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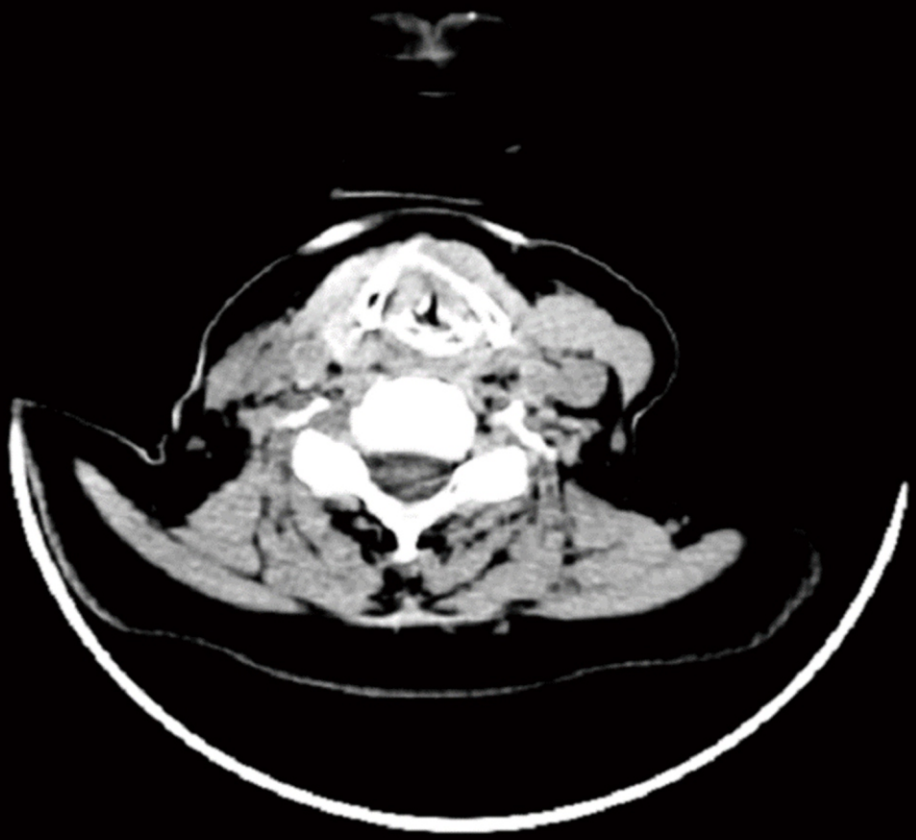

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The figure on the front cover is from the article published in Case Reports in Clinical Medicine, 2016, Vol. 5, No. 10, pp. 347-352 by Stanley Baba Amutta, *et al.*

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Laryngeal Stenosis from Trapped Overflowed Head Scarf in the Wheel of a Moving Motor Cycle: A Case Report

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Abstract

Introduction: Laryngeal stenosis is partial or circumferential narrowing of the endolaryngeal airway from congenital or acquired causes. It can present with life threatening upper airway obstruction, and the goal of treatment is restoration of good quality voice, respiration and laryngeal competence. We report a case of laryngeal stenosis following strangulation by a trapped overflowed head scarf, whilst being transported on a motor cycle and highlighted the treatment challenges. **Methodology:** A case of laryngeal stenosis studied, clinical findings, investigation results and treatment analysed. **Results:** A 70-year-old Nigerian elderly woman presented with three weeks' history of hoarseness and progressive difficulty in breathing, following pulling of her long head scarf into the back wheel of the motor cycle taking her home. She had immediate loss of consciousness, which lasted for about 60 minutes. There was associated bout of cough while eating. Examination revealed life threatening upper airway obstruction. X-ray soft tissue neck showed soft tissue mass obliterating larygotracheal air column. Flexible nasopharyngolaryngoscopy showed grossly distorted laryngeal inlet with invisible vocal cords. CT scan of the larynx showed multiple and displaced fractures of the laryngeal cartilages. Microlaryngoscopy findings were pin-hole laryngeal lumen with firm collapsed mucosa. Emergency tracheostomy was done to relieve the upper airway obstruction. Attempts were made to excise the collapse mucosa and insert a stent proved difficult. Referral for endoscopic laser excision was caution because of the potential risk of aspiration. She was counselled and coping well with the tracheostomy.

Keywords

Laryngeal Stenosis, Strangulation, Treatment, Sokoto

1. Introduction

Laryngeal stenosis is a congenital or acquired narrowing of the airway that may affect the supraglottis, glottis and subglottis [1]. The subglottis is the most common site of involvement [1]. Adult laryngeal stenosis can arise from the following causes: external laryngotracheal trauma from penetrating tissue injury, high or low velocity impact blunt force neck trauma, endolaryngeal trauma from endotracheal intubation, post-tracheostomy, post-microlaryngeal resection and post radiotherapy [2] [3]. The other less common causes include granulomatous infection from tuberculosis, scleroderma and fungal histoplasmosis. Chronic inflammatory diseases like sarcoidosis seldomly lead to laryngeal stenosis. Moreover, collagen vascular diseases such as wegener's granulomatosis and relapsing polychondritis often result in laryngeal stenosis [4]. Benign and malignant laryngeal neoplasia can also lead to laryngeal stenosis and extrinsic compression from giant multinodular goitre and thyroid malignancy [2].

An essential part of the management is endoscopic evaluation of the airways in the operating room [2]. Treatment options are endoscopic or open surgical approaches. However, the choice of treatment option depends greatly on patient's symptoms, site of involvement and degree of stenosis [5].

We present this case because of the treatment challenges encountered in her management.

2. Case Report

A 70-year-old Nigerian woman presented with three weeks' history of hoarseness and progressive difficulty in breathing, following pulling of her long and overflowed head scarf into the back wheel of the motor cycle on which she was being conveyed home. She had immediate loss of consciousness, which lasted for about 60 minutes. There was associated bout of cough while eating suggesting aspiration. Examination revealed features of life threatening upper airway obstruction and barely audible speech. X-Ray soft tissue neck showed soft tissue mass obliterating larygotracheal air column **Figure 1**, flexible nasopharyngolaryngoscopy showed grossly distorted laryngeal inlet with invisible vocal cords and its movement as shown in **Figure 2**. Serial axial slices of the CT scan of the larynx showed multiple and displaced fractures of the laryngeal cartilages, isodense translaryngeal mass and pin-hole laryngeal lumen as shown in **Figures 3-5**. Microlaryngoscopy findings were pin-hole laryngeal lumen with firm collapsed endolaryngeal mucosa.

She had an emergency tracheostomy and was hospitalized in our Centre for five weeks because of the problem of aspiration during meal. Aspiration stop after three weeks on admission in the hospital. Additionally, the tracheostomy was complicated by excessive crusts formation below the tip of the tracheostomy tube in the trachea. The crusts usually formed a plug, which cause upper airway obstruction. She experienced this problem one to two times every week for the first three weeks on admission. The plug of crusts was successfully managed by instilling about one millimeter of 0.9% normal saline into the trachea via the tracheostomy tube to soften, and then sucked it

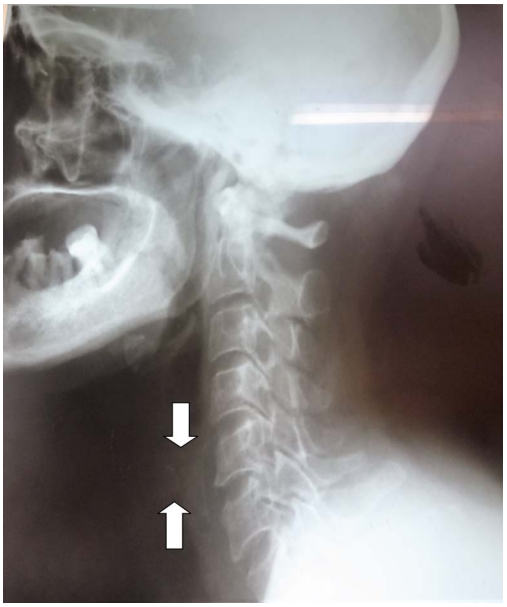

Figure 1. Lateral view of X-ray soft tissue neck showing soft tissue mass obliterating laryngotrachael air column (between the white arrows).

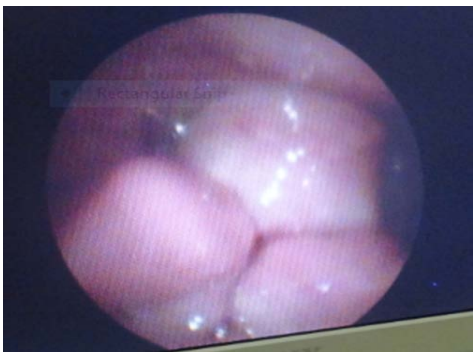

Figure 2. Distorted view of laryngeal inlet on flexible laryngoscopy.

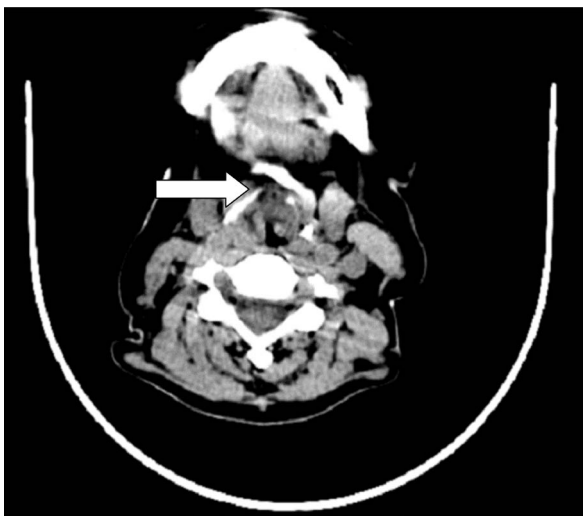

Figure 3. Displaced fracture of the thyroid cartilage (white arrow).

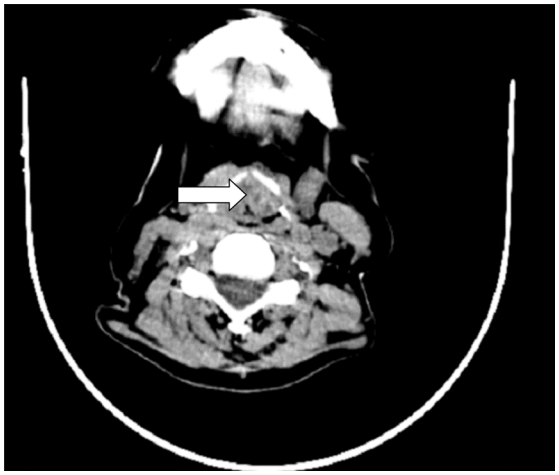

Figure 4. White arrow shows isodense translaryngeal mass.

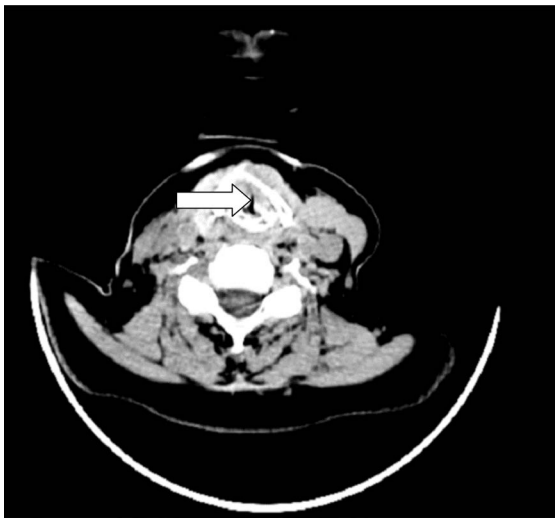

Figure 5. Pin-hole laryngeal lumen showed by white arrow.

out with suction machine. Sometime, the tracheostomy tube had to be completely removed and tracheostoma kept open with a trachea dilator, whilst patient was encouraged to cough to expel the mucoid crusts via the tracheostomy stoma. Tracheostomal swab and swab from suction tubings, to rule out peristomal bacteria colonization after the tracheostomy, yielded no growth. However, she was placed on empirical oral antibiotic (Tablet Augmentin 1 g 12 hourly and Metronidazole 400 mg 8 hourly for fourteen days).

Attempts to excise the collapse mucosa endoscopically and insert a stent proved difficult. Referral for endoscopic laser excision was caution because of the potential risk of aspiration. Therefore, she was counselled to make do with the tracheostomy and she is coping well.

2.1. Discussion

Soft tissue damage of the laryngeal lumen can result in: 1) mucosal loss, 2) Adhesions,

3) Organization of haematoma within paraglottic, pre-epiglottic and interarytenoid space [2].

Glottic insufficiency can result from web formation, arthrodesis of arytenoid and damage recurrent laryngeal nerve [2]. Displaced fractured cartilaginous framework usually heal with fibrosis with its's fibrocyte possessing directional memory, therefore, incising and separating fibrous tissue often result to a dense fibrous tissue. Possible solution is excision and grafting (rib, hyoid, thyroid cartilage, auricular and nasal septal cartilage) to re-establish structural support [6]-[9]. It is worthy of note that none of these graft is ideal. Enough mucosa should be preserved when the structural support is re-established. This can be augmented by skin or buccal mucosa graft. Endoscopic approach in the surgical management decreased morbidity, shorter hospital stays and tolerance of repeated procedure [10]. In 1972 Strong and Jacko first reported endoscopic treatment of laryngotracheal stenosis with CO_2 laser [2].

The patient in this case report had both mucosal and displaced cartilaginous damage with resultant dense fibrosis, therefore, the choice of laser resection and dilatation were considered inappropriate and discarded. Furthermore, laser excision will worsen her mild aspiration because of the immobility of the vocal cords. Open surgical approach was another challenge. She was in advance age and the degree of the stenosis (transglottic) means that she would require multiple stage procedure, and there is no guarantee that resection and grafting will be successful.

Overall, the goal of surgery is to establish satisfactory airway and allow decanulation, good voice and laryngeal competence. The patient may never be decanulated or regain good voice if the stenosis involves the glottis or supraglottic larynx [2]. The patient in this case report was advised to make do with the tracheostomy because her laryngeal stenosis involved the supraglottic, glottic and subglottic regions of the larynx. Reconstruction may be complicated by glottic incompetence and re-stenosis. Generally, the most frequent cause of failure of treatment is scar formation and re-stenosis.

The cessation of the aspiration prior to her discharge home could be attributed to the collapsed, distorted laryngeal inlet, acceptance of the damage to her larynx couple with swallowing exercises. Excessive mucoid secretion, crusting and cough are common immediate complications of tracheotomised and laryngectomized patient [11]. Presumably, she was given empirical antibiotic treatment because peristomal infection and tracheitis could be responsible for her troublesome tenacious crusting.

She was discharged home in good mood after learning how to safely change and clean her tracheostomy tubes and had been on a 2 year, 3-month follow-up in our ENT out-patient clinic. She is coping well with the tracheostomy, and free from the aspiration and excessive crust formation.

2.2. Conclusion

Permanent tracheostomy may be the treatment of choice for severe translaryngeal stenosis in an elderly patient with mild glottis incompetence, and extensive endolaryngeal and cartilaginous skeletal framework damage.

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Only Spondylodiscitis? A Clinical Case of Multiple Septic Embolization

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Abstract

Background: Spondylodiscitis and spinal epidural abscesses are rare pathologic entities, but increasing in incidence. Group G beta hemolytic Streptococcus has been recently described associated with human infections. They often present clinically in a non-specific fashion, a fact which can lead to diagnostic delay, with serious consequences for the patient. **Case Report:** An 80-year-old man was admitted to the hospital with complaints of fever for three days, dysuria, hematuria, and back pain. Both septic embolizations and spondylodiscitis due to Group G beta hemolytic Streptococcus were detected. The patient was successfully treated with intravenous penicillin G for eight weeks, followed by oral amoxicillin for five months. **Discussion:** In all patients with spondylodiscitis, infective endocarditis should be considered, particularly in patients with heart valve disease history, since spondylodiscitis may be the presenting sign of an infective endocarditis. A high level of suspicion is therefore necessary in order correctly diagnose such entities as quickly as possible. The present case illustrates the pathogenic potential of group G streptococci in spondylodiscitis and native valve endocarditis.

Keywords

Spondylodiscitis, Group G Beta Hemolytic Streptococcus, Epidural Abscess, Embolization

1. Introduction

The group G β-hemolytic streptococci (GGS) consist of *Streptococcus dysgalactiae* subspecies *equisimilis*, *S. canis*, and *S. intestinalis* which are significant human pathogens inhabitants of the skin and mucous membranes. Although cutaneous infections

and pharyngitis are most often encountered, a wide variety of infections—including potentially life-threatening ones, such as sepsis, endocarditis and septic arthritis—have been described [1].

Asymptomatic pharyngeal carriage of GGS occurs in up to 23% of humans [2]. Symptoms of pharyngitis range from a mild upper respiratory tract infection to exudative pharyngitis.

Infective endocarditis (IE) occurs in older group who has prosthetic valves or structural heart diseases. Few of them have underlying rheumatic valve disease. *Staphylococcus aureus* and viridans streptococci are the most common causes of native valve infective endocarditis. Usually, more than 50% of causes of IE are caused by viridans streptococci.

Less than 4% of patients with endocarditis actually have concomitant spondylodiscitis [3].

Spondylodiscitis is a prolonged inflammation of two adjacent vertebral bodies and the disc between them. As a result of the avascular nature of the intervertebral disc space in adults, spondylodiscitis is rarely observed. 80% of spondylodiscitis was hematogenous, and 20% developed after spinal surgery [4]. Sources of hematogenous or contiguous spread of infection include the genitourinary tract, skin, infected catheters, endocarditis and dental infections.

Nevertheless, the primary site of infection cannot be identified in most of cases. Less common causes include infected native or prosthetic valves [5]. The insidious course with non-specific symptoms can affect the treatment.

Until this report, there has been no previous report of spondylodiscitis and native valve endocarditis due to G group *Streptococcus* in the literature.

2. Case Report

An 80-year-old man was admitted to the emergency room due to dysuria, pollakiuria, hematuria and transient episodes of urinary incontinence for one week. Increasing lower back pain, functional impairment of the lower limbs and fever up to 40˚C in the previous three days were reported.

The patient had a past history of coronary heart disease and aortic regurgitation and type 2 diabetes. The patient denyed any recent medical or dental/surgical procedure.

On admission, he was febrile (38.3˚C) and the blood pressure was normal (136/63 mmHg).

Cardiac auscultation revealed diastolic murmur in the aortic area and systolic murmur in the left sternal border and apex. Herpes labialis, hemorrhagic macular lesions in the fingerspulp, polyarthritis, pain in passive mobilization of the left elbow, knees and wrists were documented.

Neurological examination revealed paraparesis, hypoesthesia of the lower limbs with L4-L5 root distribution.

Blood tests showed a normochromic normocytic anemia (Hg 9.5 g/dL), thrombocytopenia (51,000/mcL), elevated white blood cell count (12.4×10^9 cells·l^{-1}) with neutro-

philia (85%), elevated C-reactive protein (35.4 mg/dL) and erythrocyte sedimentation rate (80 $mm \cdot h^{-1}$), a diminished creatinine clearance (0.43 $ml \cdot m^{-1}$), a positive RA test (29 UI/ml), hypoxemia (pO_2 55.7 mmHg) and erythrocyturia. Chestradiography revealed inferior lobes diffuse infiltrates.

A group G beta hemolytic Streptococcus susceptible to penicillin (MIC 0.016) was isolated in blood cultures. Urine culture and renal ultrasound were unremarkable. Skeleton X-ray showed an erosive arthritis and knee arthrocentesis showed a joint purulent fluid (negative bacteriological examination). A cranial and dorso-lumbar computed tomography (CT) had no acute changes but magnetic resonance imaging (MRI) revealed L4-L5 spondylodiscitis with lumbar epidural abscess.

Transthoracic echocardiography revealed a nodule of increased echogenicity in the mitral valve and aortic valvular insufficiency. Six days later he had a transesophageal echocardiography which showed no evidence of vegetation or perivalvular abscesses.

The diagnosis seemed difficult to establish. There was no doubt that there was spondylodiscitis with septic embolizations. Was there too IE? Which was the primary disease?

It was assumed a diagnosis of infective endocarditis by Duke criteriawith septic embolization: lumbar spondylodiscitis, peripheral septic arthritis and cutaneous septic embolization.

According to Neurosurgery, the patient should maintain complete rest during eight weeks.

The patient received penicillin G 4 million units every four hours intravenously for eight weeks. Clinical and imagiological improve with lumbar MRI showing marked reduction of disc and epidural infectious component. There was a clinical improvement of low limbs deficits without sensitivity changes. He started physical rehabilitation plan and after recovering he was discharged from hospital. Three grams daily of oral amoxicillin was administrated for five months. Epidural abscess and spondylodiscitis subsequently resolved and the patient became without deficits and pain.

3. Discussion

Spondylodiscitis is a rare cause of chronic back pain with an incidence of 0.2 - 2 cases/100,000/year. The majority are male, 50 - 70 years-old and with back pain as an isolated symptom. About 30% of the patients additionally have neurological deficits; about 10% suffer from fever and weight loss [6].

As the special blood supply of the spine, the two vertebrae and the linking intervertebral disc are affected [7].

Spondylodiscitis is rarely observed in association with infective endocarditis. The first was reported by Sèze *et al.* [8]. Le Moal *et al.* [9] reported that the prevalence of spondylodiscitis in patients with IE was of 15%. Spondylodiscitis, has rarely been described, particularly in case reports. Ninet *et al.* [10] found the prevalence of spondylodiscitis in patients with IE to be of 5.9%. Spondylodiscitis does not appear to worsen the prognosis of IE, although the need for cardiac valve replacement seems to be more fre-

quent in IE patients with spondylodiscitis. Symptoms are variable and may delay the diagnosis.

The mean duration of symptoms from onset to diagnosis ranges from two days to six months. A careful review of the patient's history and physical examination, as well as laboratory data and diagnostic imaging studies are necessary. Musculoskeletal symptoms can represent the major sign of the disease, leading to diagnostic difficulties [9]. These similar symptoms also occur in up to 45% of patients with IE and are often misdiagnosed as rheumatic or degenerative joint disease.

Arthralgia is the most common musculoskeletal complaint in patients with IE and involves the shoulder most frequently, followed by the knee, hip, wrist, ankle, and the joints of the hands and feet [11]. Joint aspiration is usually nondiagnostic [11].

Low back pain is second in frequency, affecting almost, 1/3 of patients with IE. Nevertheless, neurologic defects are usually not demonstrable in patients with back pain [11]. Destructive lesions of the sacroiliac joints have also been described in patients with low back pain due to IE leading to pain over the joints. The lumbar region is commonly involved (60%), and thoracic spine can also be affected (26%). Low back pain due to spondylodiscitis is uncommon in patients with IE. Common to all patients with IE, fever and heart murmur can be detected on physical examination and Gram-positive cocci can be isolated from blood cultures.

It is important to remember that no vegetation view in transesophageal echocardiography (under antibiotic therapy directed for 10 days and documented prior embolization) does not exclude the diagnosis of left-sided IE [10] [11], therefore this entity is the probable cause of multiple septic embolization described.

A diagnosis of spondylodiscitis can be confirmed by CT or MRI. Nevertheless, MRI is most sensitive in the acute phase [8].

4. Conclusions

The authors describe a clinical case of spondylodiscitis, where the etiological investigation proved a challenge, having been excluded a nosocomial cause. The combination of clinical and imagiological data contributed to the appropriate treatment with a favorable clinical outcome.

The authors conclude that, in patients with spondylodiscitis, IE should be ruled out, particularly in patients with a history of heart valve disease, since spondylodiscitis may be presenting sign of an IE.

Transesophageal echocardiography and blood cultures should be routinely performed in these patients.

As the taxonomy of the viridans group streptococci becomes better defined, it is likely that novel disease associations will be made with the newly recognized species.

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Maintaining Nursing Care Quality

—Clinical Care Guidelines for Cystic Fibrosis: Outpatient and Inpatient

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Abstract

The Care Committee of the Mukoviszidose e.V., headed by Cornelia Meyer, has drawn up a completely revised version of the German Guidelines to Care in Cystic Fibrosis. It addresses all nursing staff concerning children, adolescents or adults with cystic fibrosis (CF) either in an inpatient and outpatient setting or in rehab clinics. The guidelines evolve along with the increased life expectancy of cystic fibrosis patients and improved quality of life which is described by CF patients and can be observed by the therapeutic CF team. For example, the treatment of secondary diseases like CFDR (CF related diabetes) which comes along with an increased life expectancy has been added over the years. It is essential that within such a complex disease pattern, professional experience of care staff who worked in specialized CF care centers (50+ patients per year) for many years has to be transferred to other nursing stuff or beginners. This is especially important in the context of the heterogeneous characteristics of this disease. Often it can be seen that the quality of the care for CF patients depends on the know-how and professional experience of the interdisciplinary CF therapists team. Moreover, it depends on the knowledge which the patient has gathered by himself by experience or learning. And, of course, it depends also on the knowledge of the relatives especially parents or partner respectively.

Keywords

Cystic Fibrosis, Clinical Nursing, Guidelines

1. Introduction

Cystic fibrosis (CF) is one of the most common life-shortening inherited diseases. In Germany about 8000 people are affected [1]. Even though there is still no cure for the disease, improvement in symptomatic therapy has enhanced life expectancy to around

40 years. Cystic fibrosis is caused by the mutation of a gene called cystic fibrosis transmembrane conductance regulator (CFTR). This gene defect results in the production of thick mucus in the internal organs causing inflammation, frequent lung infections and digestive problems. Long-term issues include difficulty breathing and coughing up mucus as a result of frequent lung infections. Other signs and symptoms include sinus infections, poor growth, fatty stool, clubbing of the fingers and toes, and infertility in males, among others. Different people may have different degrees of symptoms. Lung transplantation may be an option if lung function continues to worsen. Lung problems are responsible for death in 80% of people with cystic fibrosis. Although technically a rare disease, CF is ranked as one of the most widespread life-shortening genetic diseases [2].

Life expectancy of CF patients has been doubled to nearly 40 years of age within the last 20 years. This is mostly based on newly developed medication and a profound knowledge of the physiological and chemical processes in the human CF cell; furthermore, through dense treatment within interdisciplinary teams like medicine, care, physical therapy, sports therapy, psychotherapy, nutrition therapy and social educators; and furthermore through the empowerment of the patient him-/herself. An important key issue of the therapy is the education and support of the autonomy of the patient aside from medication management, physical therapy and sports.

Patients' life expectancy has been steadily increased over the years (and hopefully will do in future), but causes simultaneously that the patient and the nursing staff have to face new challenges. Nowadays, to live with cystic fibrosis still means to maintain a disciplined daily lifestyle for more than 40 years, maintain motivation and handle the disease in a salutogenesis way by strengthening the sense of coherence [3]. Despite all the positive developments we still see difficult ethiopathology in which the CF patient still dies, in some cases as a child, or its survival depends on the last line of treatment, the lung transplantation. This holds also for patients in the early teenage years. This revised version of the guidelines offers updated and helpful support for optimal patient care. The guidelines show in a practical manner which benefit might arise by using it for the caring of cystic fibrosis patients and which advantages come along for the other departments.

2. Guidelines in Cystic Fibrosis

The guidelines, as a kind of handbook, aim at comprehensive support for all those involved in CF nursing for children and adults. The guidelines address primarily nursing professionals, close relatives and all others concerned. The 5th revision of the German Guidelines to Care in Cystic Fibrosis are a loose-leaf edition. The page numbers and numerical structure have intentionally been left out. This allows for uncomplicated additions of updates. Individual subject matters are highlighted. The authors have carefully compiled cystic fibrosis specific measures of action and presented them after scientific evaluation and emphasis on quality and safety. Strong emphasis is also taken on appreciation of the complex work of nursing. The new edition of the guidelines offers comprehensive up-to-date support in nearly all caring situations.

> "Furthermore, patient care is facing increasing challenges because the patients are fortunately increasing in age but also becoming highly complex patients at the same time. These patients may develop additional complications such as osteoporosis, high blood pressure, depressive episodes, pain, diabetes mellitus and many other disorders which patient care must be able to handle. Adaption to this new situation is necessary for a good patient care and appropriate specialised training have to be implemented." (Dr. C. Schwarz, Medical Advisor, Charité Berlin, Preface [4]).

The preface is followed by a detailed description of the CF disease pattern [5]. This is particularly helpful for beginners who have been given a complete overview over the complexity of the disease. The following seven chapters contain the central themes:

- Hygiene.
- Nutrition.
- Inhalation treatment.
- Outpatient IV antibiotic treatment.
- Inpatient IV antibiotic treatment.
- Long-term oxygen therapy.
- Noninvasive ventilation.

Each chapter contains aspects being used practically or are of great importance, especially in combination with hygiene. The main subject of hygiene had been excluded from the other chapters and had been included in a separate chapter. Specific hygiene subjects, for example, nebuliser sterilisation, can be found in the corresponding chapter. The topic of hygiene will become more and more an important issue throughout the progression of the disease and it is particularly important for the hospital setting especially for disinfection reasons and in cases of patient isolation. In future more work must be done to cover the rapidly increasing knowledge due to germs and drug resistance. Further, the guidelines describes CF-relevant lung bacteria like Pseudomonas aeruginosa and how to deal with it in the clinical setting. Also, procedures and processes of bacterial isolation are being described together with up-to-date references to multiresistant Pseudomonas sp. (MRGN) [6] [7].

3. Using the Guidelines

By creating a fictional case report we will demonstrate how the guidelines are to be used. We picked out the issue of nutrition which is another key issue in the treatment of CF [8]. In a cross sectional and longitudinal analysis from Steinkamp *et al.* (2002) there find evidence for the hypothesis that a near normal weight is associated with a better lung function in CF [9]. In consequence a higher life expectancy can be assured.

Julia, a nine years old child with CF, is receiving inpatient treatment. Her weight is within the 10*th percentile and her height is within the* 25*th percentile. She has had recurrent infections which has caused the hospital stay. She is concerned about her diagnosis and would like most to "get rid of CF". Her mother cooks additionally hypercaloric meals and supervises the enzyme dosage over day in the hospital. The moth-*

er-daughter interaction is limited to Julia's treatment (*eating*, *inhalation*, *physical therapy*). *The attending nursing staff is aware that the mother is well-informed and that she* "*only want the best for Julia*".

What do the guidelines say? In this case the guidelines (Ch. 2: Nutrition) emphasize on the encouragement of the patients' self-reliance. This should be in Julias' own interest. Considering her age she should be able to know about the correct dosage of enzymes by estimating how much fat the food contains. Also, she should carry the enzymes by herself and disperses them autonomously over the meals. She should be able or should be encouraged to ask questions to determine the correct dosage of the enzymes. The guidelines offer helpful informations for the nursing staff about correct dosage or derivation of an adequate formulas depending on the meals amount of fat. As she is still a growing child she requires a higher energy density of the food. Assistance for choosing the right food items is been given by using the "nutrition cube" as recommended by the study group "Nutrition" of the Mukoviszidose e.V. A nutrition protocol should be drawn up regularly during the inpatient stay to check for Julias' adequate energy supply. This have to be done by the nursing staff. Furthermore, the nursing staff suggest recommendations which raise the appetite level of the patient and finally discusses them with Julia and her mother. Further, the possibility to get additionally calories by using hypercaloric meals has to be offered. A daily blood sugar profile might also be of use to elucidate why Julia has increased frequency of infection and persisting malnutrition. For an extremely reduced nutrition status the guidelines suggest the use of a stomach tube (PEG). In future, Julias' height and weight need to be continuously monitored and readjusted. At least, the contact to an educated dietician have to be established.

It is important to realize that there are things Julia can handle by herself (by the mean of salutogenesis) in order "to move towards health", *i.e.* to avoid the "get rid of cf" way of thinking. She have to take responsibility for her own disease and not despair due to the diagnosis. This is a problem especially evolving during puberty. As mentioned before, CF means a disciplinary lifestyle—forever! Therefore it is important to get into action as soon as possible and to counteract negative developments in time.

4. Conclusions

Since the share of inpatient stay has drastically decreased, it has become increasingly important that the possibility for the nursing staff to get in close contact with the patient is upheld in order to have a positive effect on the patient and his/her relatives. The consultation of the patient has to start before the patient starts to ask questions. Especially for chronic diseases, it holds the fact that the patient and their relatives have become a kind of specialist for CF and this has in any case to be taken into consideration. But this does not implicitly mean; however, there is no room for improvement or there are no possibilities for improvements within the individual daily therapy management. The guidelines are supposed to give us also a sense of safety by dealing with CF.

Since the first edition of the German Guidelines to Care in Cystic Fibrosis which had

been published in 1998 the guidelines are being revised regularly. In 2015 all chapters have been revised completely by several authors who have worked with CF patients for several years. New developments in treating CF, inpatient and outpatient, have been taken into account. For example, especially the chapter of hygiene (MRGN: multi resistant gram negative bacteria), IV antibiotic treatment (picc line catheter: Peripher Inserted Central Catheter), inhalation treatment (new hygienic standards) and nutrition (CFRD: CF related diabetes) have been updated. The 5th completely revised and amended version of the Clinical Care Guidelines for Cystic Fibrosis is available on request by Mukoviszidose e.V. (Adress: In den Daunen 6, 53117 Bonn-Germany. E-mail: info@muko.info).

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Rheumatic Mitral Valvulitis with a "Giant Vegetation"—A Case Report

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Abstract

Infective endocarditis (IE) is the infection of inner endothelial layer of the heart including the heart valves and it may present as rapidly progressive or manifest itself as subacute or chronic disease. The epidemiology of infective endocarditis has been changed over the past few decades and the incidence of IE in children in United States and Canada is 1 in 1250 pediatric hospital admissions in the early 1980s. At least 70% of infective endocarditis in children occurs with congenital heart disease whereas rheumatic heart disease in southern states of India and the degenerative mitral valve disease (myxomatous, mitral valve prolapse) in the western countries are the most underlying predisposing conditions to infective endocarditis in adolescents. The characteristic lesion of infective endocarditis is "vegetation" and a "large" vegetation >10 mm in size has been reported with an incidence of 15.9% - 62.5% in patients. The significance of vegetation size has been a subject of discussion for many years to predict the embolic episodes. Background of this case study illustrated the varying size and shape of giant vegetation attached to the anterior leaflet of mitral valve in an underlying rheumatic mitral valvulitis and its consequence of valve damage such as chordal rupture, flail leaflet and mitral regurgitation with a description of anatomic features and echocardiographic manifestations in a 10-year-old female child.

Keywords

Rheumatic Mitral Valvulitis, Infective Endocarditis, Giant Vegetation, Flail Leaflet, Mitral Regurgitation, Ping-Pong Mitral Stenosis

1. Introduction

The mitral valve apparatus consists of leaflets, subvalvular apparatus (chordae tendineae and papillary muscle), annulus and the left ventricle. It is a dynamic three-dimensional system that allows brisk left ventricular blood-inflow during diastole and ensures

unidirectional heart pump function by sealing the left atrium from left ventricle during systole. The anterior (aortic or septal) leaflet of the mitral valve originates from the fused superior and inferior cushion tissues in the left AV (atrioventricular) canal and starts delaminating from the myocardial wall shortly thereafter. The posterior (mural) leaflet forms from the left lateral cushion. The mitral valve leaflets, chordae and papillary muscles become developed at the 15th week of gestation [1]. The anterior leaflet of the mitral valve is semicircular (trapezoid or dome-shaped) and it is larger, longer and thicker than the posterior leaflet and comprises one third of the annulus circumference and is in fibrous continuity with the left and non-coronary cusps of the aortic valve with the interleaflet triangle between the aortic cusps that abuts on to the membranous portion of the interventricular septum [2]. The posterior (mural leaflet) is quadrangular in shape and comprises two-thirds of the annular circumference. The posterior leaflet has two well defined indentations (clefts) that generally form three scallops (segments) along the elongated free edge. These leaflets are attached at their bases to the fibromuscular ring and by their free edges to the subvalvular apparatus. The commissures define a distinct area where the anterior and posterior leaflets come together at their insertion into the annulus. The leaflets are having a basal zone (connecting to the atrioventricular junction), thin central clear zone and a thick rough zone at the free edge of the leaflets. The rough zone is the main area of chordal attachment, the region of coaptation (the line of contact between the leaflets) and apposition (overlap of the leaflet free edge). The mitral valve leaflet is tri-laminar, consists of fibrosa/ ventricularis, spongiosa and atrialis layers and endothelial cells cover the blood-interfering surfaces. The fibrosa is composed of dense collagen (type I—74%, type III—24%, type V—2%) [3] and it is providing the strength and stiffness to the leaflets. It is the major load bearing layer that faces the greatest pressure during valve closure, extends from the annulus into two-thirds of the leaflets and it is absent at the free edge. The spongiosa is the major component of the free edge and consists of extracellular matrix or ground substance of glycosaminoglycans and proteoglycans which are hydrophilic and attract water molecules [4]. This characteristic of water absorbent proteins causes the ground substance to expand and swell at the free edge and act as a protective buffer to ensure a tight seal along the point of apposition. Smooth muscle cells, veins and arterioles are confined to the base of the leaflets at the fibrous-myocardial junction where the leaflet inserts. Atrial myocardial cells extended into the base of the leaflets and had dense innervations and excitability, suggesting a neural regulatory mechanism [5]. The leaflets have chords (chordae tendineae), the fibrous strings that originate with highly variable branching from papillary muscle tips (heads) and insert fan-like into the ventricular aspects of the leaflets. According to the site of insertion, they are termed as primary or marginal, secondary or intermediate and tertiary or basal chords. Primary chords are inserted on the free edge of the rough zone of both leaflets and function to prevent prolapse or eversion (flail) of the leaflet margin. Secondary chords attach to the ventricular surface on the region of rough zone (*i.e.*, body of the leaflet) and relieve tension on the valves. There is a pair of large, thick secondary chords arising from the tip of

each papillary muscle to anterior leaflet, termed as "strut" chords, which are thought to be strongest and preserving ventricular shape and function. Tertiary chords are found in posterior leaflet only and attach directly to the ventricular wall [6]. Unlike the tricuspid valve, the mitral valve does not have chords anchoring the leaflets to the ventricular septum.

Complete closure (coaptation) and correct apposition (symmetrical overlap, usually a minimum of 4 - 5 mm) of both leaflets are essential in preventing regurgitation. Leaflet coaptation depends on the balance of systolic tethering and closing forces on the valve. Tethering forces are transmitted through the LV (left ventricular) wall-papillary muscle-chordal system and keep the leaflets from protruding into the left atrium. Closing forces depend on the pressure generated by the left ventricle to close the mitral valve. Disturbances of this finely tuned spatial and temporal interplay may create an imbalance of these forces and result the valve to become regurgitant. Rheumatic valvulitis may cause mitral regurgitation by retraction of tendinous chords and leaflets as well as annular dilatation, thus compromising coaptation between the two leaflets, leading to regurgitation. Infective endocarditis can cause mitral regurgitation through chordal rupture or leaflet perforation.

Review of Literature

Rheumatic disease is the etiology for stenotic mitral valves in >99% of cases. The cause of pure mitral regurgitation are multiple and include floppy mitral valves, infective endocarditis, papillary muscle dysfunction, rheumatic disease, and ruptured chordae tendineae. In a study by Allen and associates [7], the three leading causes of pure mitral regurgitation were floppy (28%), rheumatic (29%), and idiopathic chordal rupture (14%). In a study by Hanson and colleagues [8], the three leading causes were floppy (70%), papillary muscle dysfunction (24%), and infective endocarditis (2%). In a study by Olson and associates [9], the reported leading causes to be floppy (38%), rheumatic (31%), and papillary muscle dysfunction (11%), but Wallen and colleagues [10] found rheumatic disease accounted for only 3% of purely regurgitant mitral valves.

Endocarditis was first described by William Osler in 1885. It is an inflammatory process that affects the endocardium and may have an infective or noninfective origin. It is uncommon in the western world (22 cases per million), but more prevalent in developing countries and a giant vegetation blocking the mitral valve orifice is uncommon and so this case had been reported.

2. Case Report

A 10-year-old female child was referred for echocardiographic evaluation with an apical systolic murmur. The child was having recurrent episodes of rheumatic fever (febrile illness with joint pains) at the age of 5 - 6 years and taken some treatment from the local medical practitioner, but she was not taken penicillin prophylaxis earlier. The child was remained afebrile for long period and no precipitating factors of infective endocarditis such as dental or genitourinary procedures in the past. General examination re-

vealed normal growth and development, no cyanosis and clubbing and peripheral signs of infective endocarditis such as Osler's nodes, Janeway lesions, Roths spots and splinter haemorrhages were not present and they are relatively rare in children. Physical examination revealed a grade 3/6, blowing, high pitched, holosystolic murmur with a constant intensity and duration on dynamic auscultation and loudest at the apex with a radiation to left axilla and transmitted to the left infrascapular area and vertebral coloumn and it is due to the flow generating the murmur is directed posterolaterally within the left atrial cavity, suggesting the murmur of mitral regurgitation due to the rupture of chordae tendineae of anterior mitral leaflet. Blood cultures were negative. Blood chemistry revealed the positive serum ASO (anti-streptolysin O) titer, suggesting a recent streptococcal infection and other parameters were normal. X-ray chest revealed moderate cardiomegaly and ECG revealed a left ventricular volume overload pattern of eccentric hypertrophy due to LV dilatation as a result of severe mitral regurgitation and a normal sinus rhythm. Transthoracic echocardiography revealed a giant vegetation "popcorn" like in **Figure 1**, **Figure 3** and **Figure 4** and "cucumber" like in **Figure 2**, mainly attached to base and apical portion of anterior mitral leaflet as shown in **Figure 31** and manifested in various size and shapes as shown in **Figures 1-37**. A flail anterior leaflet with a disorganized mitral regurgitation jet as shown in **Figure 21** and the posterior leaflet is embedded with vegetation and resulting in "kissing forms" as shown in **Figures 13-15** in echocardiography imaging. Tricuspid valve is also thickened

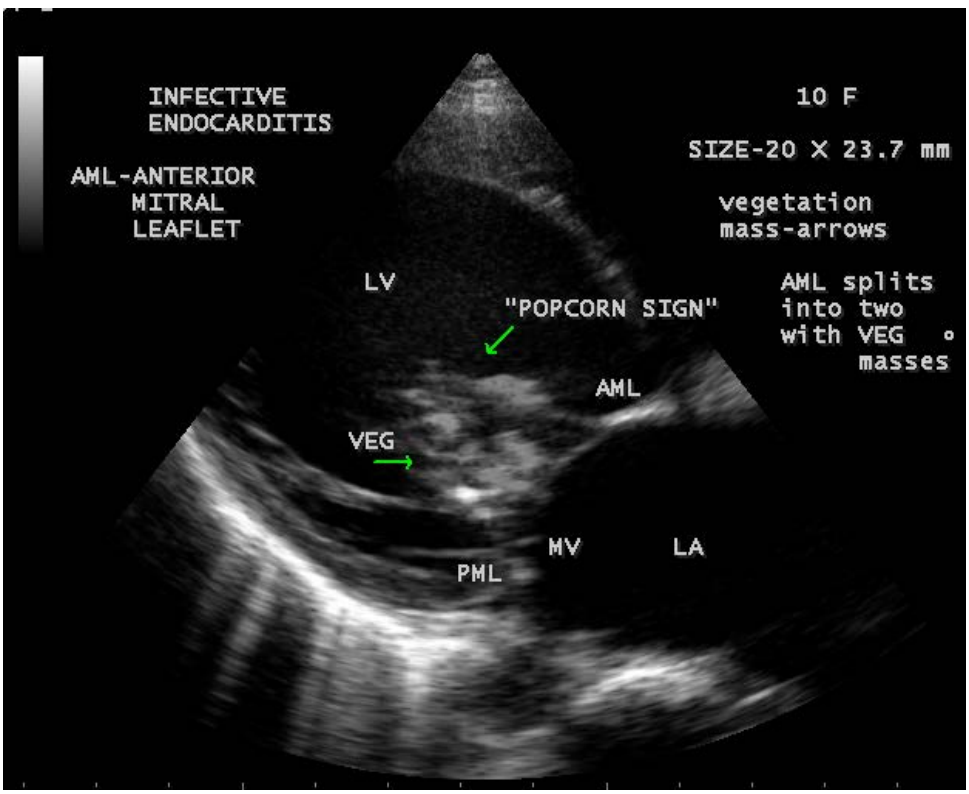


Figure 1. A large "popcorn" like vegetation obstructing the mitral valve—"giant vegetation" ([36], Figure 3).

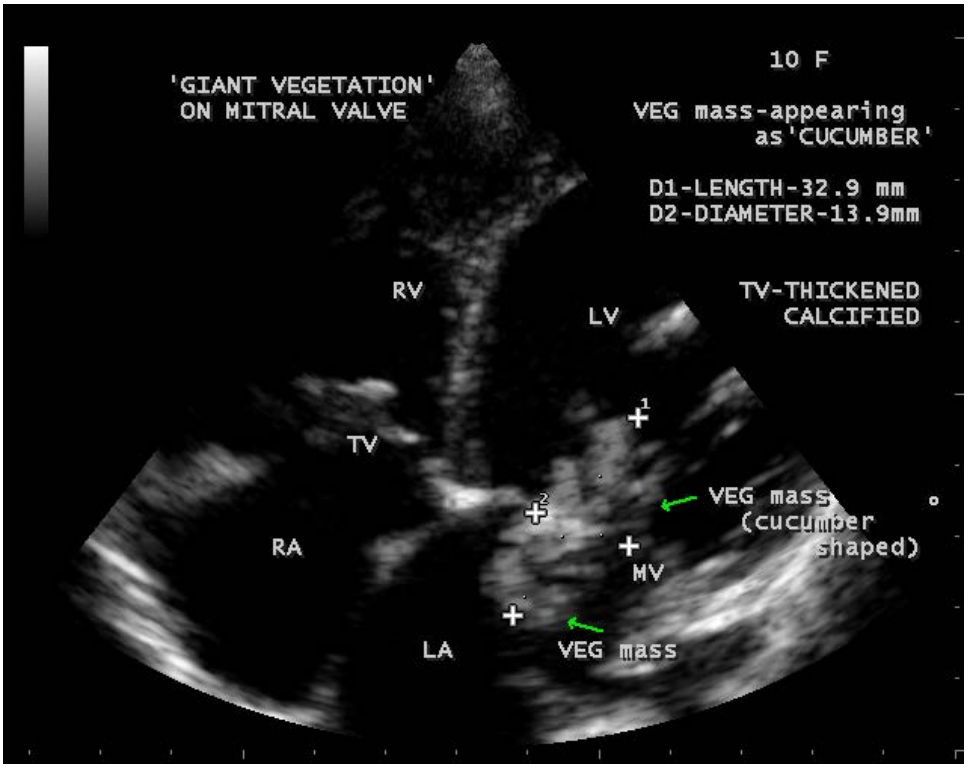


Figure 2. A large "cucumber" like vegetation obstructing the mitral valve—"giant vegetation". TV (tricuspid valve) also thickened and calcified due to rheumatic process.

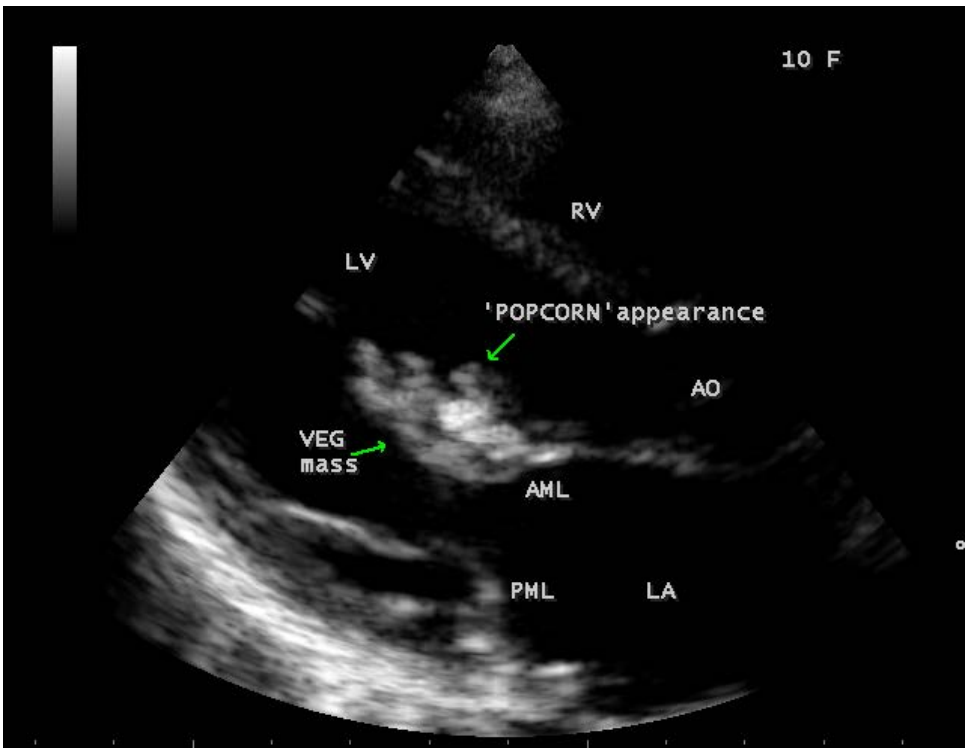


Figure 3. A "popcorn" like vegetation attached to the anterior mitral leaflet moving into the left ventricle along with valve leaflet.

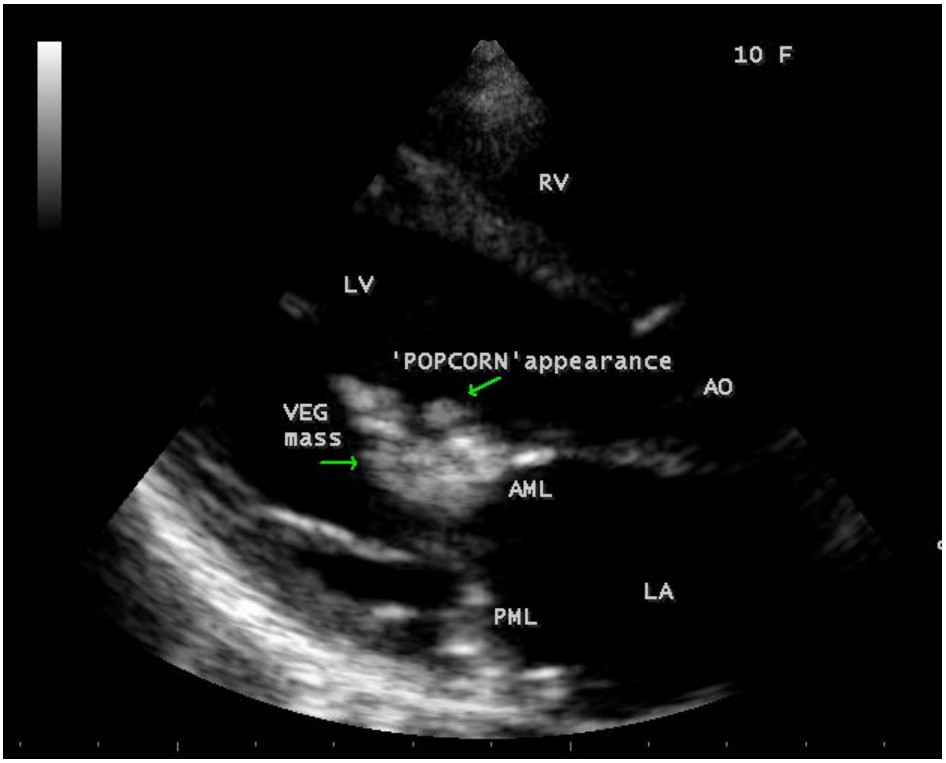


Figure 4. A "popcorn" like vegetation attached to the anterior mitral leaflet moving closer to the mitral valve orifice.

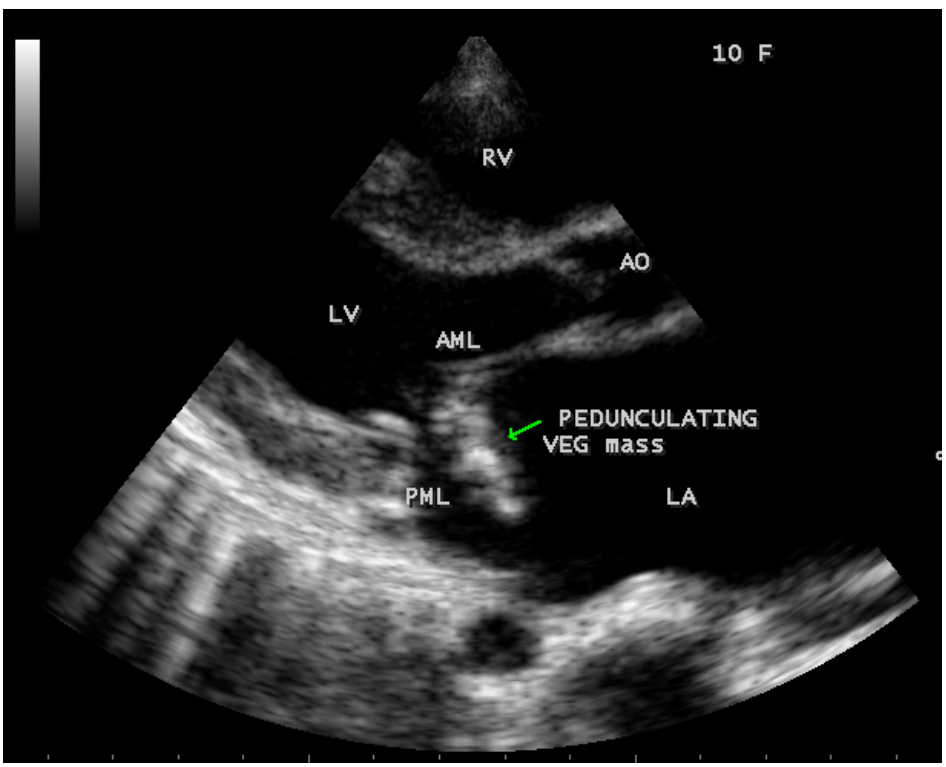


Figure 5. Flail anterior mitral leaflet with a pedunculated, partially calcified, vegetation mass into the left atrium (LA) ([33], Figure 13.1).

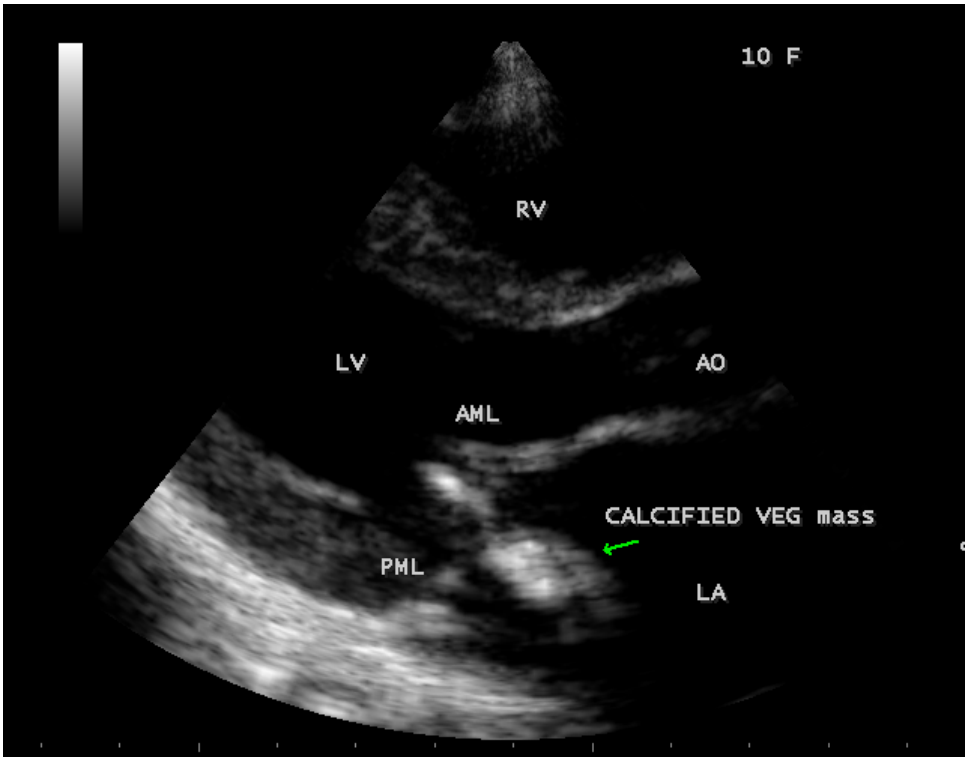


Figure 6. Healed mass of vegetation (calcified) attached with AML (anterior mitral leaflet) into LA (left atrium).

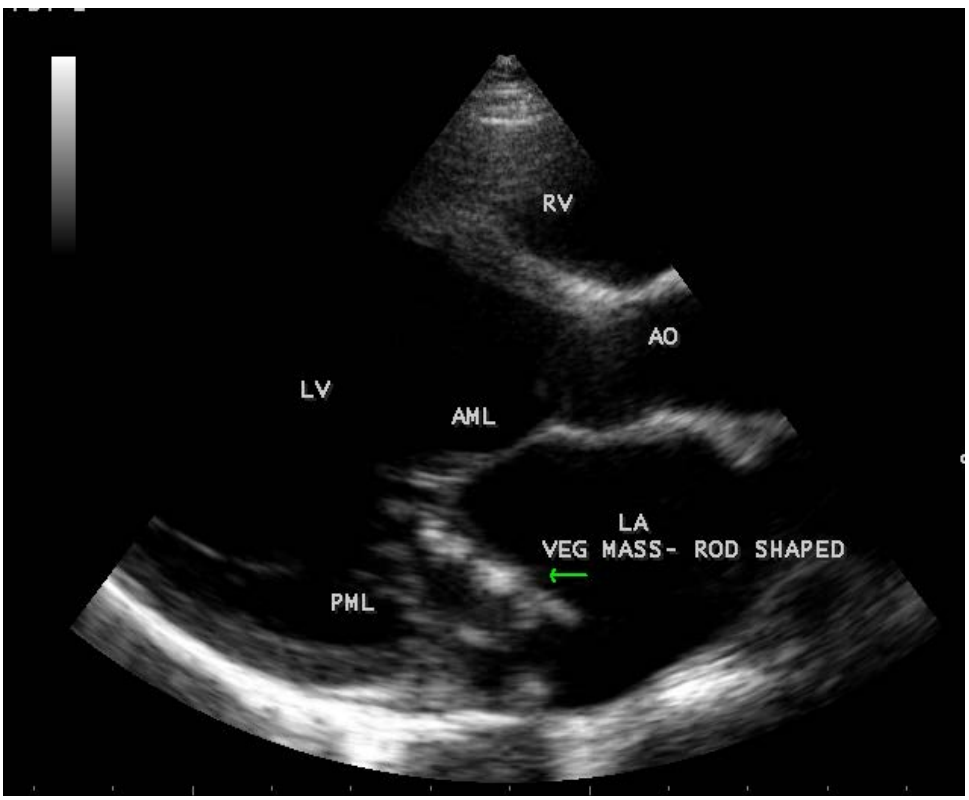


Figure 7. Vegetation seen as "rod-shaped" into LA (left atrium).

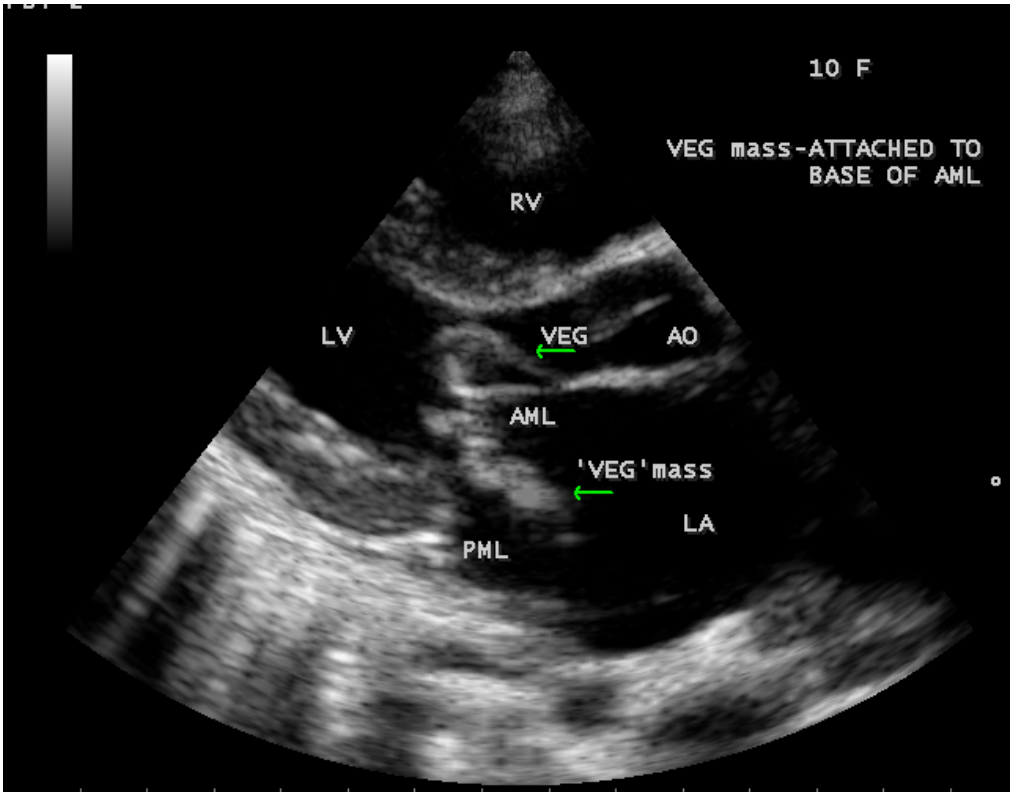


Figure 8. Vegetation seen as attached to the base of AML (anterior mitral leaflet).

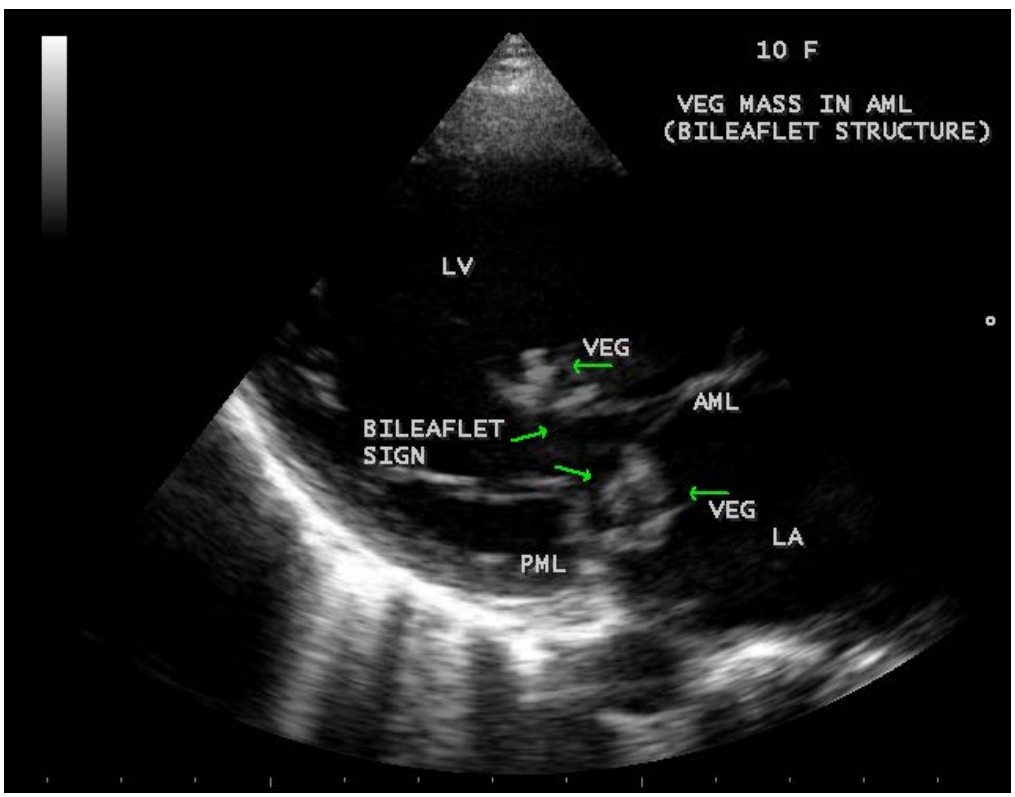


Figure 9. Vegetation seen as "bileaflet structure" attached to AML.

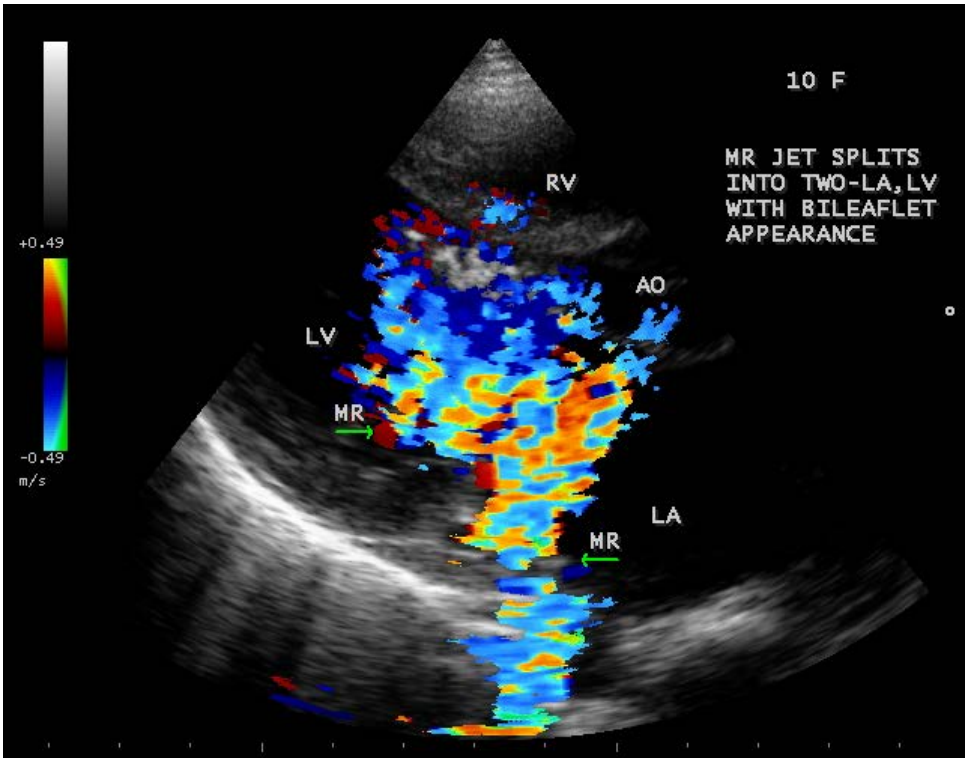


Figure 10. Color Doppler imaging showing the MR (mitral regurgitation) jet as bileaflet appearance—simultaneously into LA and LV.

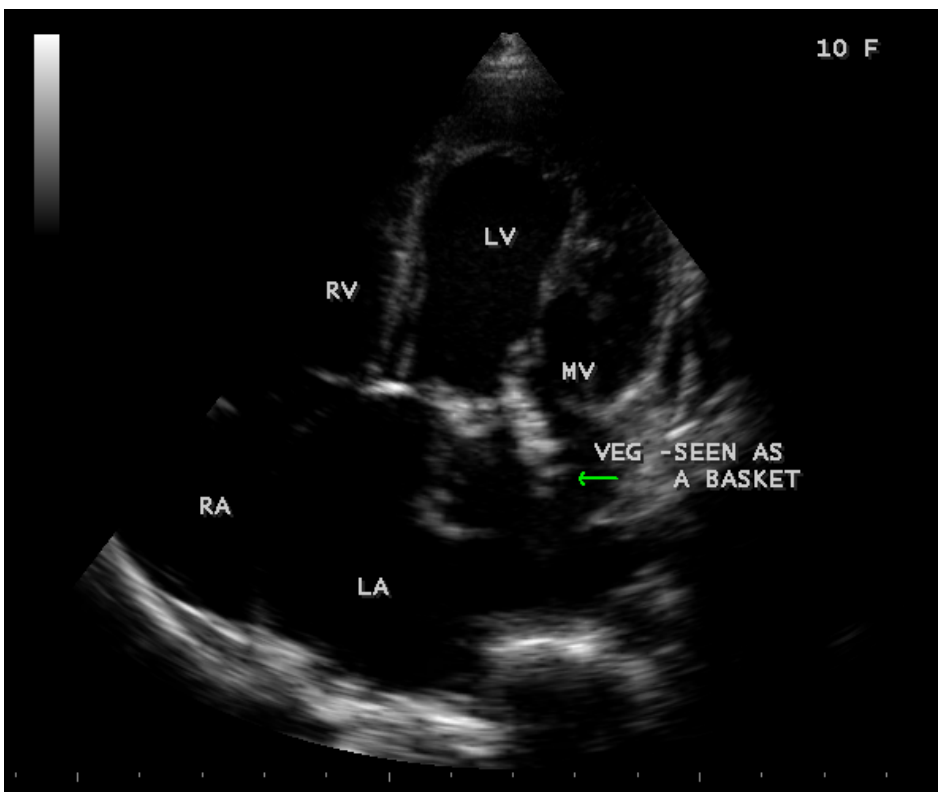


Figure 11. Vegetation seen as "basket" shaped in mitral valve orifice ([33], Figure 13.3B).

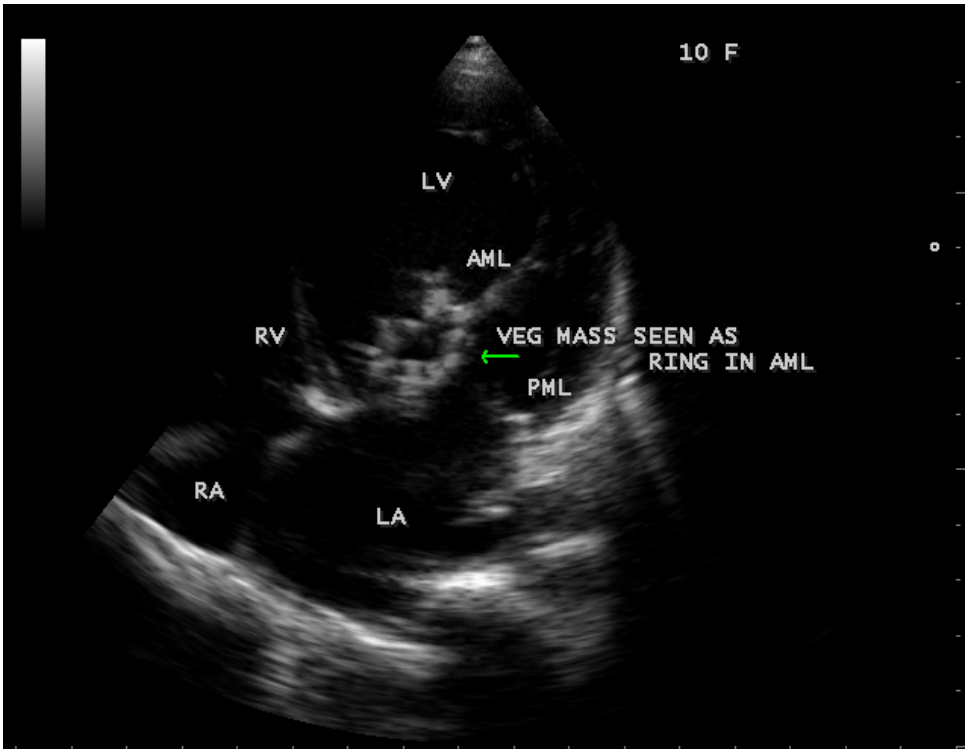


Figure 12. Vegetation seen as "ring" attached to AML (anterior mitral leaflet).

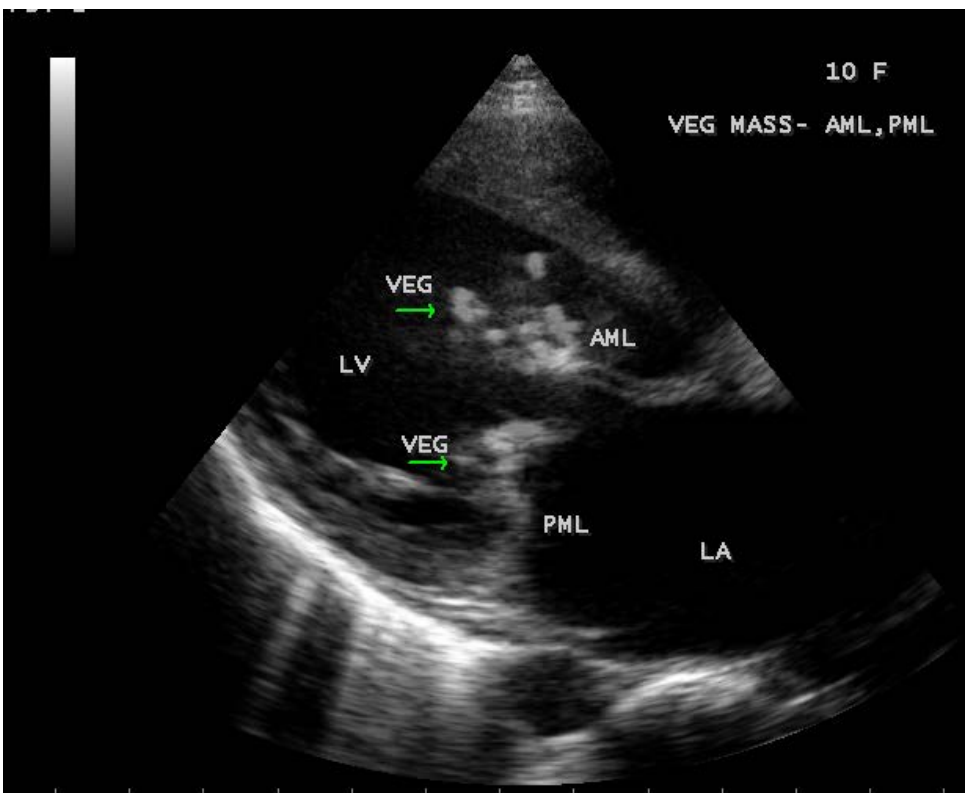


Figure 13. Vegetation seen as "kissing" type in parasternal long axis view-both AML and PML having the vegetation masses.

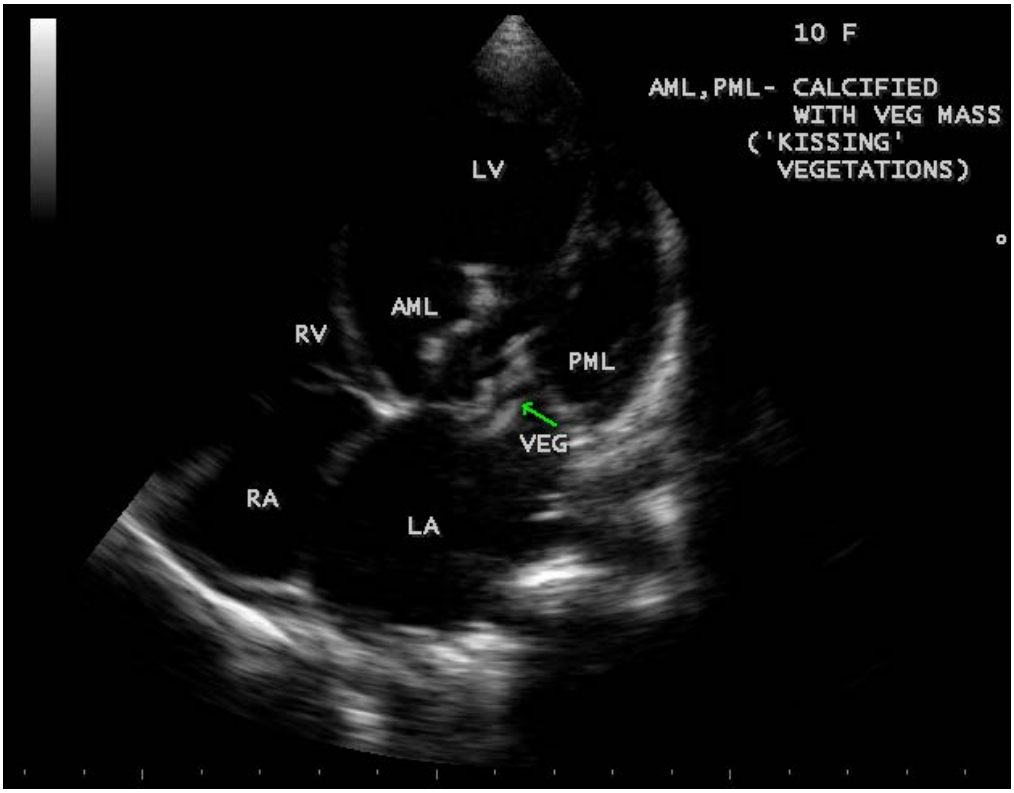


Figure 14. Vegetation seen as "kissing" type in apical four chamber view.

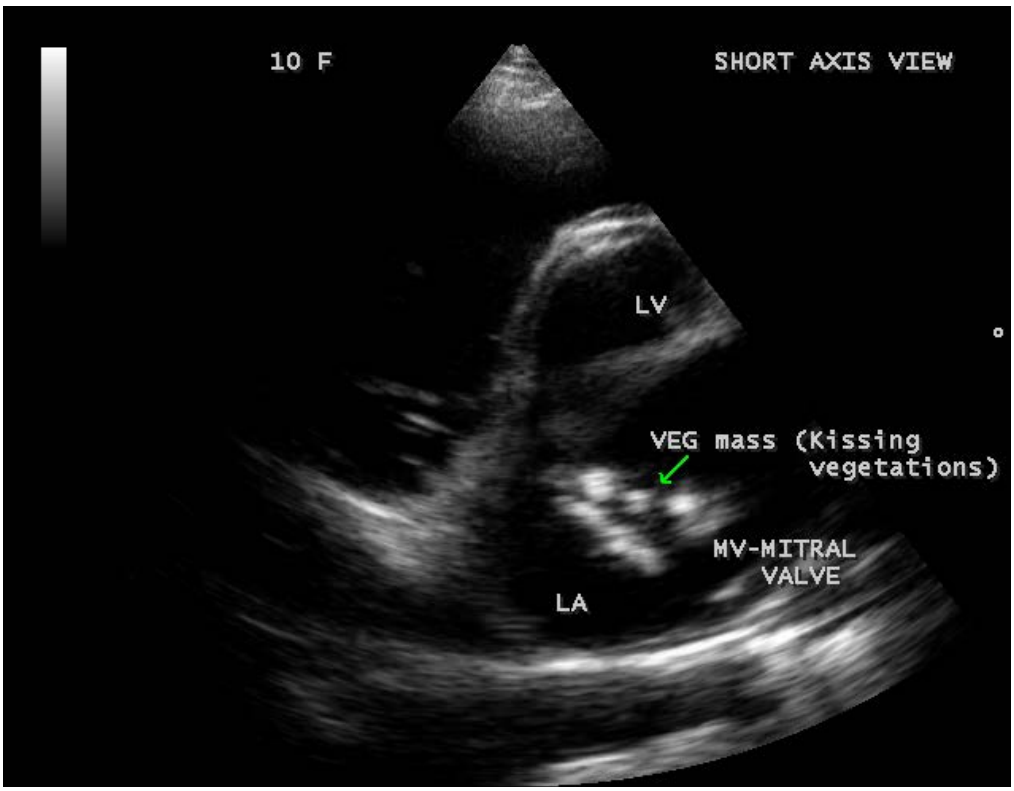


Figure 15. Vegetation seen as "kissing" type in short axis view.

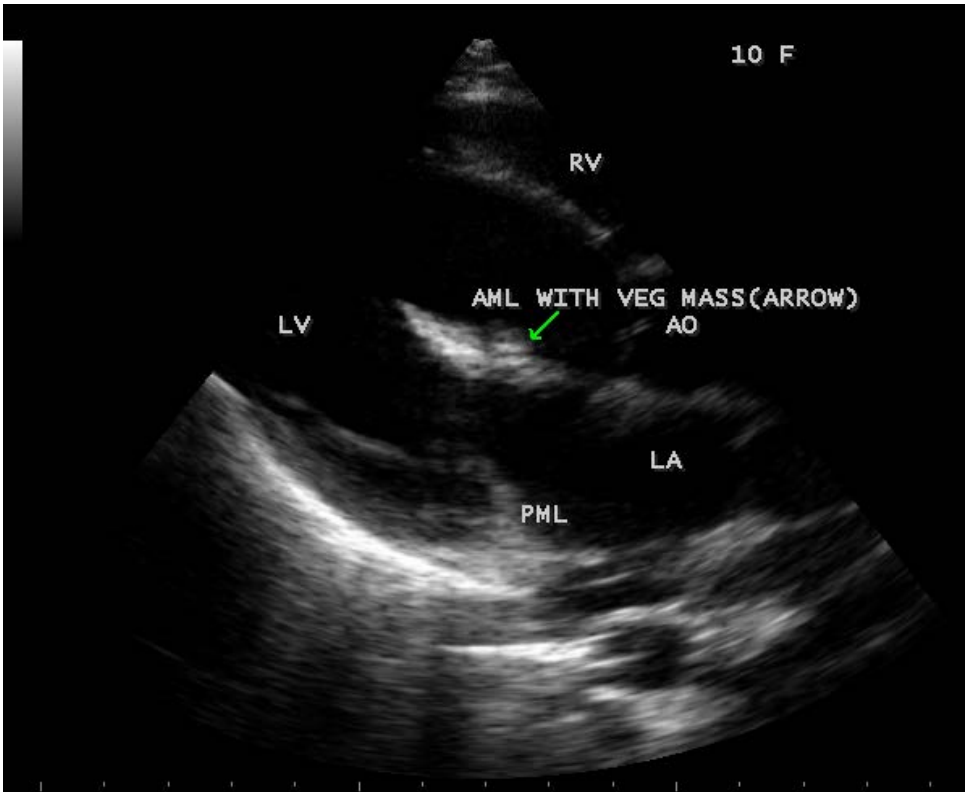


Figure 16. Vegetation embedded on AML in parasternal long axis view ([33], Figure 13.7A).

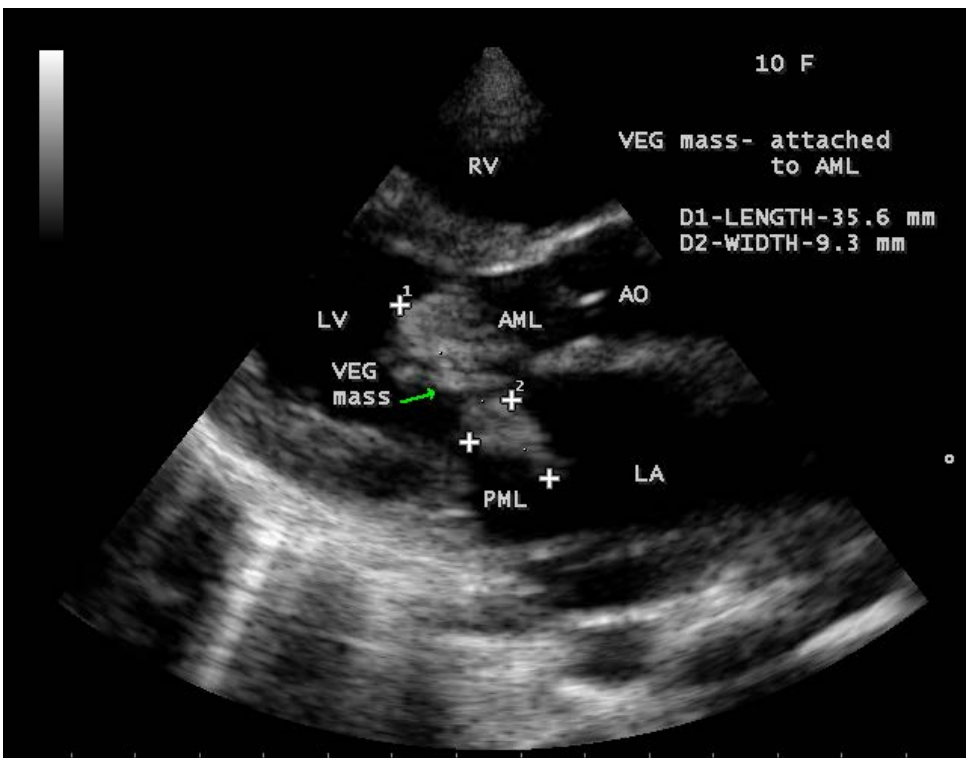


Figure 17. Vegetation attached to AML (anterior mitral leaflet) showing the size in parasternal long axis view).

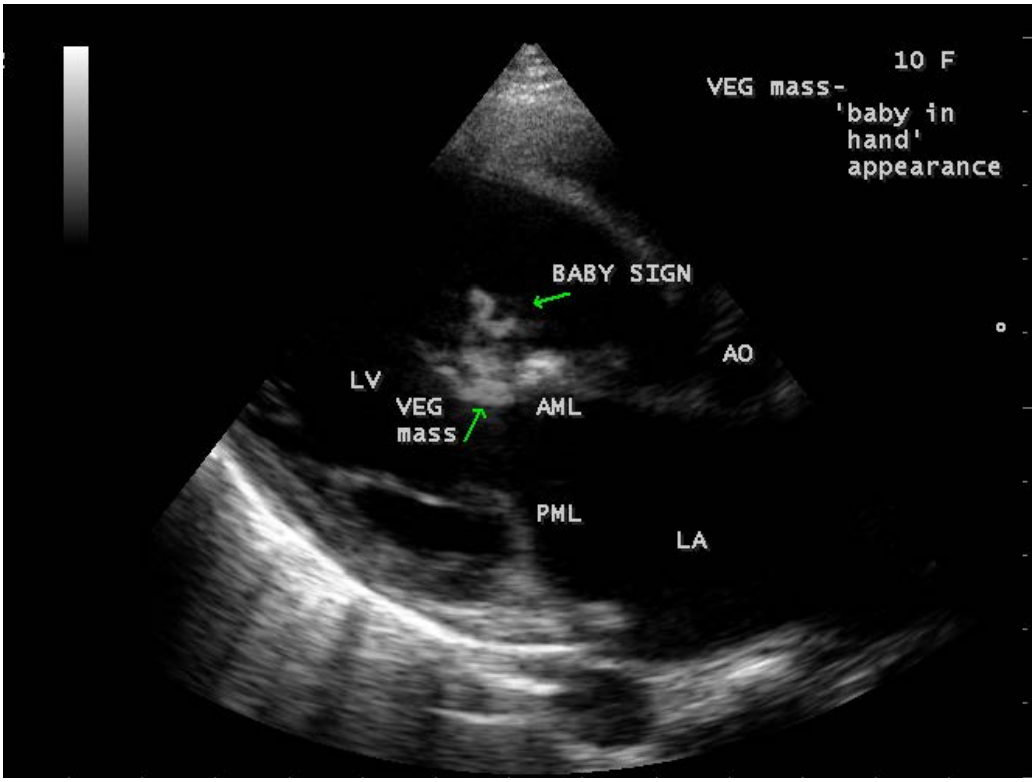


Figure 18. Vegetation seen as "baby in hand" appearance on AML (anterior mitral leaflet).

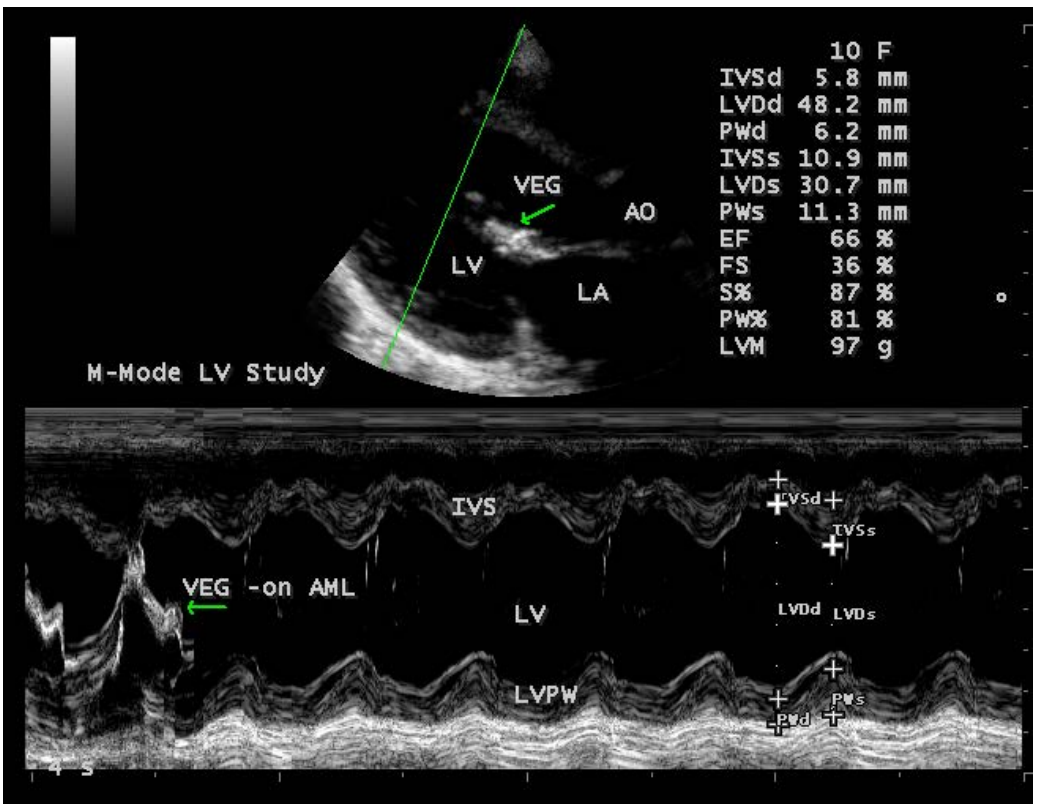


Figure 19. M-mode LV function study.

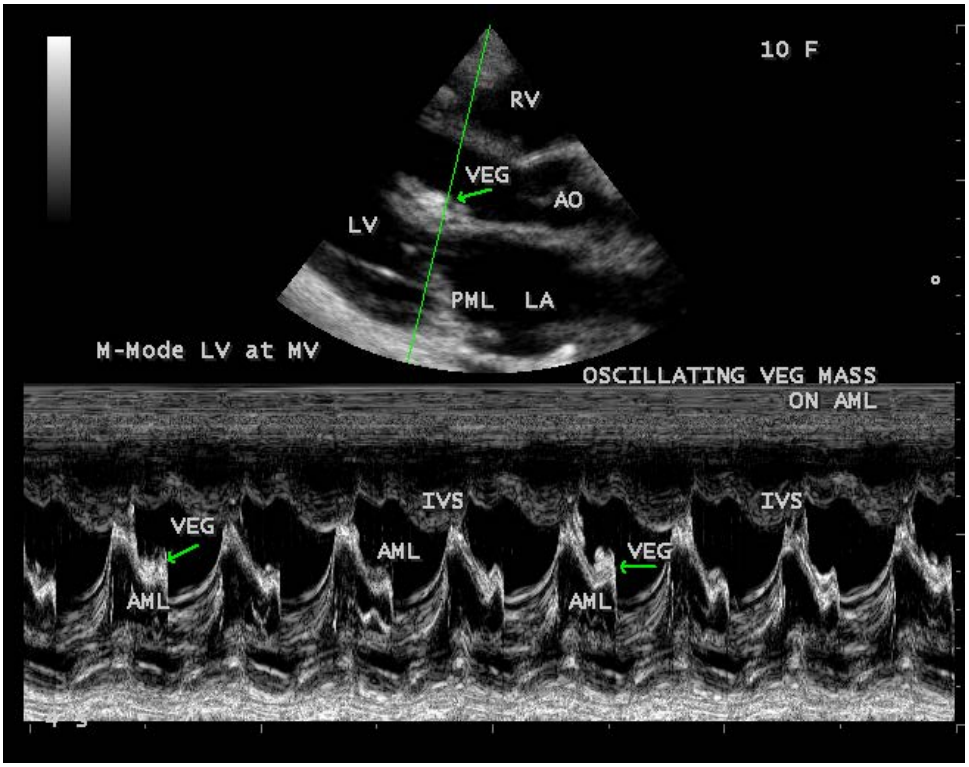


Figure 20. M-mode LV at mitral valve level—showing vegetation on AML.

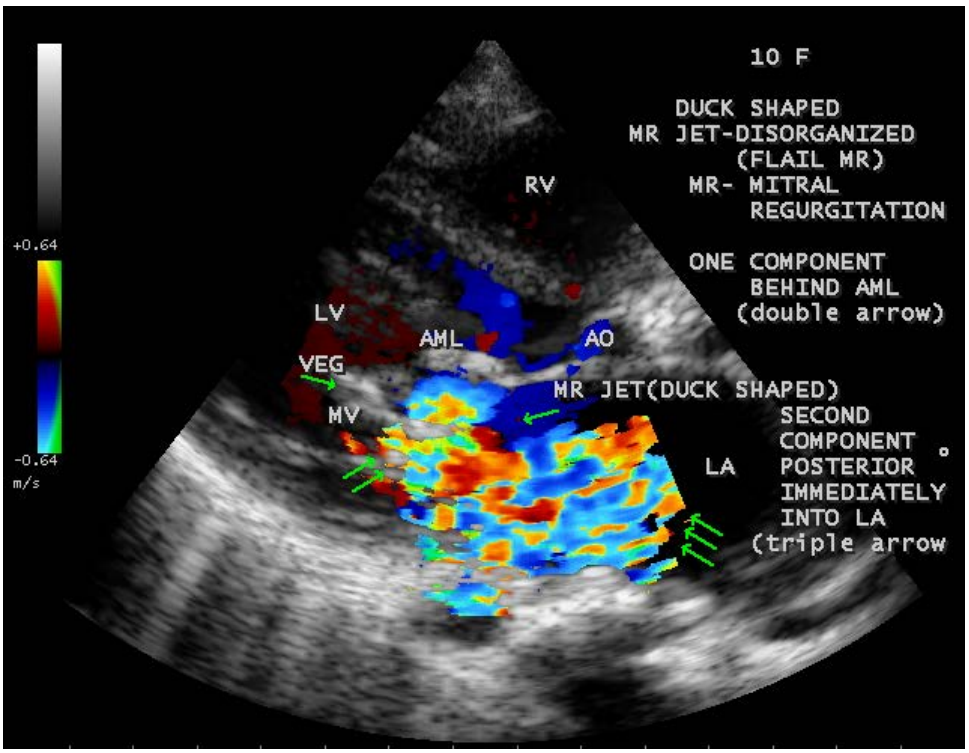


Figure 21. Disorganized MR jet (one component behind AML (double arrow) and the second component immediately posterior towards LA (triple arrow) of flail anterior mitral leaflet ([33], Figure 11.79).

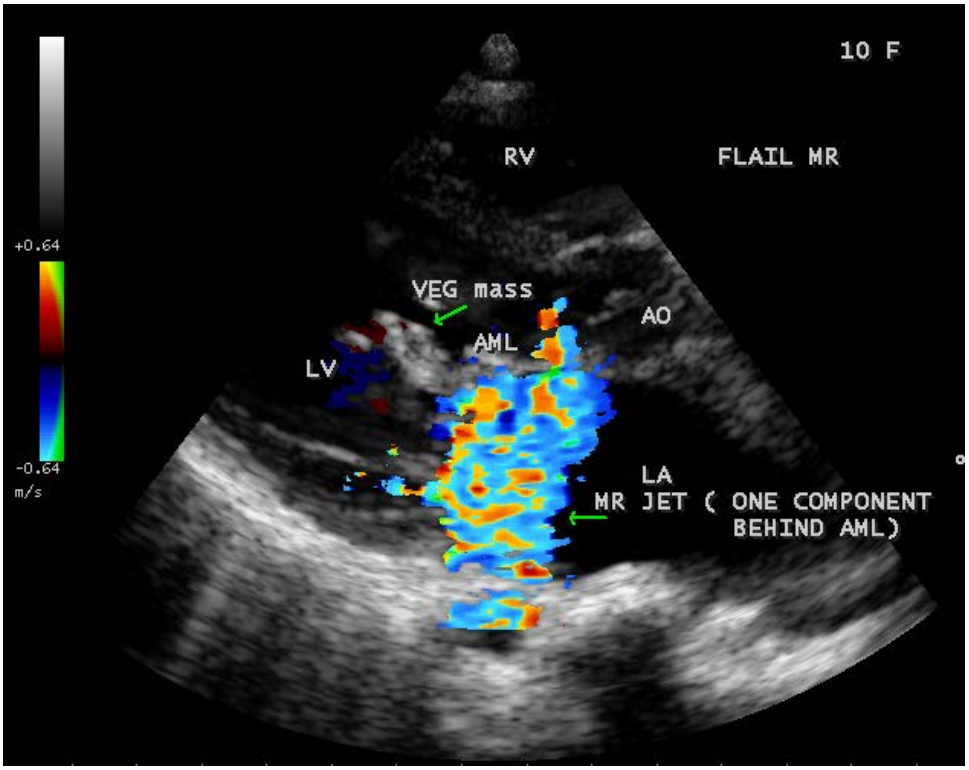


Figure 22. Disorganized Flail MR jet—one component behind AML (anterior mitral leaflet)—highly eccentric jet.

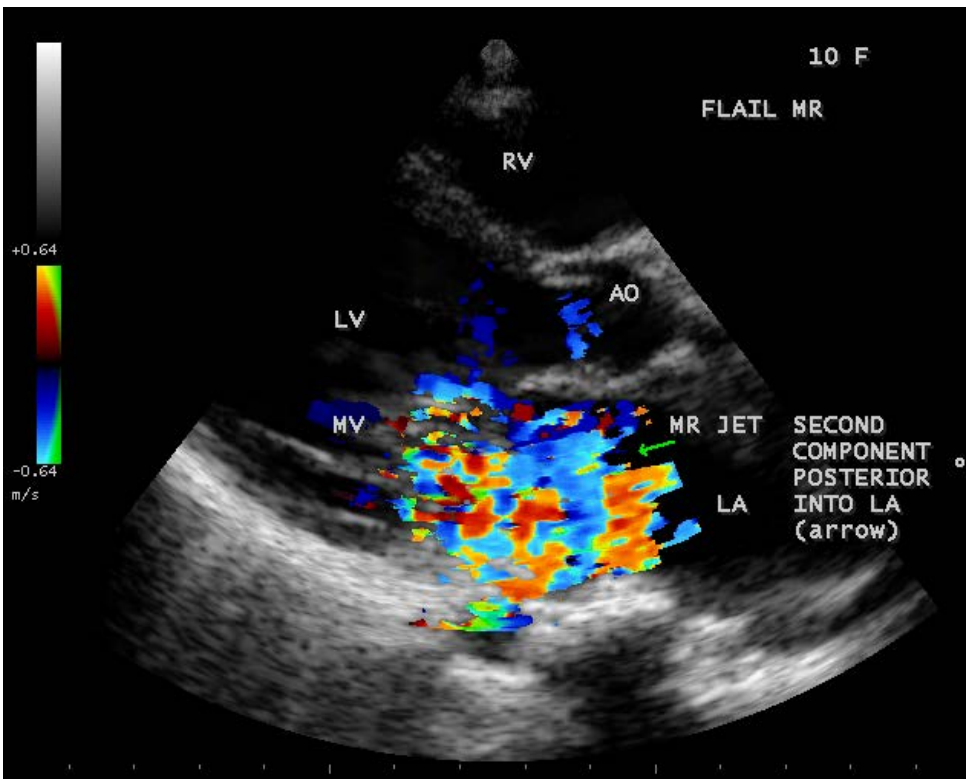


Figure 23. Disorganized MR jet—second component posterior towards LA (left atrium).

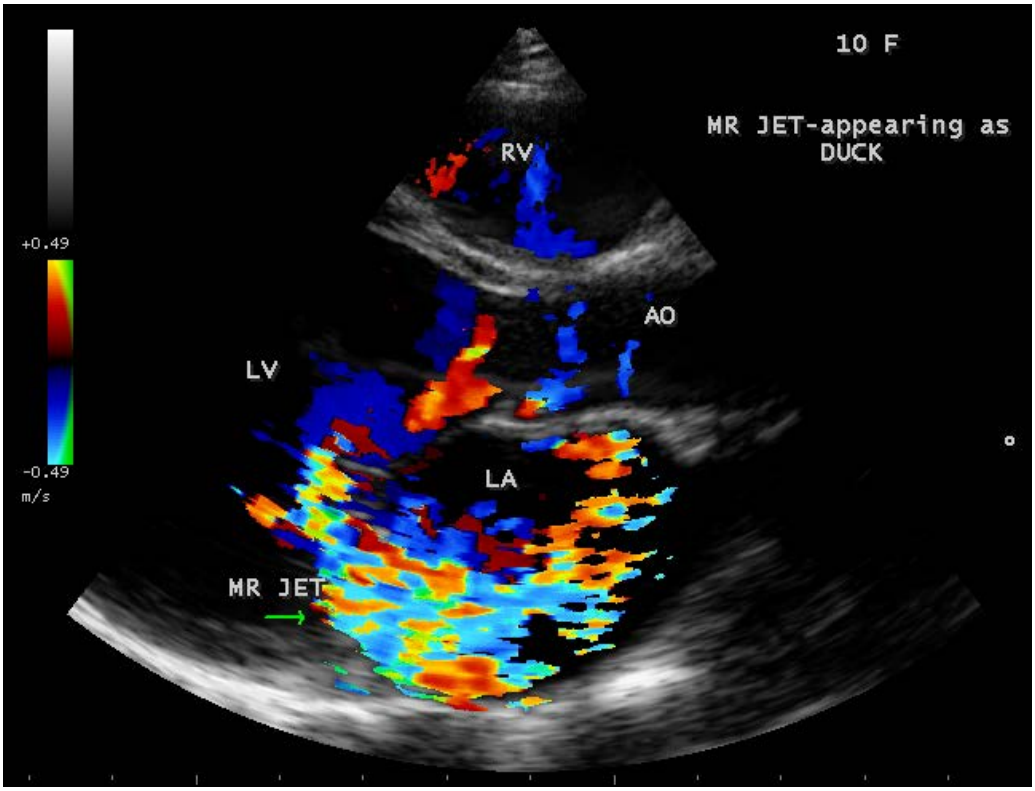


Figure 24. The "duck" shaped MR jet—posterior towards LA.

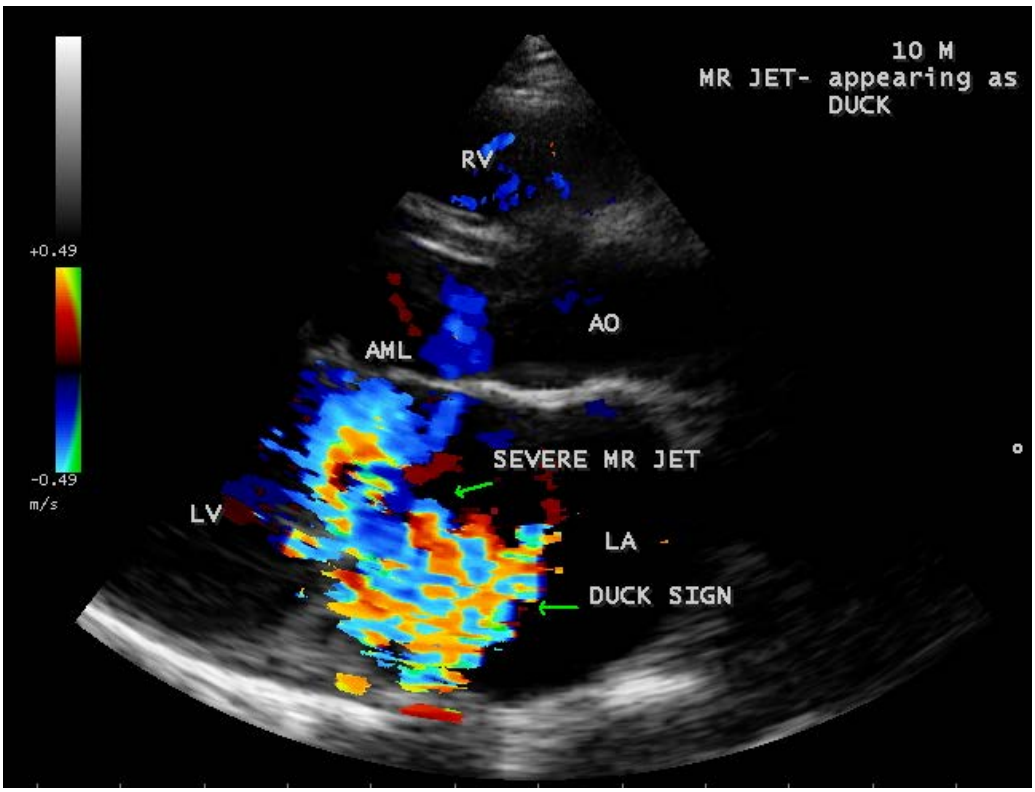


Figure 25. The "duck" shaped MR jet—hugging the LA wall suggesting severe regurgitation.

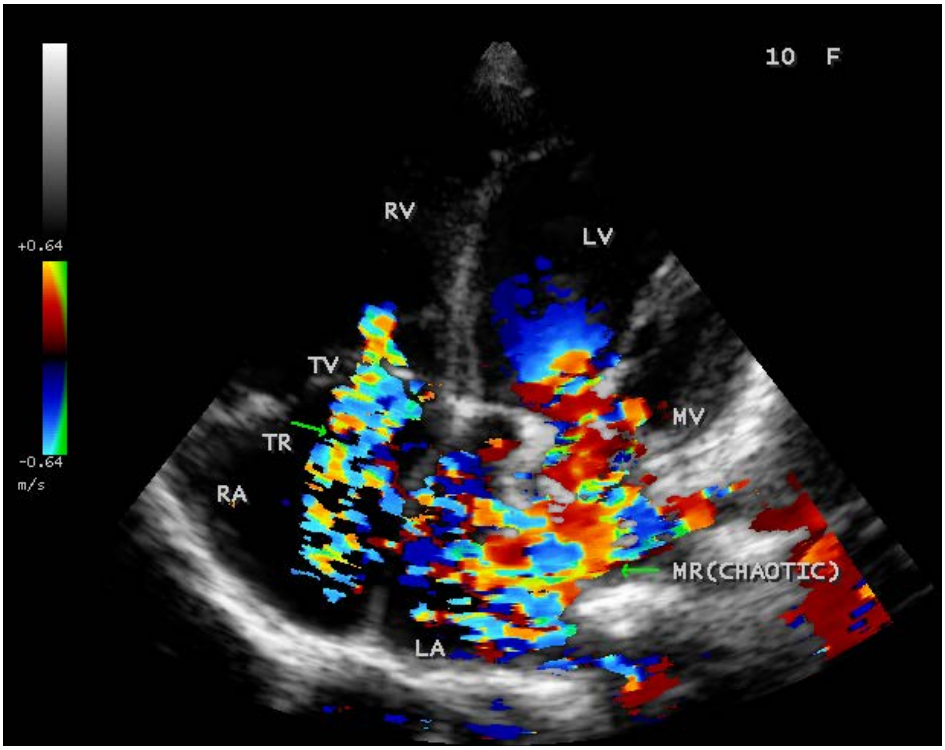


Figure 26. Apical four chamber view showing the chaotic MR (mitral regurgitation) jet, TR (tricuspid regurgitation) jet.

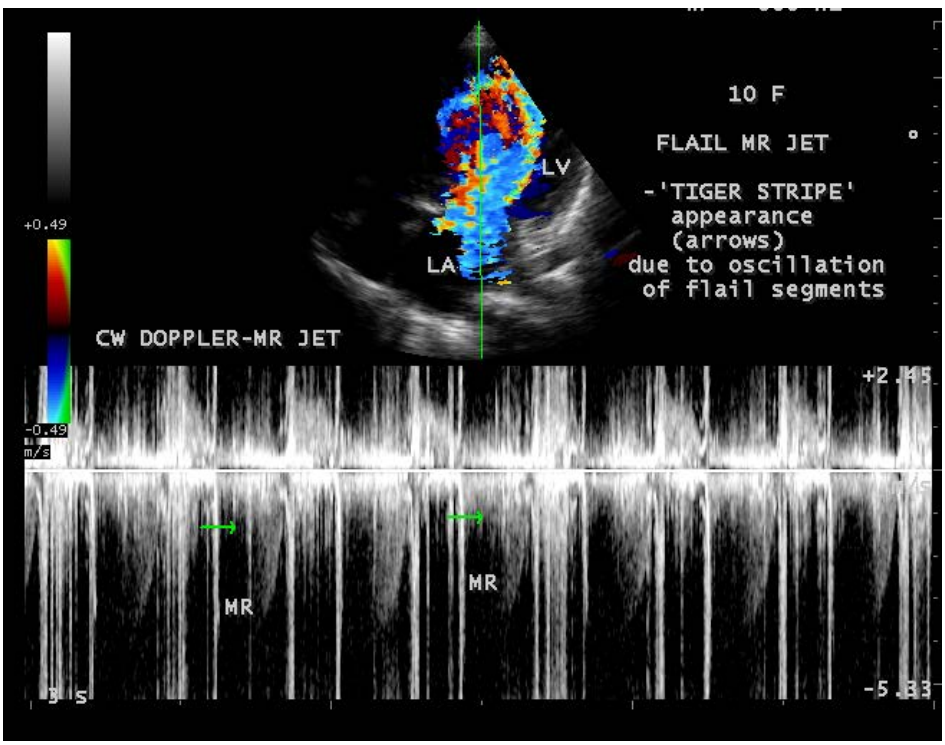


Figure 27. CW (continuous wave) Doppler showing the "tiger stripe" appearance (arrows) on spectral Doppler of MR jet due to oscillating flail segments in the regurgitant stream ([33], Figure 11.85).

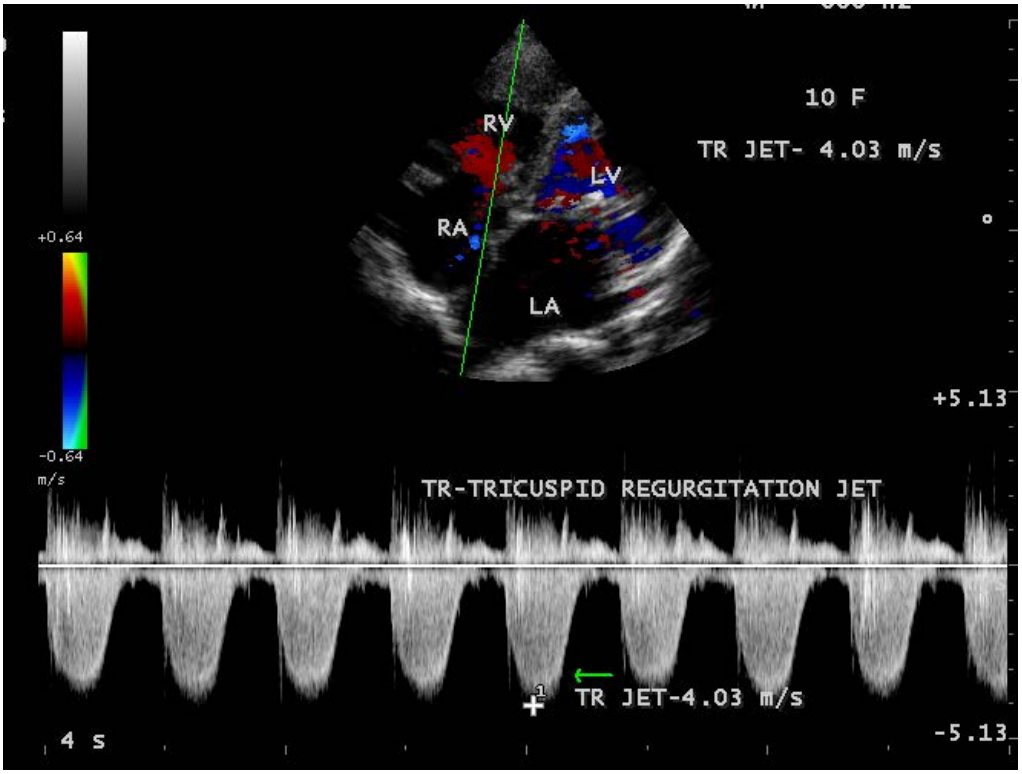


Figure 28. CW (continuous wave) Doppler showing the TR (tricuspid regurgitation) jet velocity.

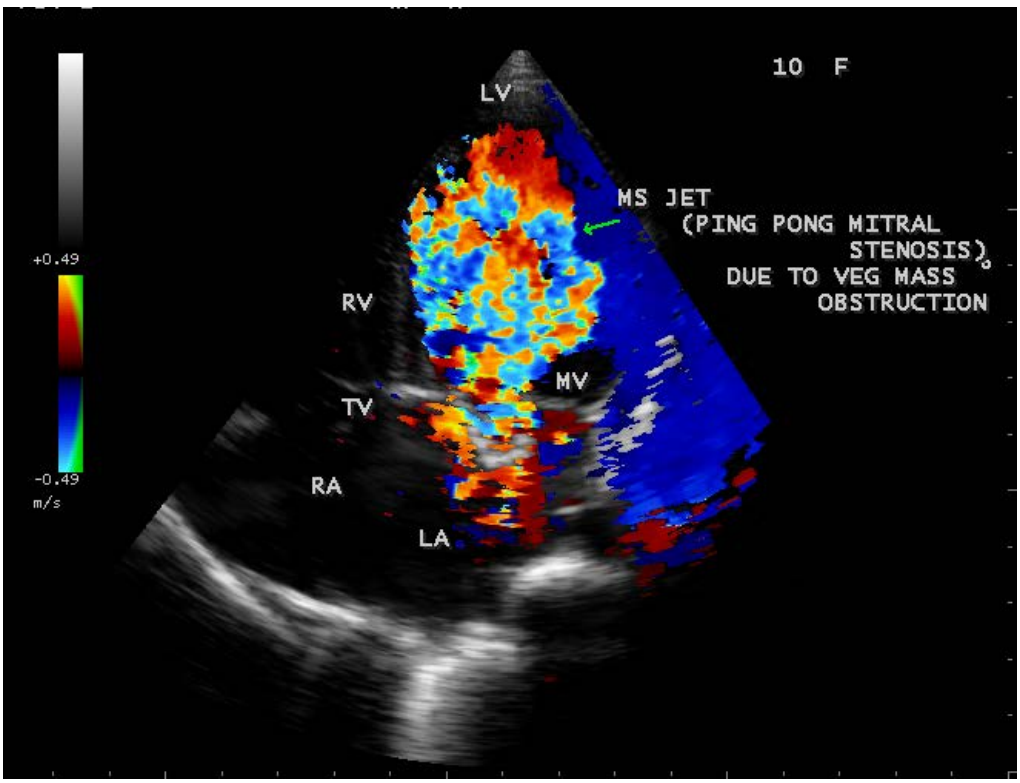


Figure 29. Showing the functional MS (mitral stenosis—"Ping-Pong" mitral stenosis) due to the mass effect of vegetation.

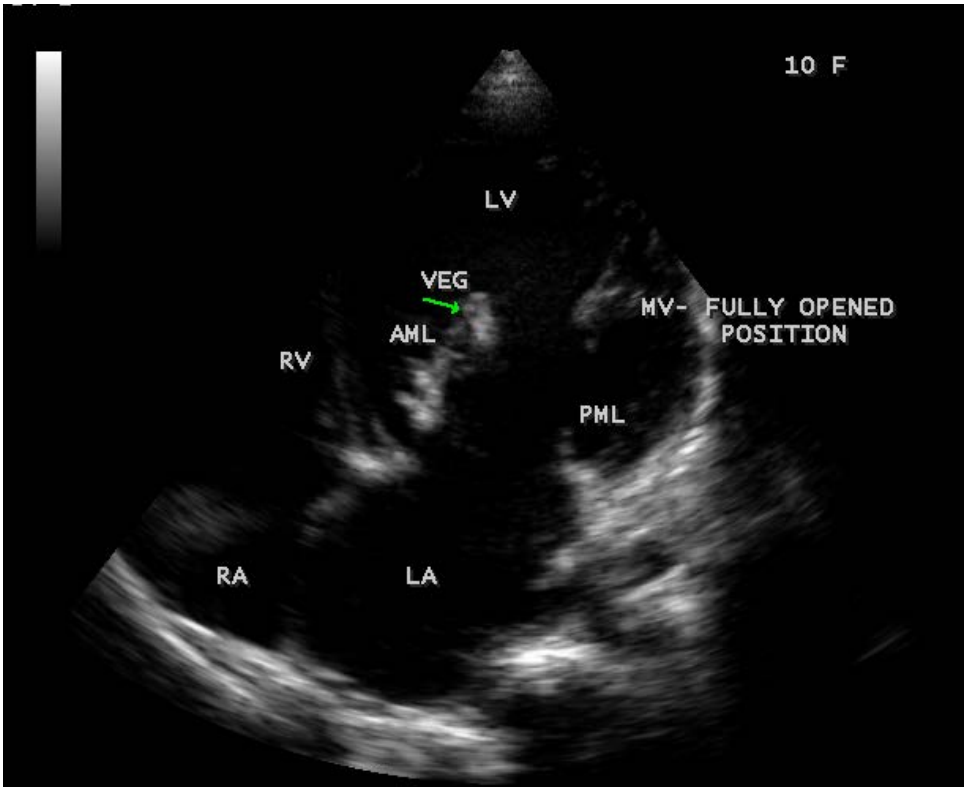


Figure 30. Vegetation mass attached to AML (anterior mitral leaflet)—mitral valve in a fully opened position ([33], Figure 13.7A).

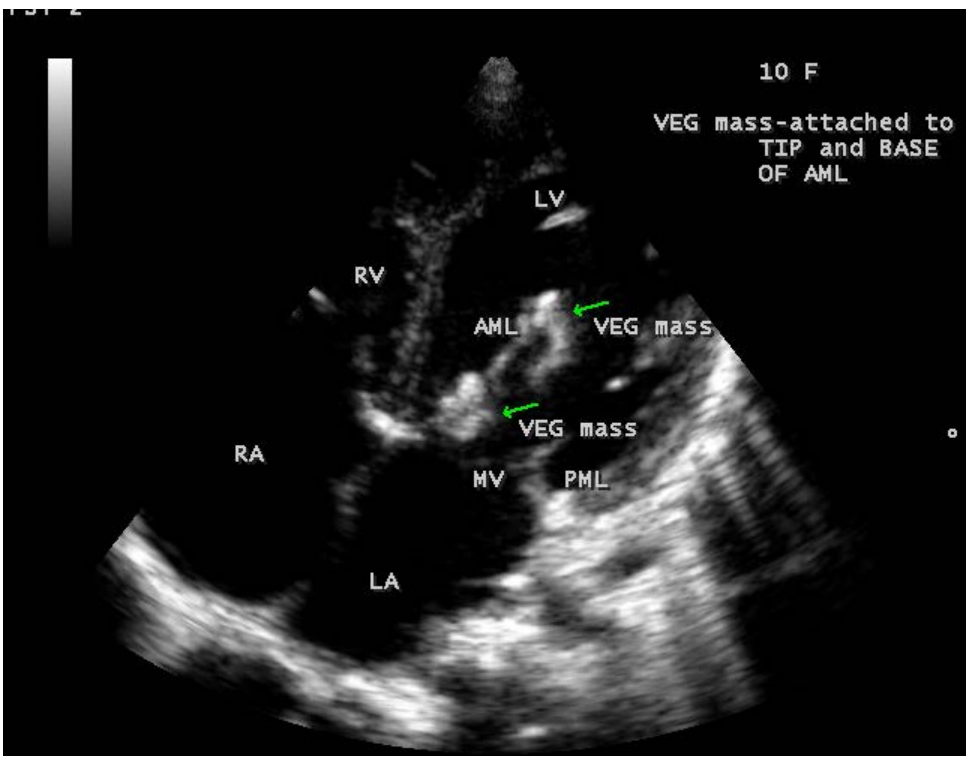


Figure 31. Vegetation mass is attached to the base and apical portion of the anterior mitral leaflet.

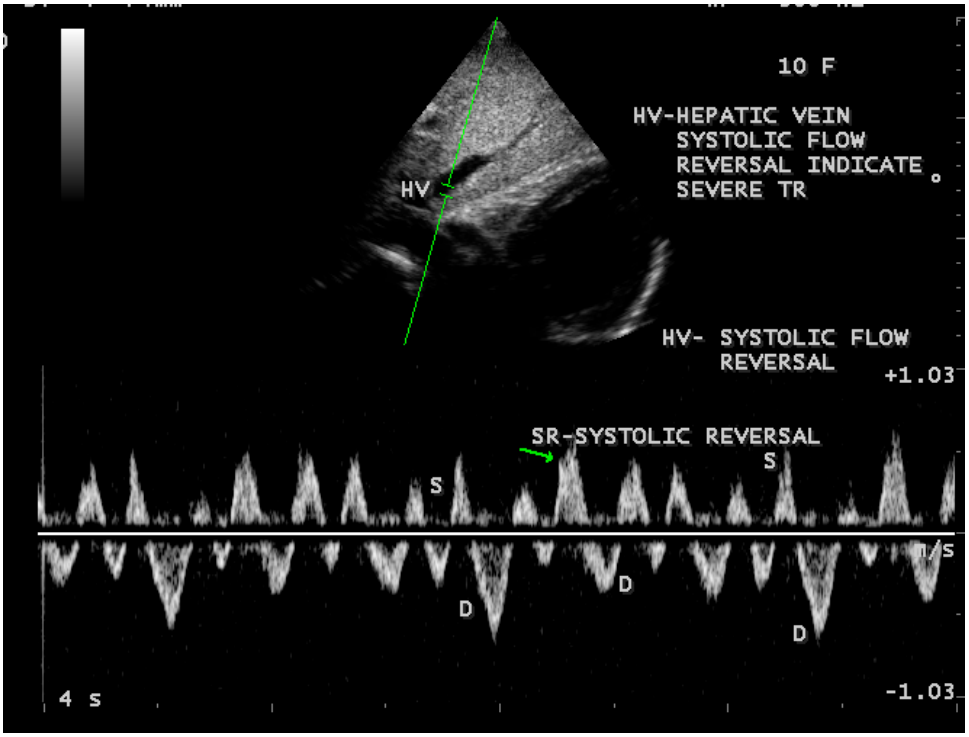


Figure 32. Pulsed Doppler—showing the hepatic vein systolic flow reversal suggesting severe tricuspid regurgitation.

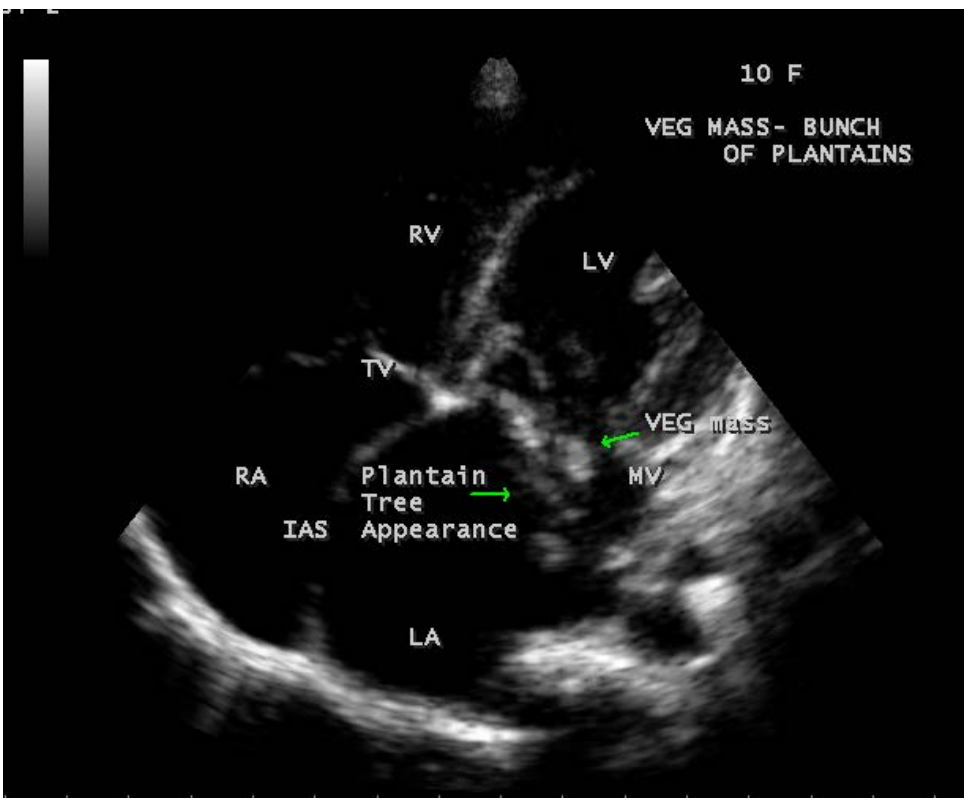


Figure 33. Vegetation mass appearing as "bunch of plantains"—plantain tree appearance.

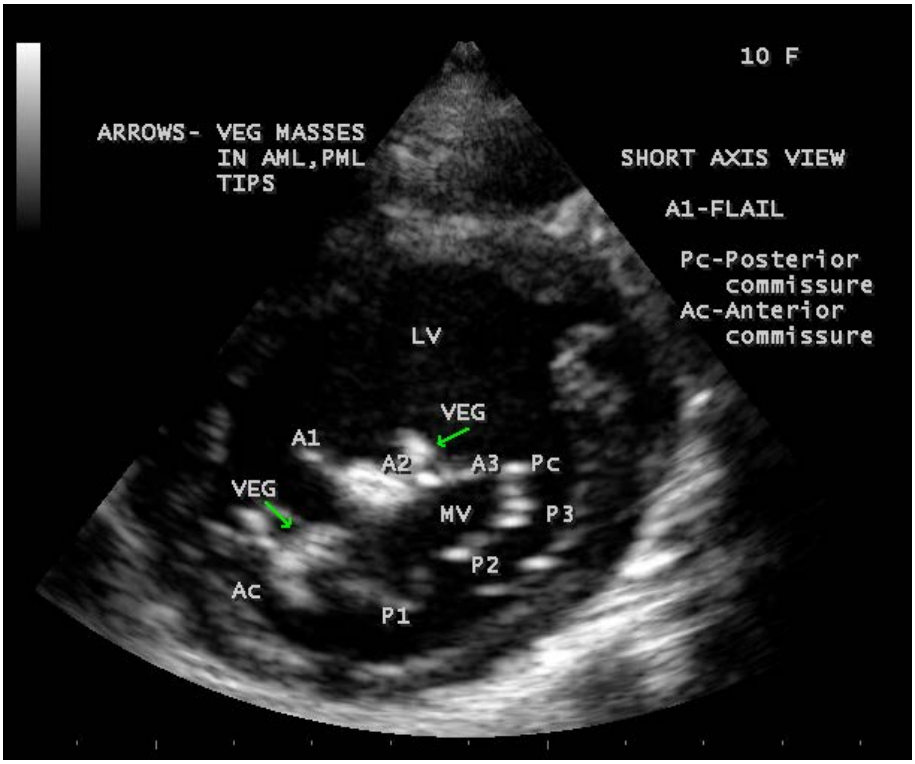


Figure 34. Short axis view showing the vegetation masses in the tips of mitral valve leaflets. P_1 (anterior), P_2 (middle), P_3 (posterior)—are the scallops (clefts or indendations) of PML (posterior mitral leaflet), A_1, A_2, A_3—are the corresponding segments of AML (anterior mitral leaflet). A_1 is Flail. Pc (posterior or posteromedial commissure), Ac (anterior or anterolateral commissure).

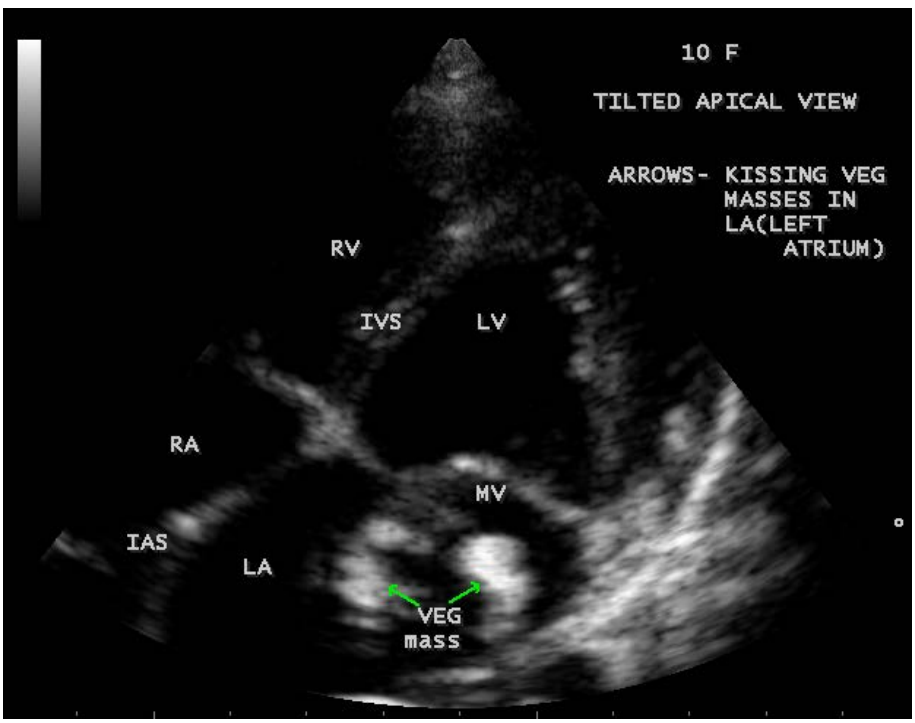


Figure 35. Short axis view showing the kissing form of vegetation masses in the LA (left atrium).

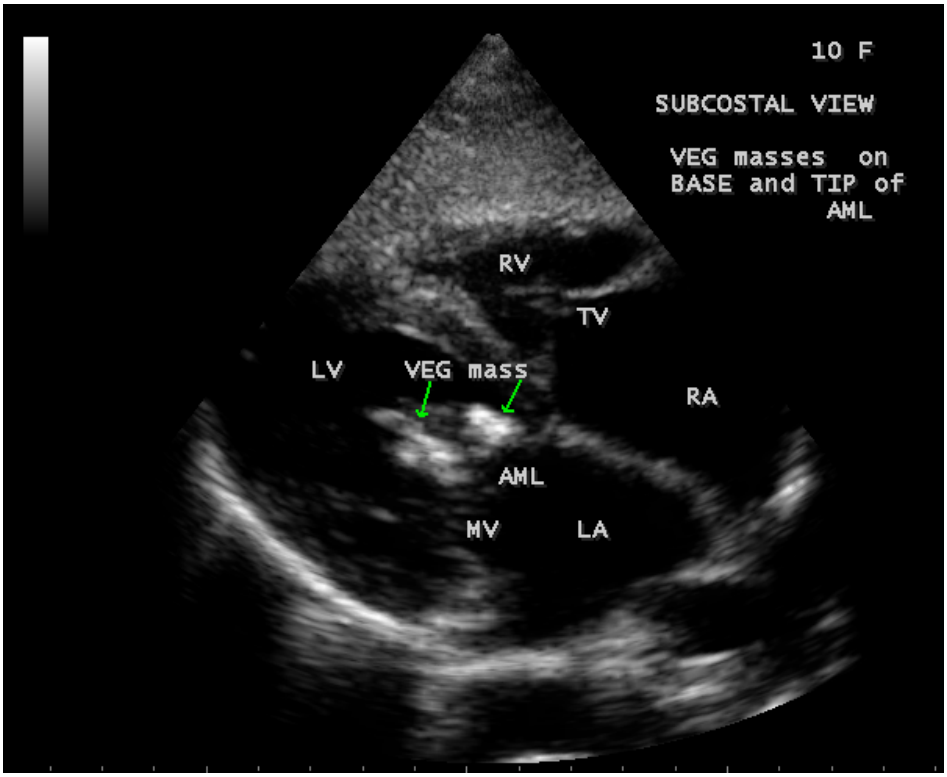


Figure 36. Subcostal view showing the vegetation on the base and tip of AML.

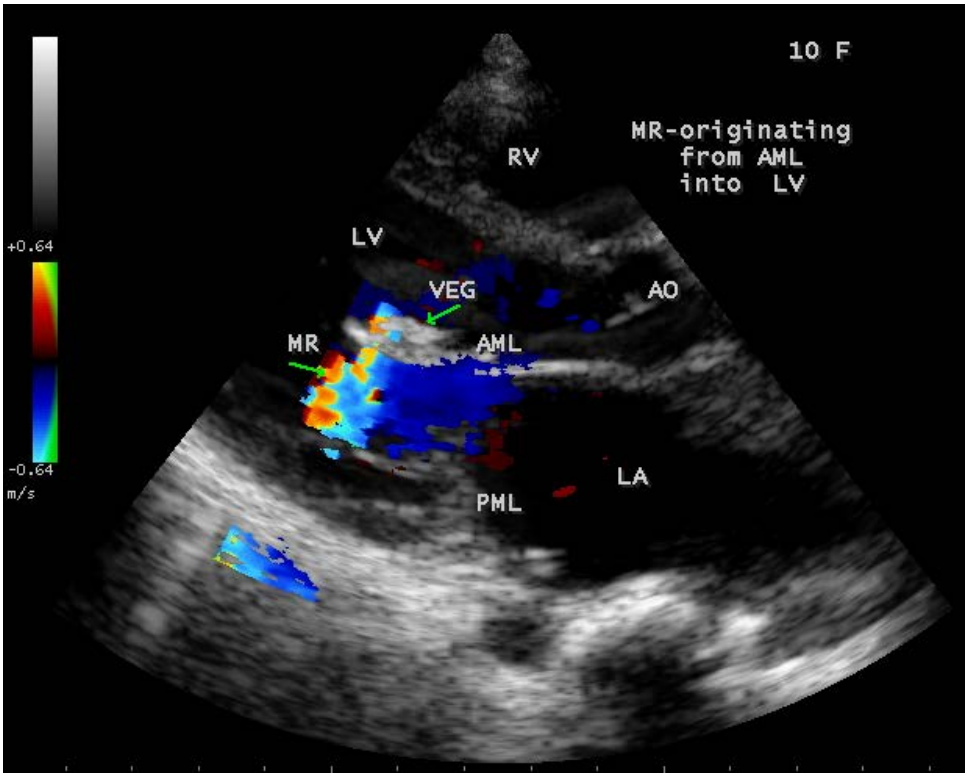


Figure 37. MR (mitral regurgitation) jet originating from the tip of AML (anterior mitral leaflet) at the site of attachment of vegetation into LV (left ventricle).

and calcified as shown in Figure 2 in addition to thickened and calcified mitral leaflets, suggesting an underlying rheumatic valvulitis predisposing to the formation of vegetation. The child was given 1.2 million units of intramuscular benzathine penicillin G injection as a therapeutic and initial prophylaxis dose for rheumatic fever and advised every 3 weeks for life long. Small doses of digoxin and diuretics are also prescribed and advised early surgery (mitral valve replacement).

3. Discussion

3.1. Etiopathogenesis

The mitral valve apparatus is a very complex structure and all of its components must work together for proper valve function. Mital regurgitation can occur when any one of these elements fails through different mechanisms that affect leaflet coaptation. Intrinsic valvular involvements by degenerative, rheumatic and infective endocarditis produce organic (primary or structural) mitral regurgitation whereas abnormal function of normal leaflets due to impaired ventricular function caused by ischemic heart disease and dilated cardiomyopathy [11], produce functional (secondary) mitral regurgitation as a result of an imbalance between tethering forces (annular dilatation, LV (left ventricular) dilatation, papillary muscle displacement, LV sphericity) and closing forces (reduced LV contractility, global LV and papillary muscle dyssynchronies and altered mitral systolic annular contraction). Papillary muscle rupture secondary to myocardial infarction defined an organic ischemic MR (mitral regurgitation). A descriptive classification of mechanism was developed by Carpentier in 1983 based upon the movement of leaflets as normal, excessive or restricted [12] as shown in Table 1 by understanding the papillary muscle-chordal-leaflet scallop relationship which has been defined anatomically by Lam *et al.* and it is modified by Carpentier himself in 1995 to include a mechanism of leaflet restriction during systole causing regurgitation as Type IIIb.

Kumar, *et al.* [13] proposed a classification (Duran classification) based on chordal insertion from the two groups of papillary muscles as lateral half of both leaflets is designated with 1 and the medial half with 2. Thus, anterior leaflet is divided into A_1 with chordal crossing from the anterolateral papillary muscle and A_2 with chordal crossing from the posteromedial papillary muscle. The posterior leaflet scallops are designated

Table 1. Mechanism of MR (mitral regurgitation) based on leaflet motion—Carpentier's functional classification.

Types	Leaflet motion	Mechanism
Type 1	Normal motion	Annular dilation, clefts, leaflet perforation
Type II	Excessive motion	Prolapse, flail chords, ruptured papillary muscle
Type III	Restricted motion	
Type IIIa	Restriction during diastole and systole	Commissural fusion due to rheumatic heart disease
Type IIIb	Restriction during systole only	Chordal tethering, papillary musle displacement

as P_1 (anterolateral), P_2 (posteromedial) and a large middle scallop as PM. The PM is a larger scallop and subdivided as PM_1 and PM_2 based on chordal origin.

When a part of the mitral valve body protrudes into the left atrium beyond the mitral annulus and producing mild regurgitation with a preservation of coaptation is termed as "billowing valve". It is stated that the mitral valve billows slightly into the left atrium normally and an exaggerated finding should be termed as "billowing mitral valve", extreme form of billowing is "floppy valve" and when chordal rupture, the prolapsed mitral valve is "flail". A morphologic abnormality with thickened leaflet (diastolic thickness > 5 mm) due to redundant tissue is termed "floppy valve". When the coaptation line is beyond the annular plane, it is termed as mitral valve prolapse, the leaflet tip is directed towards LV and its most common phenotype is diffuse myxomatous degeneration (Barlow's disease) in which the middle spongiosa component of the leaflet is unusually prominent and the quantity of acid mucopolysaccharide is increased. When the free edge of the leaflet is completely reversed into the left atrium (LA), the leaflet tip directed towards LA, it is termed as "flail leaflet", usually as a consequence of chordal rupture [13]. In moderate prolapse, when the leaflet tip remains in the left ventricle, it is called as "billowing valve" and in severe prolapse when the leaflet tips bulges into the left atrium, it is called as "flail leaflet".

Rheumatic valvulitis is characterized by variable thickening of the leaflets at their free edges, chordal fibrosis, rigidity and reduced motion of posterior leaflet in diastole and in some patients, the posterior leaflet remains in a semi-open position throughout the cardiac cycle and the friction of anterior leaflet in systole produce a false aspect of prolapse. This friction causes endothelial damage and results in platelet-fibrin deposition which is more susceptible to colonization by microorganisms. The initially sterile platelet-fibrin nidus called as nonbacterial thrombotic endocarditis (NBTE) become secondarily infected by microorganisms circulating in the blood, either from distant source of focal infection or as a result of transient bacteremia from a mucosal or skin source [14] and establishing an infectious nidus or vegetation on the endocardium and most commonly they are found at the valve closure-contact (coaptation) line on the atrial surface of the mitral valve [15]. Following successful medical therapy, the vegetative lesions may heal by a process of endothelialization of the surface phagocytes of bacterial debris, sometimes with calcification and subsequent organization by fibroblasts. Vegetation can be attached to any part of the valve and move with the leaflet but in a more chaotic (oscillating) manner and prolapse through the valve when it opens. Vegetation can prevents leaflet coaptation, and valvular retraction during the healing phase of endocarditis and result in mitral regurgitation. Large vegetation particularly at the mitral valve may result in functional valve stenosis and hemodynamic deterioration [16]. When the infection extends beyond the valve leaflet, distortion of leaflet and chordal rupture may occur, leading to severe regurgitation [17]. Ruptured mitral chordae tendineae (RMCT) are increasingly reported as an important cause of mitral regurgitation [18]. Anterior chordae tendineae rupture of the mitral valve was common in chronic rheumatic valvulitis (CRV) and infective endocarditis. In myxomatous dege-

neration, the posterior leaflet chordal rupture is more common and the posterior leaflet becomes "flail" with a "saloon door effect".

Rheumatic mitral regurgitation has a benign course as stated by Bland and James [19] in the analysis of the cases of rheumatic valvular lesions over a 20-year period. Levine and Friedberg have suggested that there are two groups of patients with mitral regurgitation, one group showing rapidly progressive and the other group showing a prolonged, stable and benign course. In most patients with severe primary MR (mitral regurgitation), left ventricular compensation is maintained for years, but ultimately the prolonged hemodynamic overload leads to myocardial decompensation.

3.2. Echocardiographic Features

Infective endocarditis is the microbial infection of the endocardial (endothelial) surface of the heart and the formation of vegetation (a variably sized amorphous mass of platelets and fibrin in which abundant microorganisms and scant inflammatory cells are enmeshed) is the hallmark of the disease and the vast majority of vegetations, however, occur on valve leaflets. The classic approach to the diagnosis of endocarditis by von Reyn does not include echocardiographic findings and it is mainly focused on pathological, clinical and laboratory evidence (positive blood cultures). In 1994, the Duke criteria for the diagnosis of infective endocarditis [20] defined "positive echocardiogram" as vegetation, an oscillating intracardiac mass, a new valvular regurgitation and microbiological evidence was established with a high sensitivity and specificity (generally about 80%). Steckelberg and Wilson [21] suggest that the incidence of endocarditis in the general population is approximately 5 cases per 100,000 persons-years. Valve redundancy and thickened leaflets (>5 mm) by echocardiography identify a population at increased risk for infective endocarditis. The relative risk of infective endocarditis in mitral valve prolapse ranges from 3.5% to 8.2%. Rheumatic heart disease is the predisposing cardiac lesion in 20% to 25% of cases in 1970's and 1980's [22], in Europe, it is 7% - 18% [23]. In children, it is less than one in ten cases of infective endocarditis [24] and the mitral valve is most frequently affected in women while the aortic valve in men.

Echocardiography is the only noninvasive method available for direct visualization of endocarditis-induced lesions. Echocardiographic finding in patients with infective endocarditis was initially observed by Dillon [25] and Spangler, *et al.* [26]. The vegetation will grow in size, either as a sessile clump or a highly mobile and even pedunculated mass with the potential for embolization. Vegetation can be detected when the valve attached mass reaches a diameter of ≥2 to 3 mm [27]. In both children and adults, 2-D echocardiography is usually the more sensitive technique with sensitivity in children up to 80% [28]. Valvular dysfunction due to tissue disruption or large obstructing vegetation can be visualized and quantitated by echocardiogram with Doppler [29]. The detection of a large eccentric jet adhering, swirling, and reaching the posterior wall of the LA is in favour of significant MR (mitral regurgitation) as shown in **Figure 22**, **Figure 24** and **Figure 25**.

3.2.1. Vegetation

The most common and direct evidence of infective endocarditis is the vegetation and it begins as a microscopic focus of infection and gradually grows into a conspicuous mass. It is typically an irregularly shaped, highly mobile, echogenic mass attached to the free edge of a valve leaflet (most commonly at the coaptation line) and tends to develop on the "upstream" side of the valve leaflets (*i.e.*, the ventricular side of aortic valve and the atrial side of mitral and tricuspid valves). They may be sessile or pedunculated, but usually has an oscillating or fluttering motion, a typical feature of most vegetations. Vegetation move with the leaflet in a more chaotic ("oscillating") manner and it may prolapse through the valve into the LV (left ventricle) as it opens as shown in **Figure 3**, **Figure 4** and **Figure 16** and into LA (left atrium) as it closing (**Figure 5** and **Figure 6**). The mass of vegetation is typically homogeneous with echogenicity similar to that of the myocardium. The infectious process often alter the valvular structure and function. Extensive involvement of the leaflet may result in chordal rupture, leading to severe regurgitation as shown in **Figure 21**. Direct and typical signs of RMCT (ruptured mitral chordae tendineae) were chain-flail or whiplash-like changes and had an incidence of 86.7%, causing severe regurgitation and mitral chordal rupture is the leading cause of flail mitral leaflet [30]. A large vegetation may obstruct the valve orifice as shown in **Figure 1** and **Figure 2**, sometimes termed as "obstructive-type bacterial endocarditis" and producing a functional valve stenosis (Ping-Pong mitral stenosis [31]) similar to left atrial myxoma as shown in **Figure 29**.

The shape and size of vegetation are quite variable and mostly it is polypoid [32]. The typical vegetation is a "sessile" or "pedunculating" valve-attached mass. A mobile vegetation showed a pedunculating part prolapsing into the ventricle as shown in **Figure 3** and **Figure 4** or atrium as shown in **Figure 5** ([33], Figure 13.1) in a 10-year-old female child. A vegetation was considered as "definite" when shaggy echoes in the M-mode study as shown in **Figure 20** and a corresponding mass without restricted valve motion in the two-dimensional echocardiogram were found as shown in **Figure 16** and **Figure 30** ([33], Figure 13.7). The vegetation vary in size, often being just a few mm and sometimes reaching to 2 - 3 cm. A vegetation must be at least 3 to 6 mm in size to be reliably seen. The mean size of vegetation was 0.6 mm (range 3 to 28) and vegetation >10 mm in diameter was defined as "large" and those ≤10 mm in diameter was defined as "small" and ≥15 mm is "very large". Vegetations resulting from fungal infections (candida, aspergillus) are usually much bigger than bacterial vegetations and can be so big to be mistaken for a cardiac tumor. The large vegetations are at increased risk for embolic complications [34], especially on the anterior leaflet of the mitral valve with mobility [35]. A vegetation size of 3.2 × 4.4 cm is called as "giant vegetation" on the mitral valve with a fibrillary appearance of the mass ([36], Figure 3) as shown in **Figure 1** is an important predictor of embolic phenomena in patients with infective endocarditis, causing severe mitral regurgitation as "Duck" shaped jets (**Figure 24** and **Figure 25**), disorganized (**Figure 21**) and sometimes the regurigitant jet splits into two components as one into LA and the second one into LV simultaneously as bileaflet jets (**Figure 10**) similar to bileaflet structure of AML with vegetation masses (**Figure 9**) and it originates

from tip of AML(anterior mitral leaflet) at the site of attachment of vegetation mass as shown in **Figure 37**. The size of the largest vegetation reported on the mitral valve in the literature in patients with bacterial endocarditis is 7 × 4 cm in a 29-year-old female at postmortem examination [37]. In a study of Nunes, *et al.* [38], vegetation size > 13 mm was the only independent predictor of mortality, but some studies [39] [40] did not had an increased embolic risk in patients with vegetation focused only on its presence and size and not on their location. Embolic complications may occur in infective endocarditis (20.6%) and were not more prevalent in the groups with large vegetations [41]. However, Wong, *et al.* [42] found an increased need for surgery in patients with a large vegetation (>10 mm).

The size and shape of vegetation vary due to curling of vegetation. The size of vegetation in this child is 35.6 × 9.3 mm as in **Figure 17**, 20 × 23.7 mm as in **Figure 1**, 32.9 × 13.9 mm as in **Figure 2**.

The shape of vegetation varies in this child as "popcorn" like (**Figure 1**, **Figure 3** and **Figure 4**), rod-shaped (**Figure 7**), basket shaped (**Figure 11**) ([33], Figure 13.3), "baby in hand" appearance (**Figure 18**), "cucumber" shaped (**Figure 2**) and a "bunch of plantain" appearance (**Figure 33**), ring shaped (**Figure 12**), bileaflet structure (**Figure 9**) with bileaflet MR jet as shown in **Figure 10**. and kissing forms (**Figure 13**, parasternal long axis view, **Figure 14**, apical four chamber view, **Figure 35**, tilted apical four chamber view and **Figure 15**, **Figure 34**, short axis views)

3.2.2. "Flail" Mitral Regurgitation (MR)

The anatomic disruption of a portion of the mitral valve apparatus due to the underlying rheumatic valvulitis with predisposing infective endocarditis which form a vegetation, resulting an eccentric regurgitation jet with orientation opposite in direction of the leaflet having the anatomic defect such as "flail". In the presence of "flail leaflet", the mitral regurgitant spectral signal may have an atypical appearance and the flail portion oscillates in the spectral signal of regurgitant flow stream to produce a "tiger stripe" appearance as shown in **Figure 27**, associated with "whistling" sound on auscultation ([33], Figure 11.85). The mitral regurgitation (flail MR) jet is chaotic as shown in **Figure 26**, highly eccentric (**Figure 22**) and disorganized with one component behind the anterior mitral leaflet and the second component directed posterior immediately as in **Figure 21** ([33], Figure 11.79).

The severity of eccentric MR is underestimated because of coanda effect. If the regurgitant jet area fills <20% of the left atrium, it is mild and >40% indicates severe regurgitation. The vena contracta (the neck or narrowest portion of the jet), typically imaged perpendicular to the commissural line in parasternal long axis and apical four chamber views is well defined in both central and eccentric jets, but not in chaotic, disorganized jets due to flail leaflets. Its width < 3 mm indicates mild MR, >7 mm defines severe MR and a mean value of >8 mm indicates severe functional MR. The flow convergence method based on PISA (proximal isovelocity surface area) may not applicant for eccentric and multiple jets or complex and elliptical regurgitant orifices to assess the

severity of mitral regurgitation. The adaptation of LV to the increased volume overload is reflected by LV dimensions and ejection fraction. In chronic compensated phase, the forward stroke volume is maintained through an increase in LV ejection fraction >65% and the patient could be asymptomatic. In chronic decompensated phase of MR, the forward stroke volume decreases and the LA pressure increase significantly. The patient may be still asymptomatic and the LV ejection fraction may be in the low normal range despite the presence of significant muscle dysfunction. The contractile function decreases silently and become irreversible. In the current guidelines, surgery is recommended in asymptomatic patients with severe organic MR when the LV ejection fraction is ≤60%. However, in acute stage, the LV ejection fraction increases in response to the increased preload. The end-systolic diameter is less preload dependent than the ejection fraction and it may be more appropriate to monitor the global LV function. The end-systolic diameter > 45 mm also indicate the need for mitral valve surgery [43]. In this child, the LVESD (end-systolic diameter) is 30.7 mm and the ejection fraction (EF) is 66% as shown in **Figure 19**. New parameters are currently available for a better assessment of LV function. A systolic tissue Doppler velocity measured at the lateral annulus < 10.5 cm/s has been shown to identify significant LV dysfunction and to predict post-operative LV function in patients with asymptomatic organic MR [44]. Strain imaging allows a more accurate estimate of myocardial contractility than tissue Doppler velocities. In MR, strain has been shown to decrease even before LV end-systolic diameter exceeds 45 mm [45]. A resting longitudinal strain rate < 1.07/s (average 12 basal and mid segments) is associated with subclinical latent LV dysfunction [46] and a global longitudinal strain <18.1% has been associated with postoperative LV dysfunction [47]. The left atrium dilates in response to chronic volume and pressure overloads. LA remodelling (diameter > 40 - 50 mm) may predict the onset of atrial fibrillation and poor prognosis in patients with organic MR [48]. The excess regurgitant blood entering in the LA may induce acutely or chronically a progressive rise in pulmonary pressure and the presence of TR (tricuspid regurgitation) as shown in **Figure 26** and **Figure 28** permits the estimate of systolic pulmonary arterial pressure and mitral valve surgery is recommended when it is >50 mmHg at rest and LA reverse remodelling may occur after surgery. The severe TR may cause a decrease in hepatic vein systolic velocity and systolic flow reversal may occur as shown in **Figure 32** and its sensitivity is 80% [49]. The TR (tricuspid regurgitation) jet velocity in this child is 4.03 m/s as shown in **Figure 28** which corresponds to a systolic pulmonary artery pressure of 65 mmHg.

3.3. Treatment

3.3.1. Pharmacological Therapy

Pharmacological therapy aims to alleviate symptoms and to prevent the progression of LV dysfunction. Afterload reduction is of particular benefit in the management of both acute and chronic forms of mitral regurgitation [50]. Afterload reduction with sodium nitroprusside is life saving in acute conditions such as chordal or papillary muscle rupture. It stabilizes the patient by reducing the impedence to the LV ejection and thus, the

regurgitant volume and LA pressure decrease. Dobutamine may be administered along with nitroprusside if hypotension exists. Afterload reduction in chronic, severe MR with vasodilators such as angiotensin converting enzyme inhibitors are beneficial in presence of heart failure, but not beneficial in its absence [51]. In addition to diuretics, digitalis glycosides are indicated in patients having severe MR and heart failure, particularly with established atrial fibrillation along with anticoagulants. IE (infective endocarditis) prophylaxis was advised during surgical procedures in these patients.

3.3.2. Surgical Therapy

Asymptomatic patients with severe MR having excellent ventricular function (EF > 70%, ESD (end-systolic diameter) < 40 mm) can be safely followed by a "watchful waiting approach" until symptoms, LV dysfunction (EF ≤ 60%, ESD ≥ 45 mm) and pulmonary hypertension develops. Mitral valve surgery is the only treatment for MR which provides substantial relief of symptoms and prevent the development of heart failure [52]. The normal function of the mitral valve apparatus "primes" the left ventricle for normal contraction. Operative procedures may interfere the annular-chordal-papillary muscle continuity, results in postoperative LV dysfunction and so the preservation of these structures are now considered as a critical feature of MVR (mitral valve replacement) [53]. Reconstructive procedures are carried out in degenerative MR due to mitral valve prolapse and chordal rupture as well as in ischemic functional MR [54]. Percutaneous catheter-based mitral valve repair procedures such as leaflet edge-to-edge repair and mitral annular reduction are currently under clinical evaluation and the preliminary results are encouraging [55]. The severely deformed valves in rheumatic heart disease are not suitable for reconstructive surgery and they require MVR [56] and the operation should be desirable before they develop marked LV dysfunction [57] and serious symptoms since severe LV dysfunction(EF < 30%) may cause high perioperative mortality [58]. Excellent survival is observed in patients with ESD < 45 mm, EF ≥ 60% and the 5-year survival rate is 40% in ischemic MR and 75% in rheumatic MR. Intermediate outcome may occur when LV ESD is 45 - 52 mm and the ejection fraction between 50% - 60%. Poor outcome is associated with values below these limits.

Surgery may be considered in mobile vegetation > 10 mm in size since the incidence of systemic embolization are increased (33%) compared to those with smaller size (19%) and particularly those on anterior mitral leaflet are uniquely associated with embolic episodes. Urgent surgery is indicated when a large vegetation is associated with embolic events, heart failure and persistent infection [59]. In patients with valvular dysfunction and in whom the infection is controlled with antibiotic therapy and cardiac function is compensated, surgery may be delayed until antimicrobial therapy has been completed. Early surgery is appropriate in patients with large vegetation who may need valve replacement in future since larger vegetations are associated with increased risk of mortality and embolization [60] [61]. Some authors suggest that the causative microorganism is associated with embolic complications rather than the size of vegetation [62].

Since this child is having a giant vegetation with disorganized severe mitral regurgi-

tation due to flail anterior mitral leaflet as the result of chordal rupture, the child was advised MVR(mitral valve replacement) with mechanical prostheses along with removal of vegetation and to continue penicillin prophylaxis with anticoagulant therapy for life long. Since the vegetation is healed, partially calcified and an organized mass, the antimicrobial regimen for infective endocarditis was not administered. The anticoagulant therapy is not preferred at this moment since the child had no embolic episodes and the role of prophylactic anticoagulant therapy is questionable in large vegetation in the absence of atrial fibrillation. The child was advised small doses of digoxin and diuretics along with penicillin prophylaxis.

3.4. Outcome

Several factors play a role in the prognosis of IE (infective endocarditis). Costa, *et al.* described the clinical and echocardiographic scores as the predictors of mortality in infective endocarditis. Age > 40 years (4 points), class IV heart failure (cardiogenic shock) (4 points), uncontrolled sepsis (6 points), conduction disease(5 points), arrhythmias(8 points), a valve with excessive damage (5 points), large and mobile vegetation(4 points) [63]. Mortality rates for scores below 10 were 5.26% and the scores over 20 were 78.9%. The child is having a large and mobile vegetation (4 points), extensive valve damage (5 points) and according to this study, the mortality rate of this child is 5.26%.

3.5. Screening of Population

Transthoracic echocardiographic screening revealed a "popcorn" like active mobile vegetation attached to the flail anterior mitral leaflet and producing chordal rupture with severe, disorganized mitral regurgitation as shown in **Figures 38-43** in a 5-year-old febrile (one week duration) boy having an underlying rheumatic mitral valvulitis with a grade 3/6 holosystolic murmur in the apex (radiating to axilla and back) and had an intermittent diastolic sound ("vegetation flop") coinciding with the physical movement of vegetation mass across the mitral valve orifice [64] at the apex. The vegetation is attached to the base of AML since the basal portion has some vascular supply at the fibrous-myocardial junction where the leaflet inserts and so the basal region is more susceptible to vegetation formation from the blood-borne infections. A small "popcorn" like mobile vegetation attached to the junction of anterior mitral leaflet and chordae is detected by echocardiography in a 46-year old febrile female as shown in **Figure 44** due to friction and trauma.

A "sessile" vegetation attached to the atrial side of posterior mitral leaflet, producing a "flail" PML with a "saloon door" effect and a "bileaflet" severe mitral regurgitation into the left atrium in a 95-year-old asymptomatic female was shown in **Figures 45-48**. Characteristically, the bileaflet flail PML (posterior mitral leaflet) MR (mitral regurgitation) jet is directed into left atrium only as in **Figure 46** and **Figure 48** whereas the bileaflet flail anterior mitral leaflet MR jet is directed into both LA and LV simultaneously as shown in **Figure 10**. A "sessile" vegetation had to be completely attached to the valve as shown in **Figure 49** and **Figure 50** in a 63-year-old male, in which a large vegetation

is attached to the atrial side of anterior mitral leaflet ([33], Figure 13.3-A), producing mitral regurgitation as shown in Figure 51. A "popcorn" like "giant" vegetation, attached to the anterior mitral leaflet which prolapse with mild mitral regurgitation in a 49-year-old febrile male was illustrated in Figures 52-62.

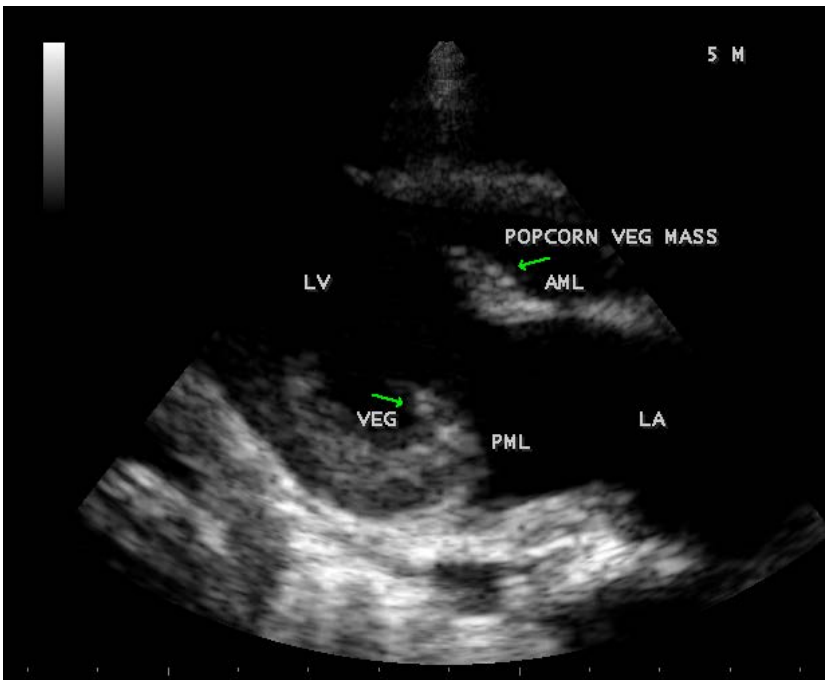


Figure 38. A "popcorn" like vegetation attached to AML in a 5-year-old febrile boy—moving into the LV along with the leaflet. PML (posterior mitral leaflet) is also having the vegetation.

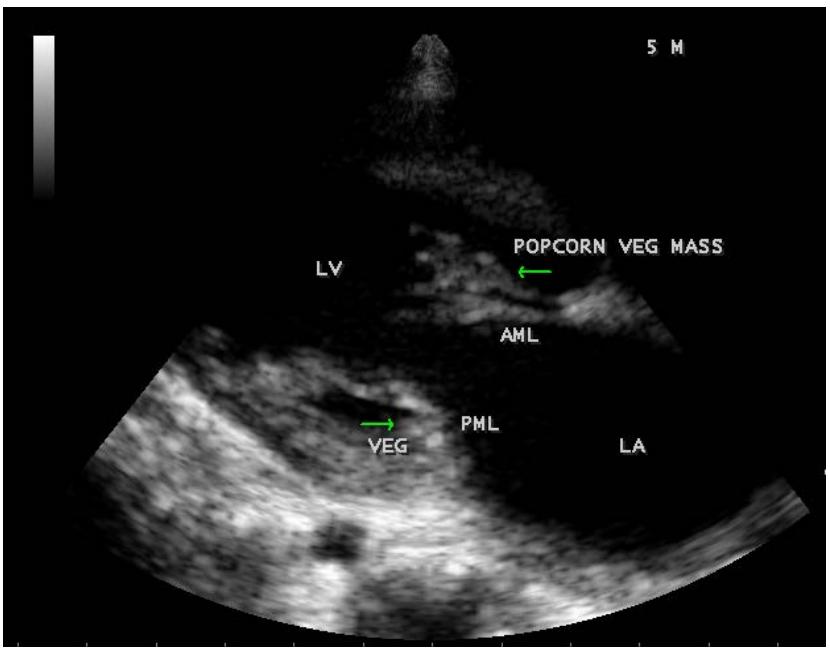


Figure 39. Vegetation masses seen in both AML and PML in the 5-year-old febrile boy—active vegetations.

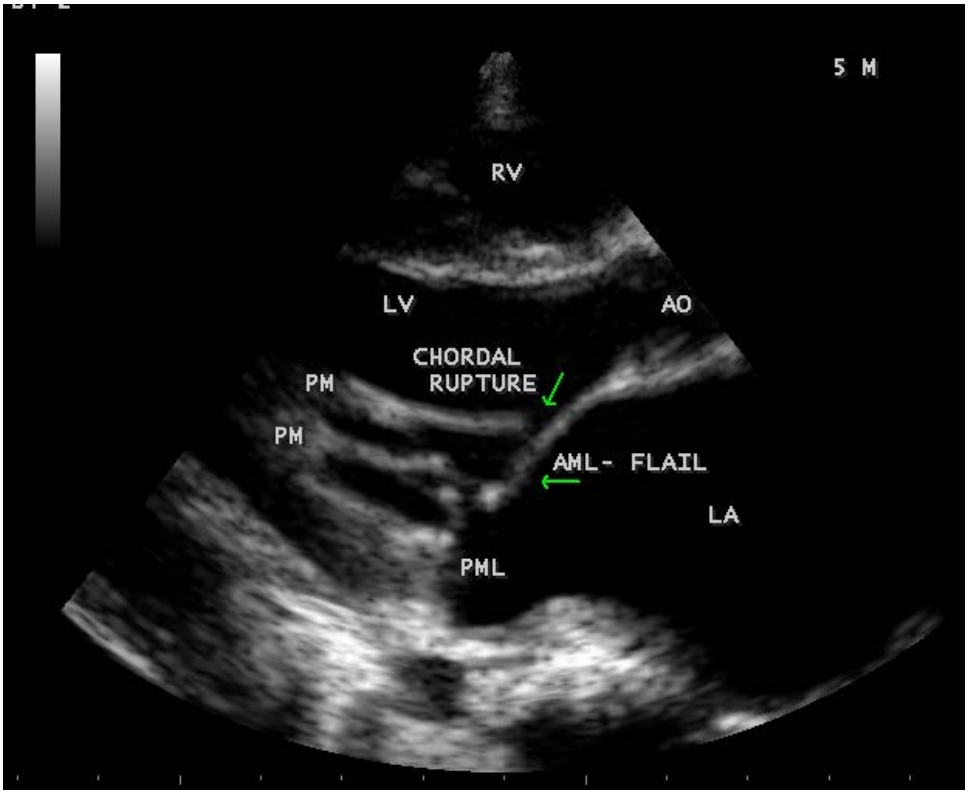


Figure 40. Chordal rupture and "flail" AML in the 5-year-old boy.

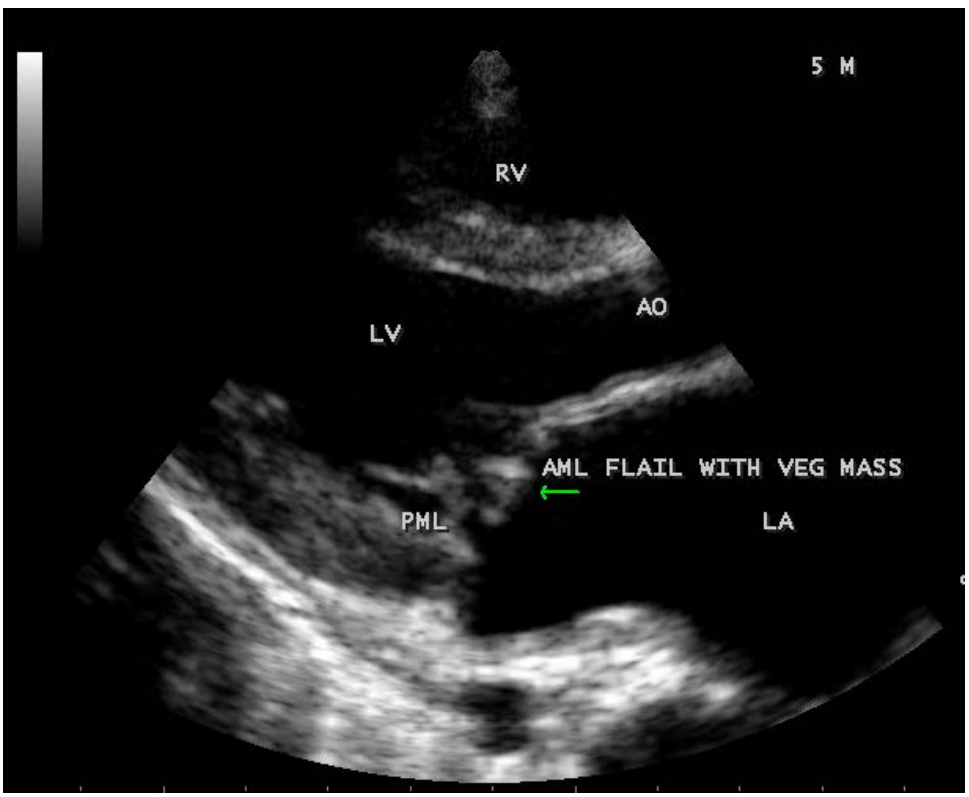


Figure 41. Vegetation mass attached to the flail AML—prolapsing into LA.

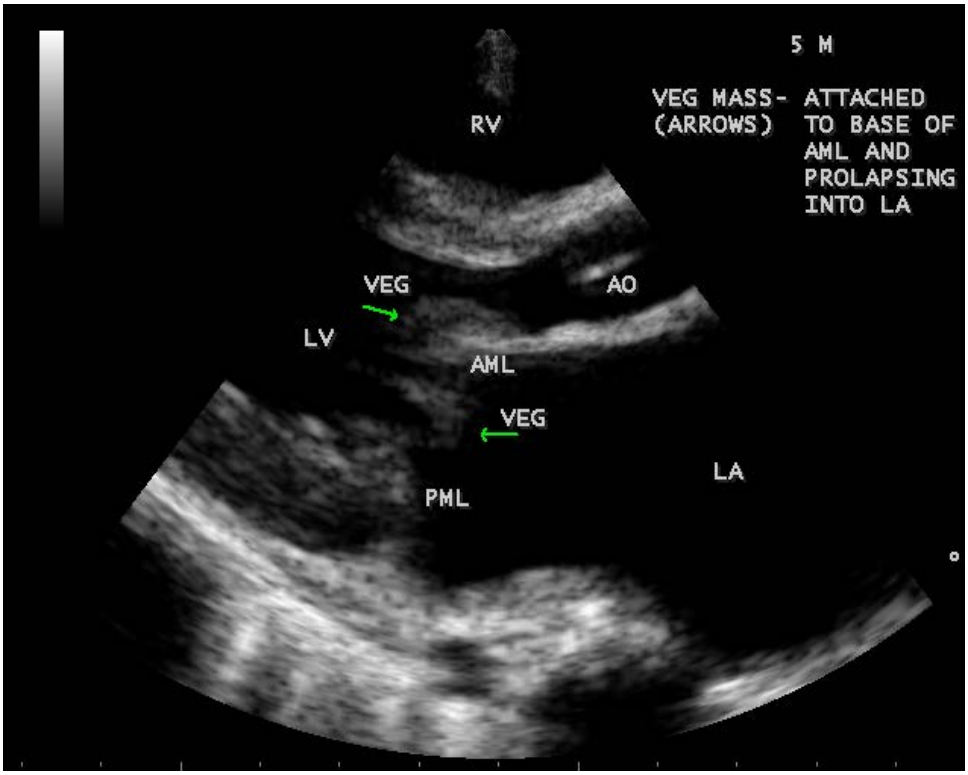


Figure 42. Vegetation mass attached to the base of AML in the 5-year-old boy.

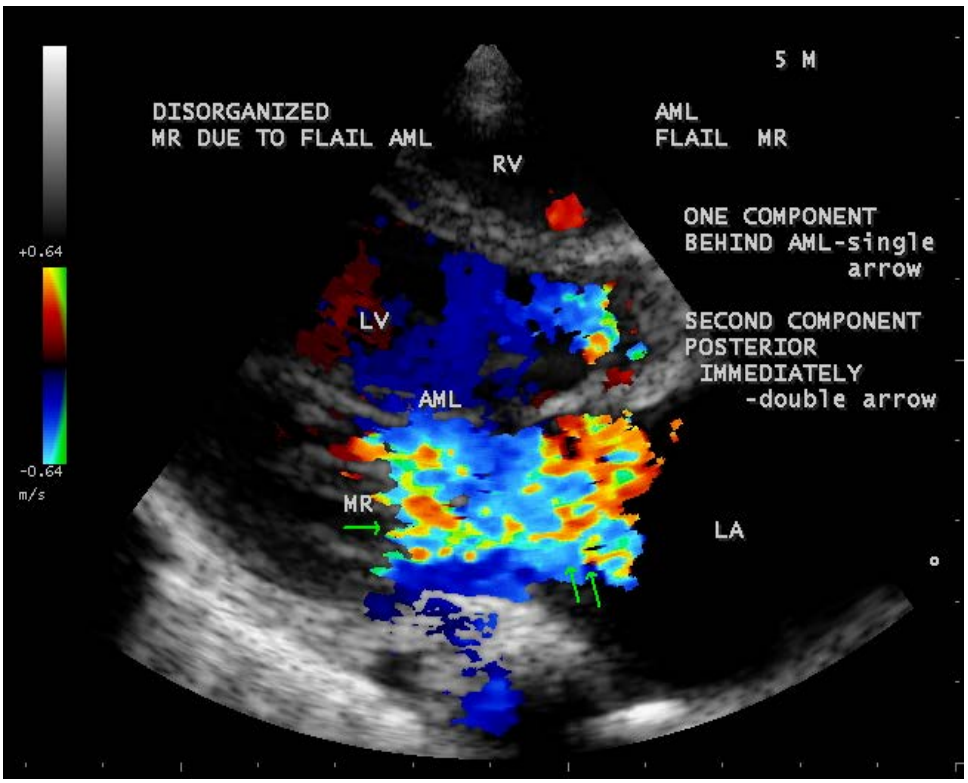


Figure 43. Chordal rupture producing severe disorganized MR jet as one component behind AML and the second component immediately posterior due to flail AML in the 5-year-old boy.

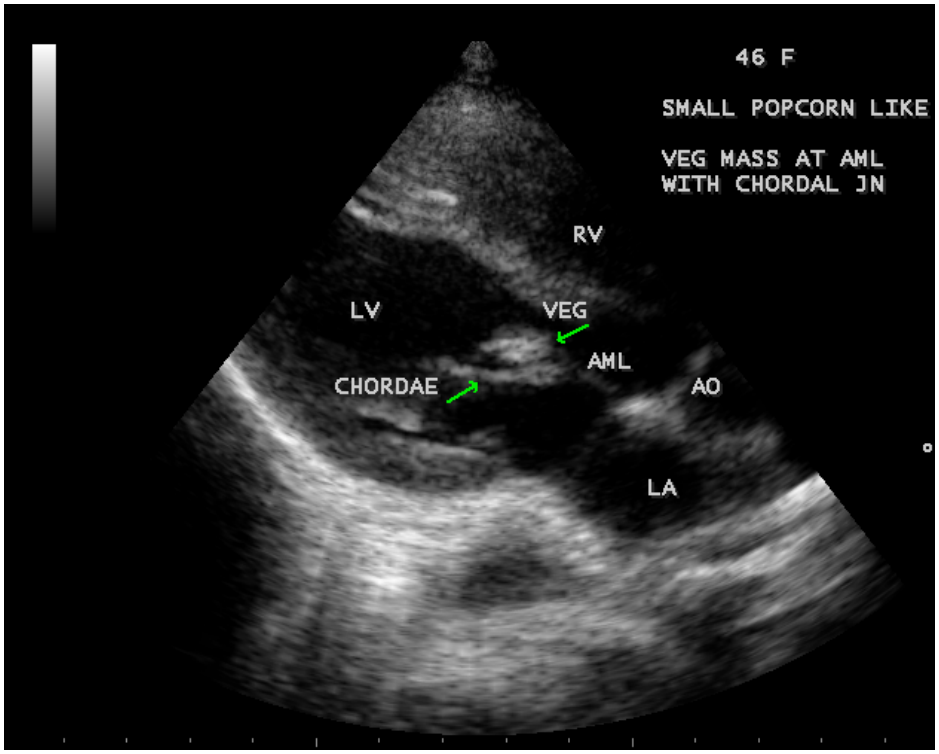


Figure 44. A "popcorn" like small vegetation seen at the junction of AML and chordal attachment in a 46-year-old febrile female.

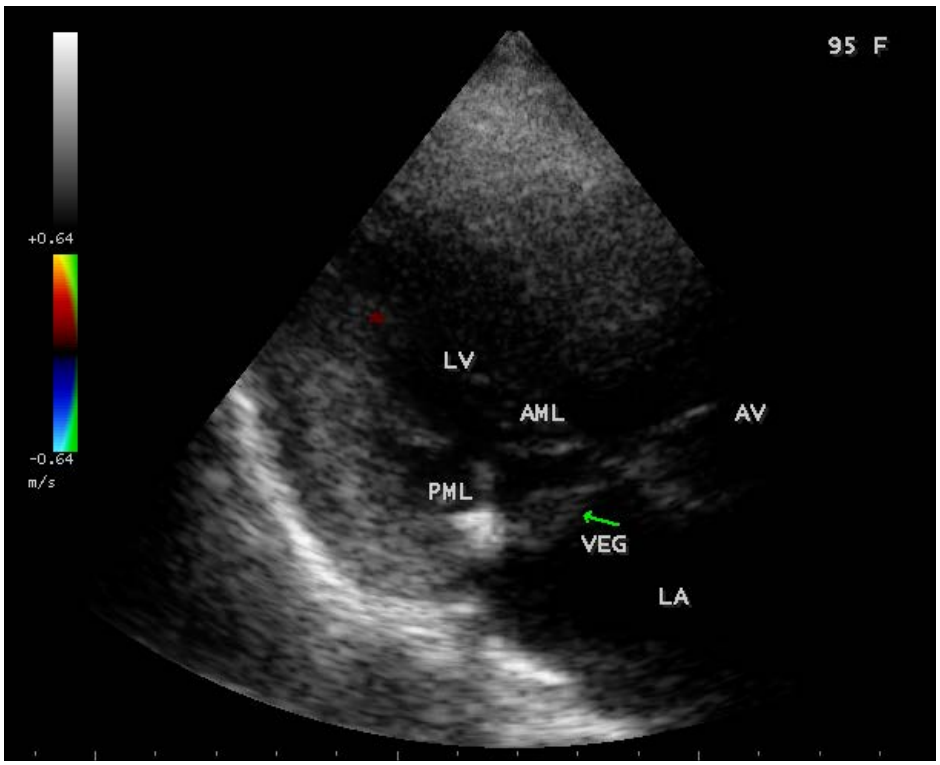


Figure 45. A sessile vegetation attached to PML (posterior mitral leaflet) in a 95-year-old asymptomatic female—parasternal long axis view.

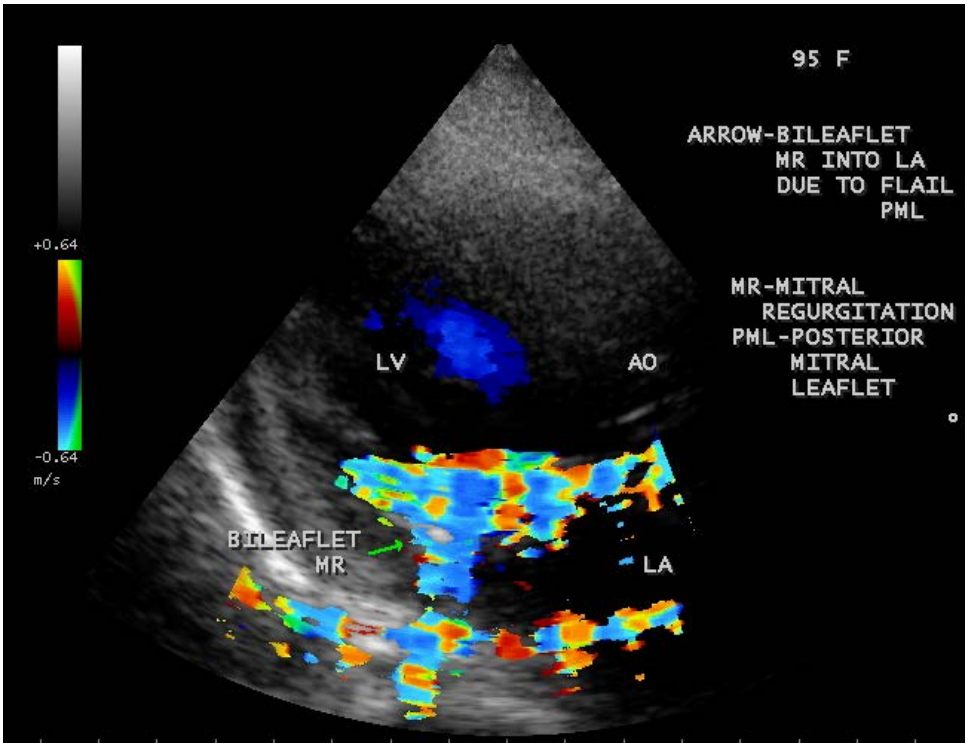


Figure 46. A sessile vegetation in PML-producing "bileaflet MR" in a 95-year-old asymptomatic female (mitral regurgitation)—parasternal long axis view.

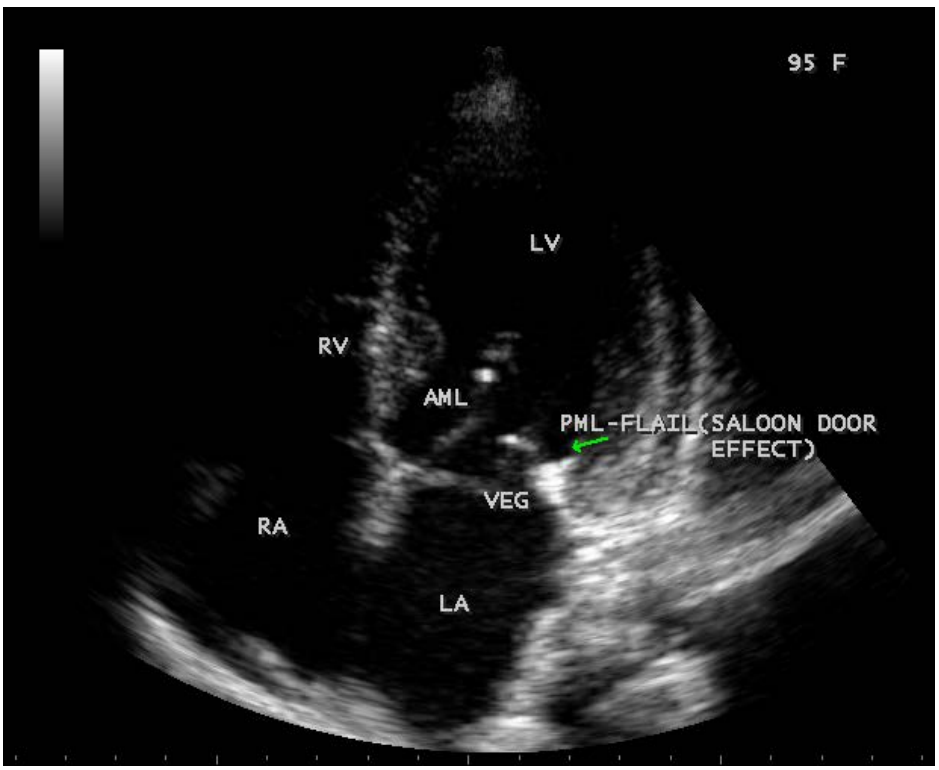


Figure 47. A sessile vegetation attached to PML—leading to chordal rupture and flail PML with "saloon door effect" in a 95-year-old asymptomatic female—apical four chamber view.

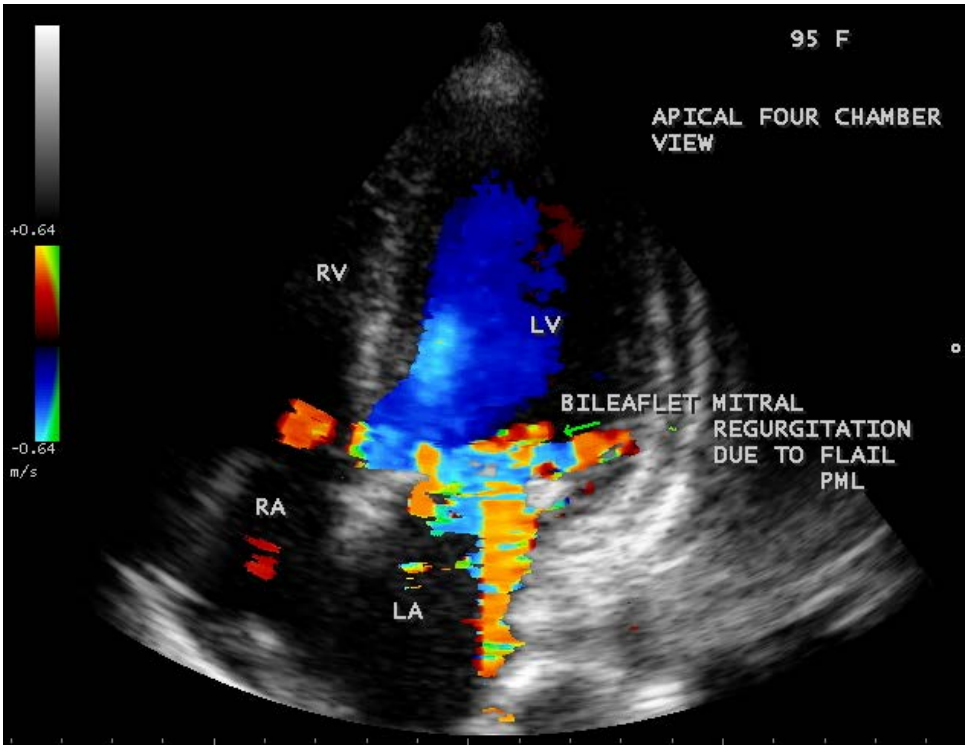


Figure 48. A sessile vegetation attached to PML-producing "bileaflet MR" in apical four chamber view in a 95-year-old asymptomatic female.

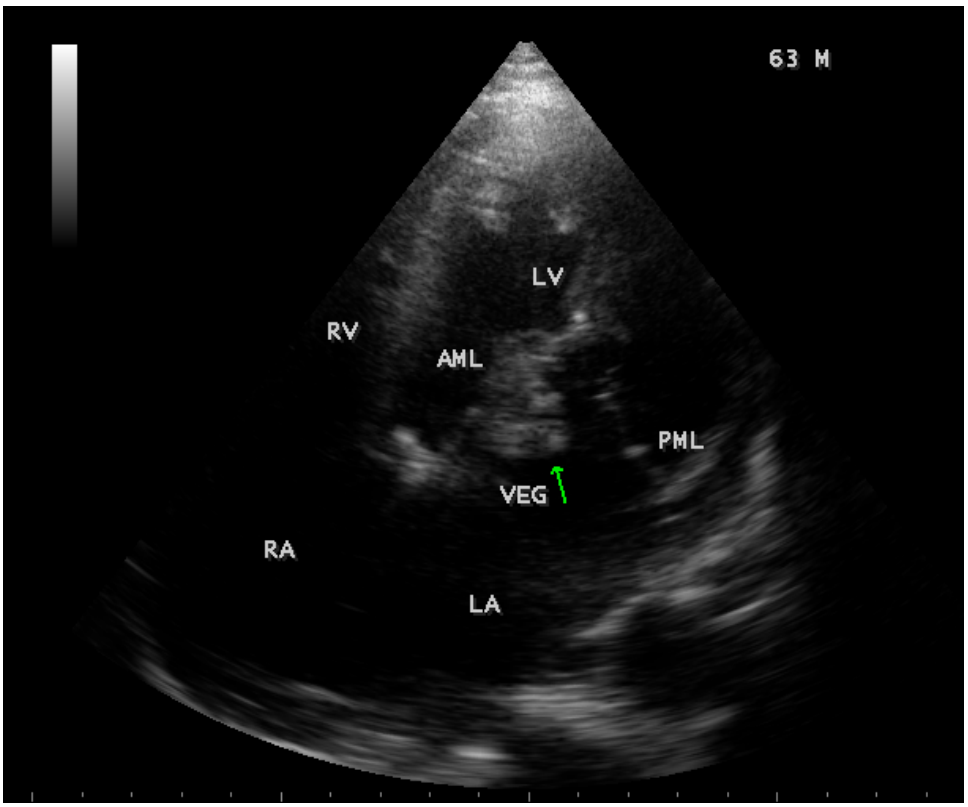


Figure 49. "Sessile" vegetation attached to AML in a 63-year-old male ([33], Figure 13.3A).

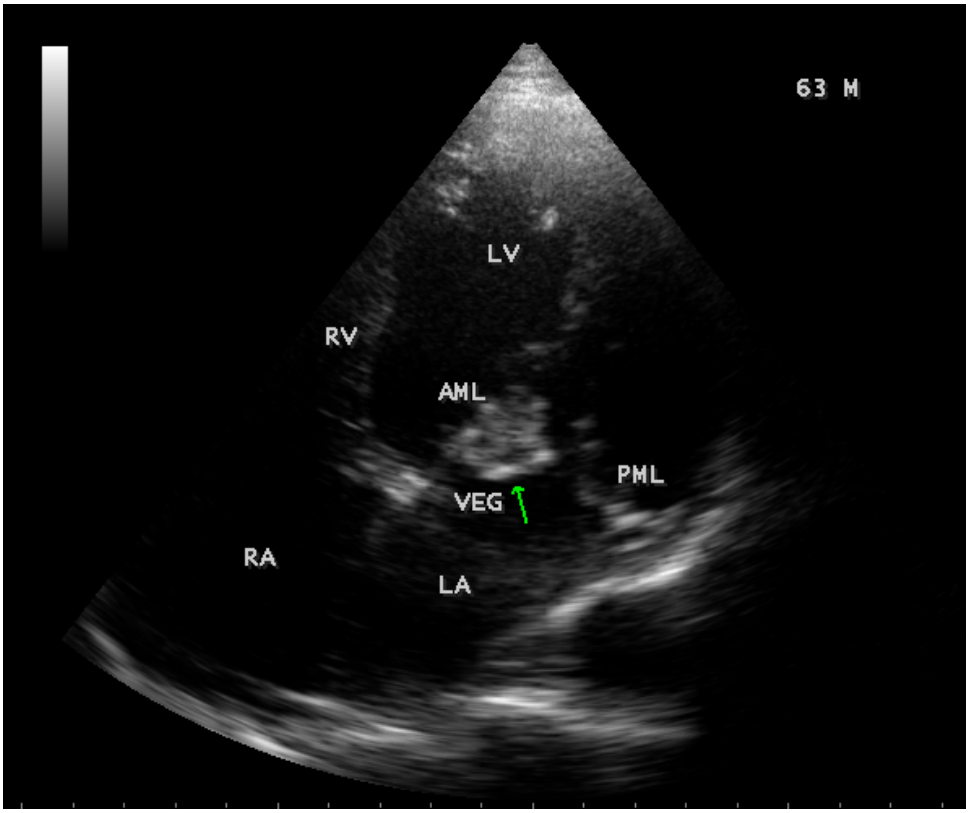


Figure 50. "Sessile" vegetation showing calcification in a 63-year-old male.

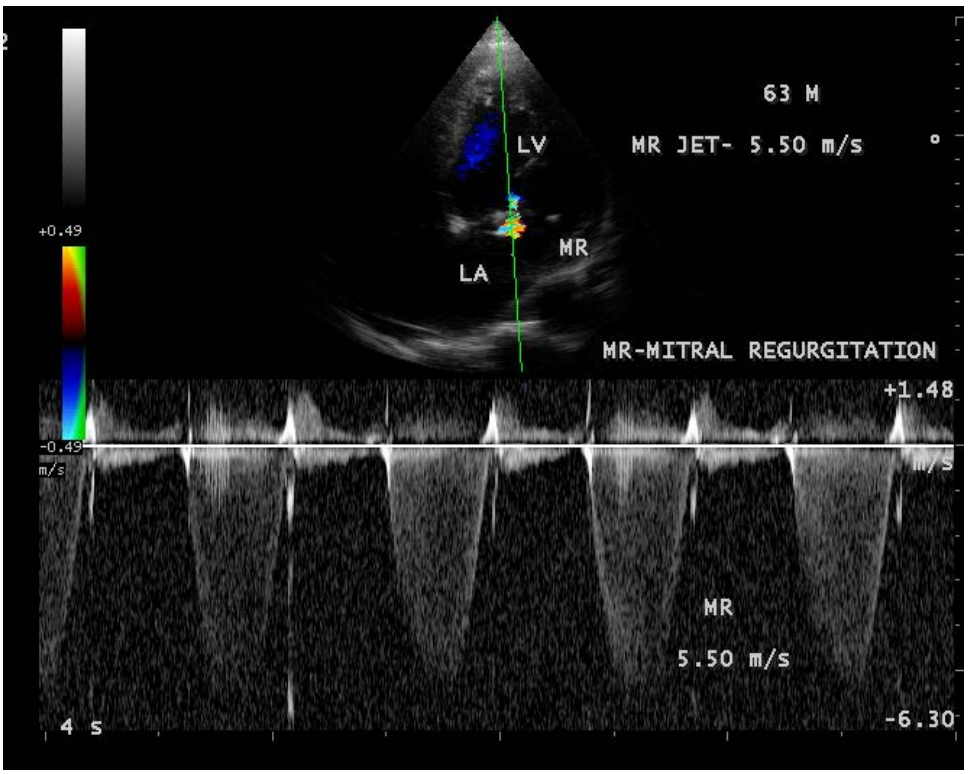


Figure 51. "Sessile" vegetation causing mitral regurgitation in a 63-year-old male.

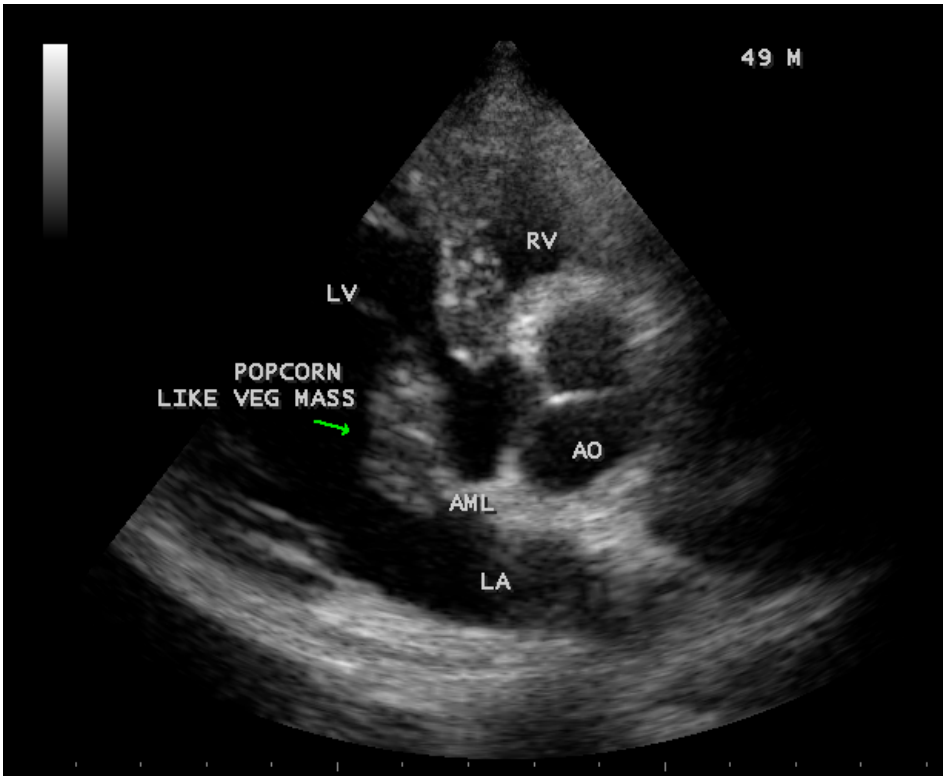


Figure 52. A "popcorn" like "giant" vegetation attached to anterior mitral leaflet (AML) in a 49-year-old febrile male.

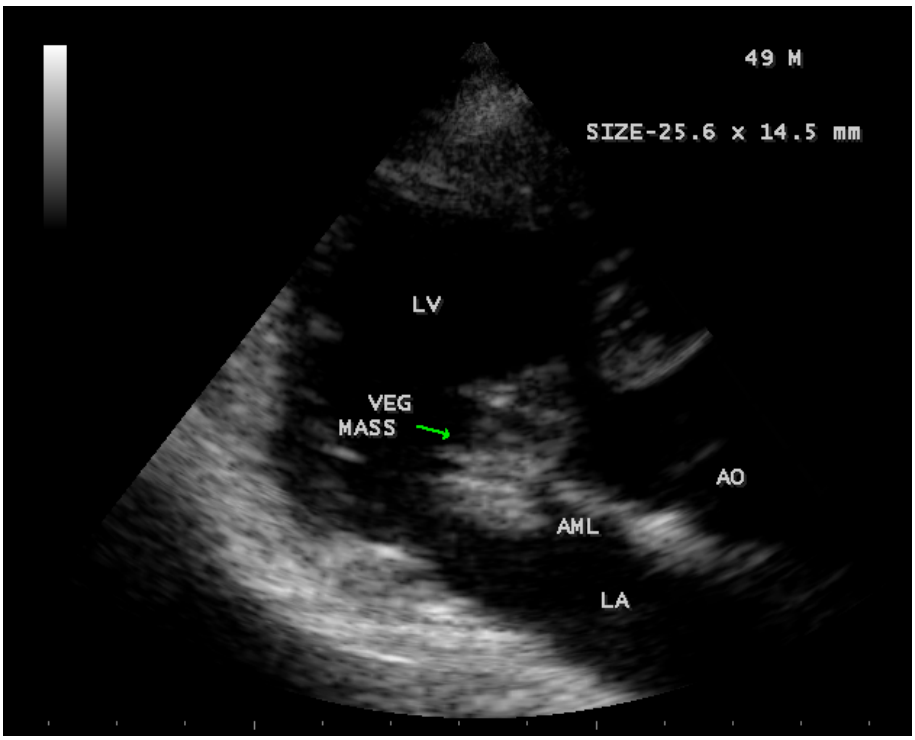


Figure 53. A "popcorn" like vegetation—seen as an active giant vegetation at the tip of AML in a 49-year-old febrile male.

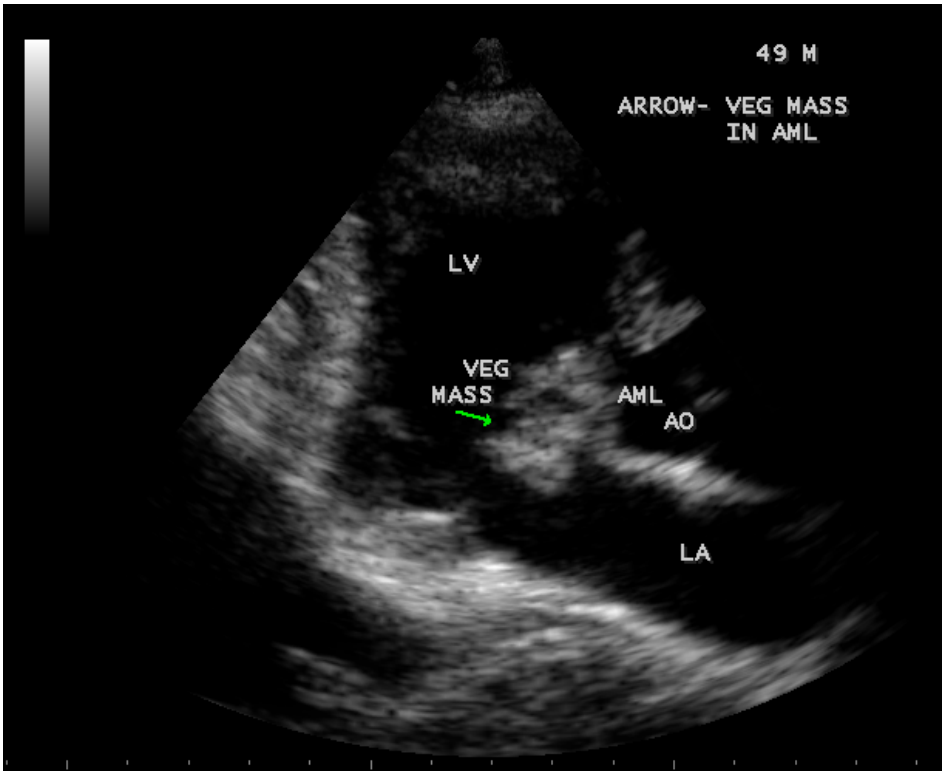


Figure 54. A "popcorn" like vegetation—seen as a calcified mass at the tip of AML in a 49-year-old febrile male.

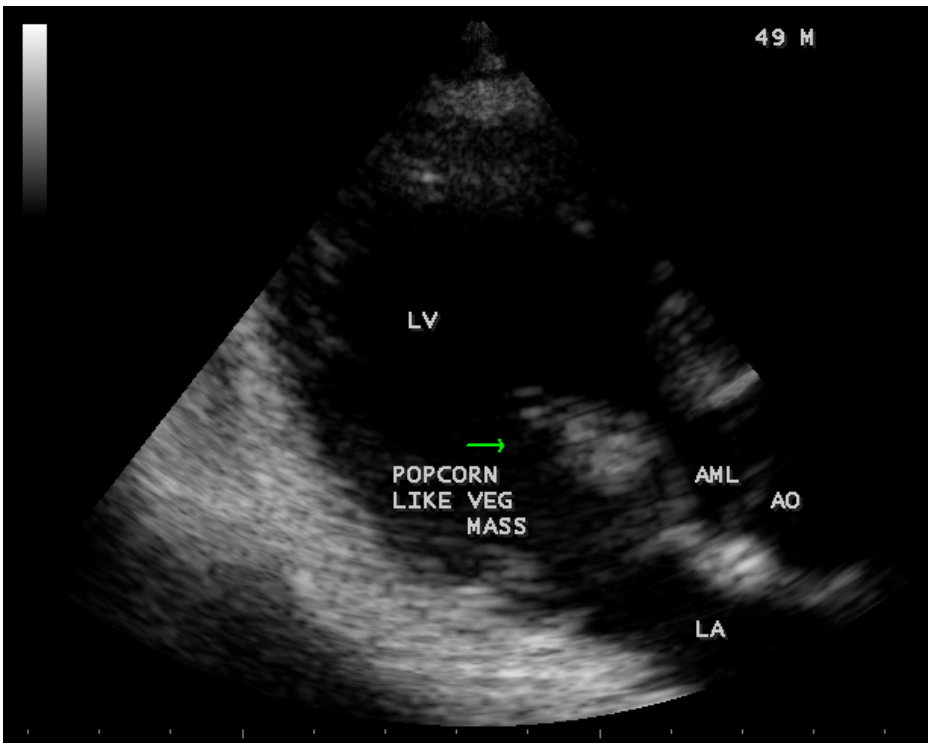


Figure 55. A "popcorn" like vegetation-prolapsing into LV along with the anterior mitral leaflet in a 49-year-old febrile male.

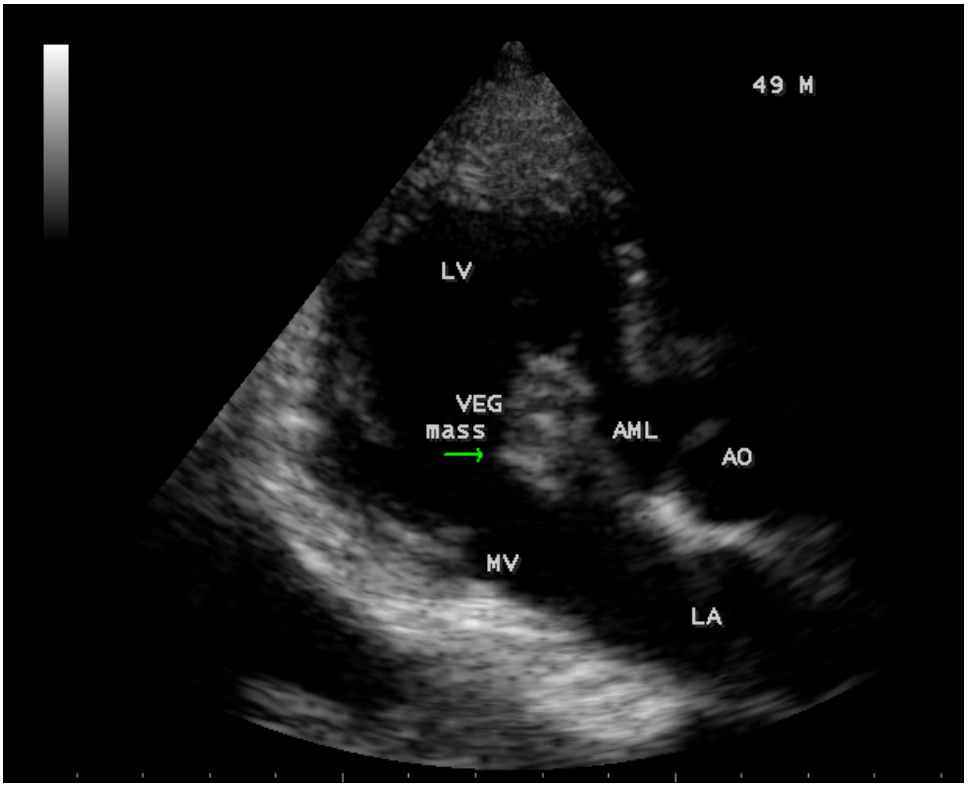
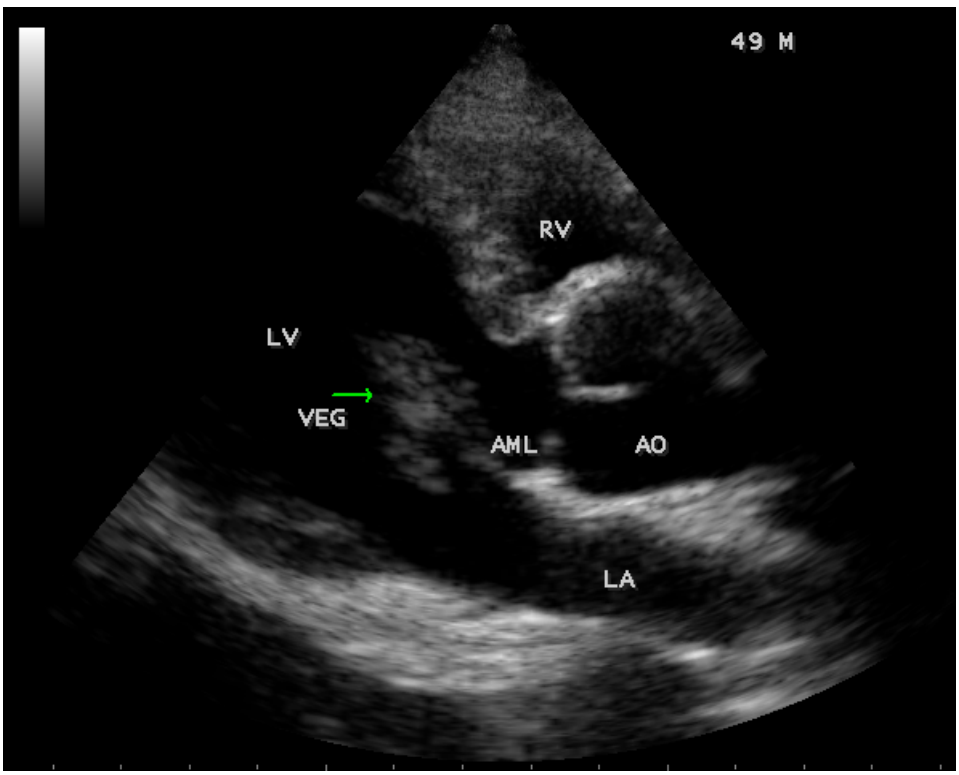
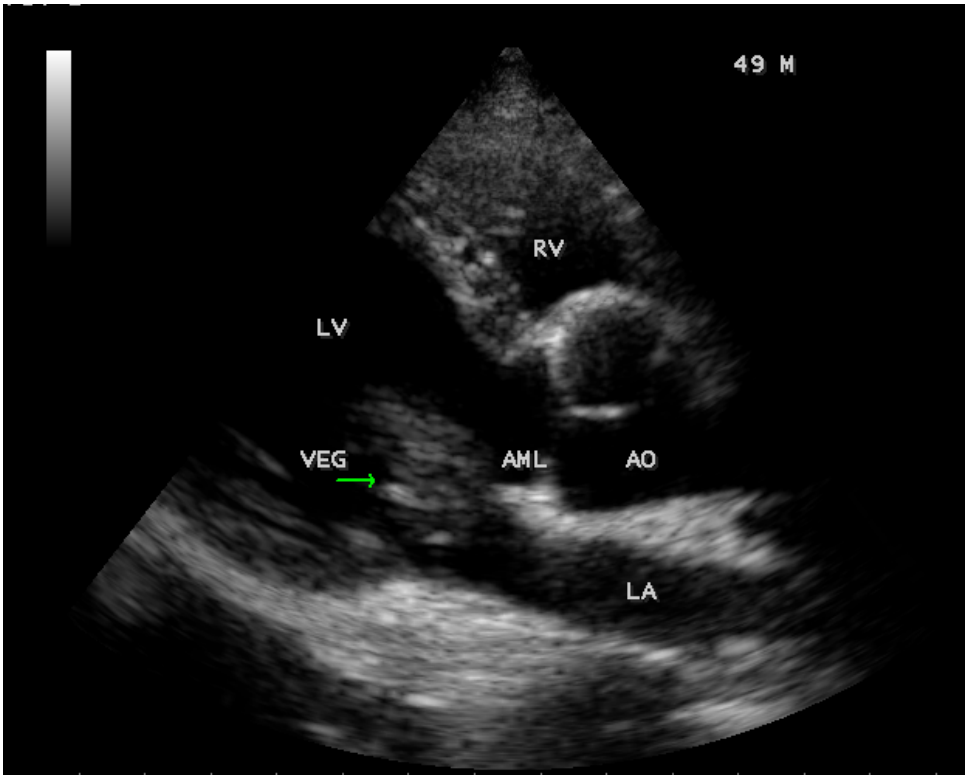


Figure 56. A "popcorn" like vegetation mass attached to the tip of AML in a 49-year-old febrile male.



(a)



(b)

Figure 57. (a) A "popcorn" like vegetation mass into the LV cavity in 49-year-old febrile male; (b) A "popcorn" like vegetation mass in AML at mitral orifice in a 49-year-old febrile male.

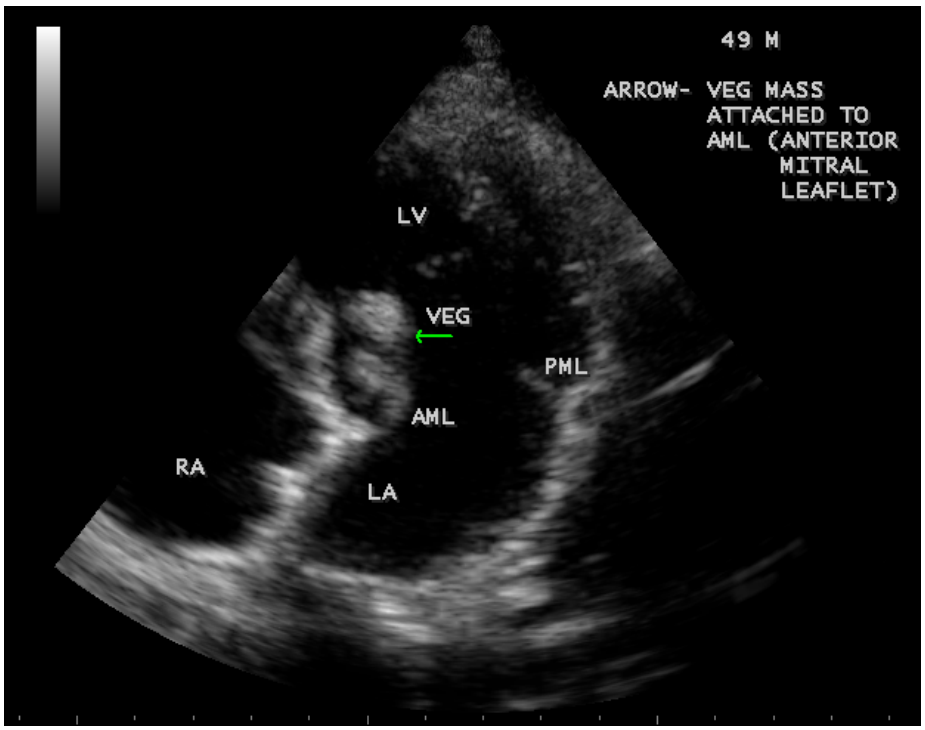


Figure 58. The vegetation is attached to AML-apical four chamber view in a 49-year-old febrile male.

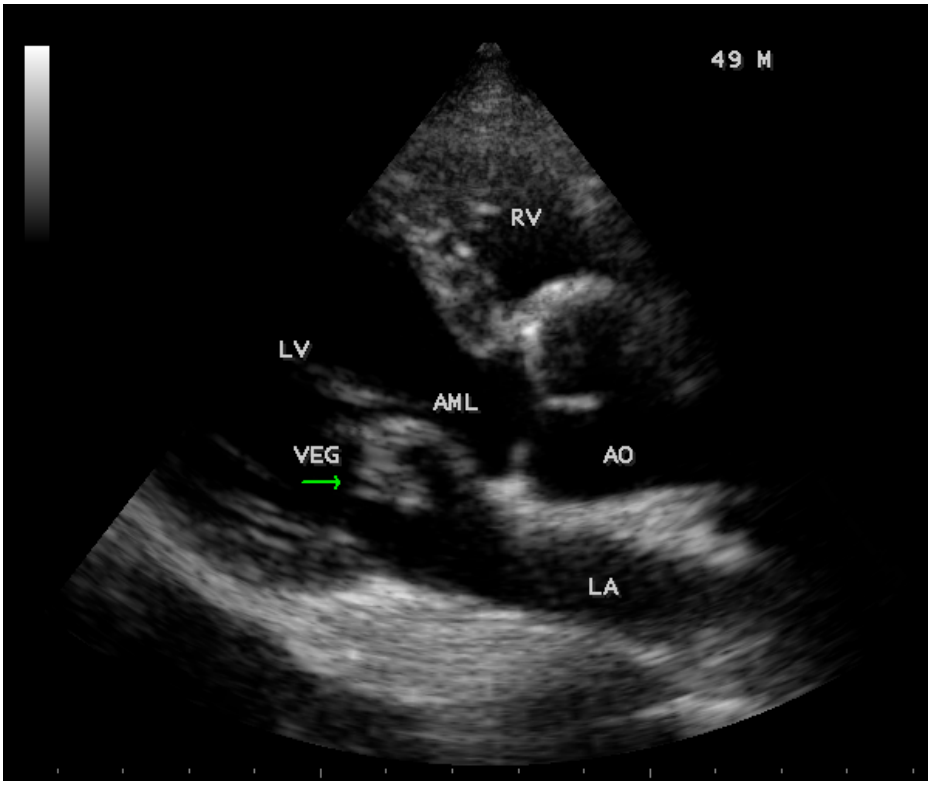


Figure 59. The vegetation mass, attached to AML (anterior mitral leaflet) seen as partially calcified mass (arrow) near the mitral orifice in a 49-year-old febrile male.

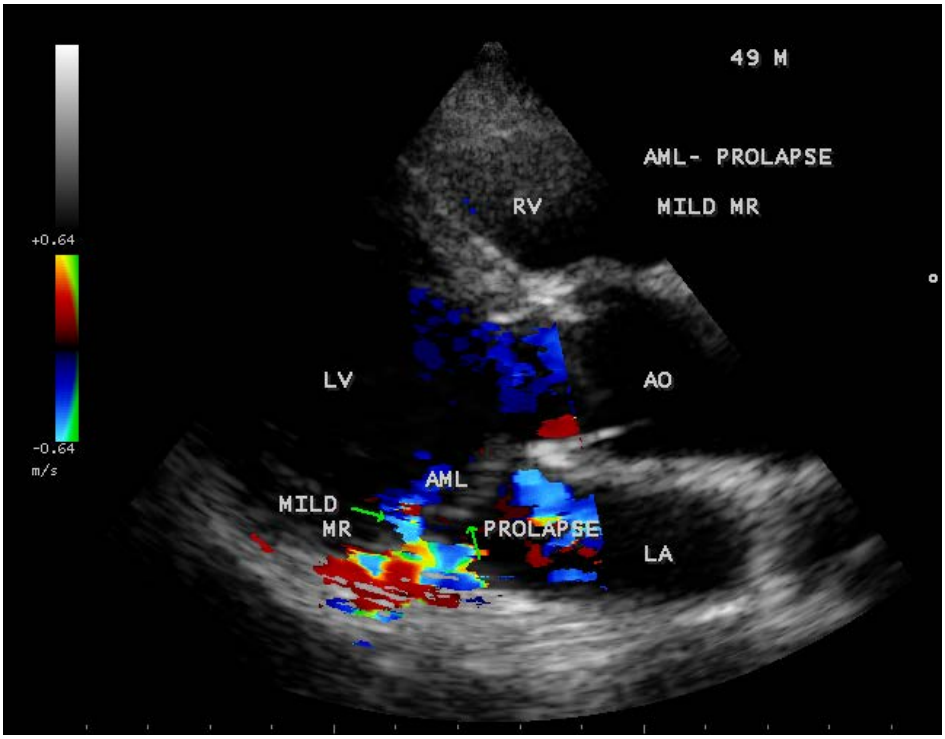


Figure 60. The AML (anterior mitral leaflet)—showing "prolapsed" (vertical arrow) with mild mitral regurgitation (MR) (left horizontal arrow) in a 49-year-old febrile male.

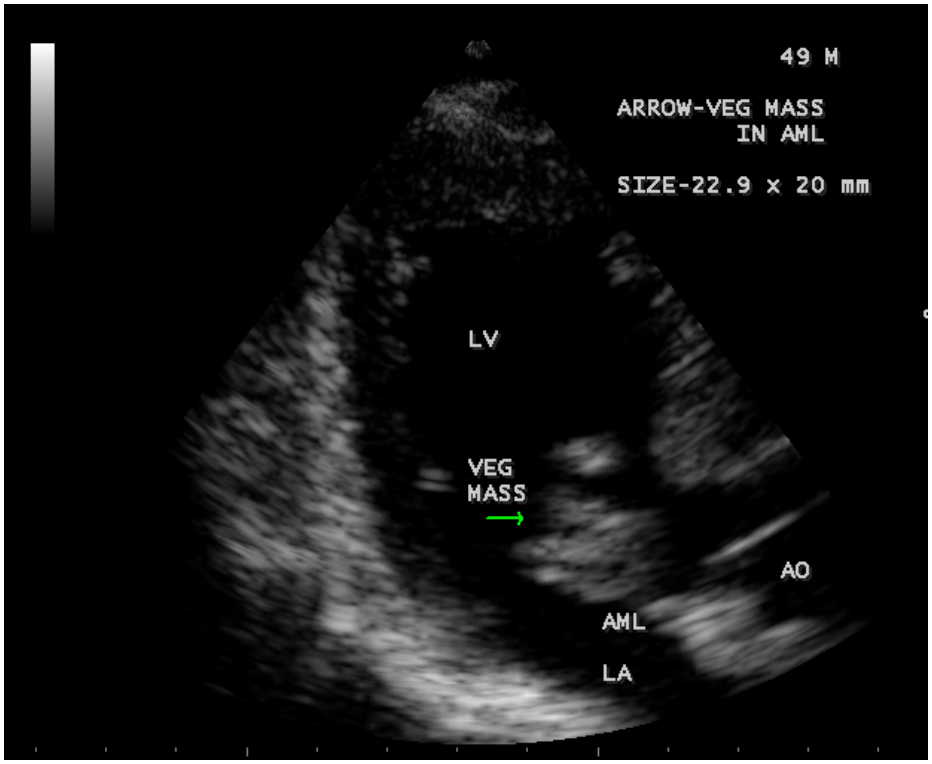


Figure 61. A "giant" vegetation attached to AML (anterior mitral leaflet) seen near the aortic orifice (LV outflow tract) in a 49-year-old febrile male.

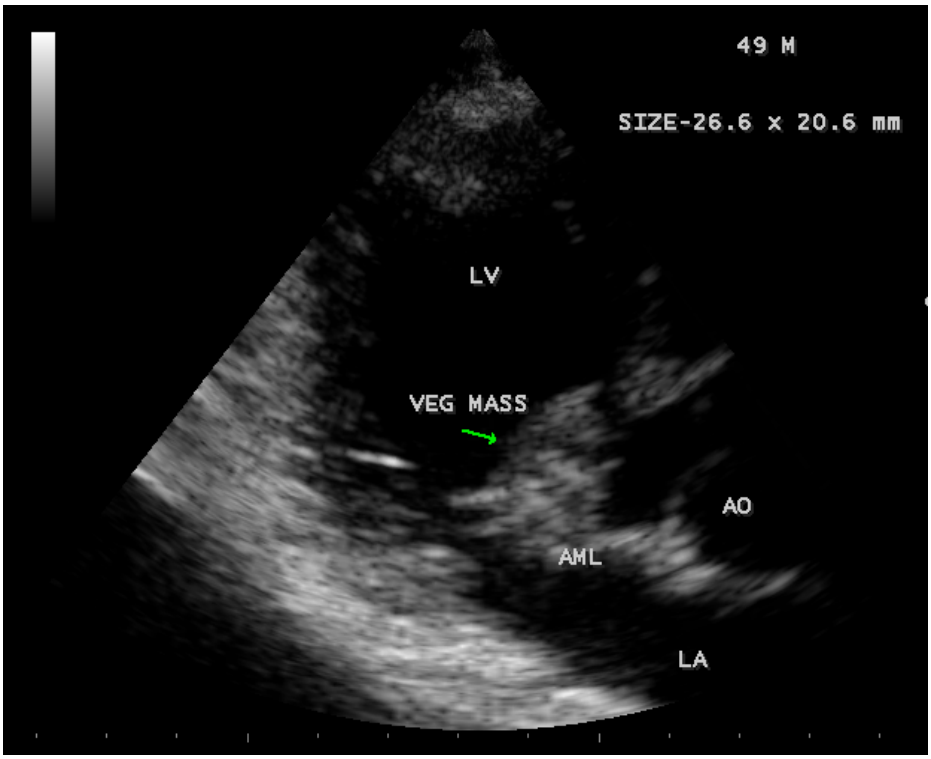


Figure 62. A "giant" vegetation attached to AML (anterior mitral leaflet) seen as moving towards aortic orifice in a 49-year-old febrile male.

4. Conclusion

A giant "popcorn" like vegetation attached to the anterior mitral leaflet and presented with various shapes in a 10-year-old female child was described by Transthoracic 2D echocardiography imaging. The child had underlying rheumatic involvement of the mitral valve and the infective endocarditis, causing chordal rupture leading to flail anterior mitral leaflet with severe mitral regurgitation. The vegetation functionally obstructs the mitral orifice and results in "ping-pong" mitral stenosis due to mass effect. The child remained asymptomatic without any embolic episodes and heart failure symptoms on follow up of two years. The "popcorn" like vegetations attached to AML (anterior mitral leaflet) in a 5-year-old boy and in a 49-year-old male were detected. The "sessile" vegetations attached to AML in a 63-year-old male with severe mitral regurgitation and attached to PML (posterior mitral leaflet) in a 95-year-old asymptomatic female with bileaflet severe mitral regurgitation were also found by Transthoracic 2D echocardiographic imaging at this region of Thoothukudi in India.

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Tuberculous Spondylitis: Clinical Features of 36 Patients

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Abstract

We report 36 cases of spinal tuberculosis who were evaluated at the Internal Medicine Department of Istanbul University between January 1990 and March 2016. Twelve cases were accompanied by active pulmonary tuberculosis while ten patients had a previous history of tuberculosis. Eight patients had diabetes mellitus; six patients were on chronic steroid treatment with a mean dose of 24 mg/day while two patients used azathioprine and methotrexate. The dominant symptom was back pain that was present in 64% of the subjects followed by low grade fever (42%), and malaise (38%). Lytic and destructive lesions were noted in various vertebrae in all of the cases while four patients had spinal compression, and two patients had iliopsoas abscess. The preliminary diagnosis was myeloproliferative disease with vertebral metastasis in eight patients. Tuberculin test was over 15 mm in 20 patients (58.8%) while ERS and C-reactive protein were highly elevated in 78%, and 84% of the patients. Diagnosis of tuberculosis was confirmed by culture of aspirated material from intervertebral disc space, collection under CT guidance, sputum or bronchial lavage, and by retrospective anti-tuberculous treatment response. MRI revealed compatible findings with spinal tuberculosis in 30 (80%) patients. In endemic countries, tuberculous spondilitis should be considered in immunosuppressed patients with back pain. Current or past tuberculosis infection is not a reliable indicator for Pott's disease in these patients. Laboratory findings were not usually useful to support the diagnosis. The low sensitivity of the tuberculin test may lead to an erronous diagnosis. Sensitivity of vertebral radiography and CT was low. MRI was the most useful radiologic investigation for the diagnosis of spinal tuberculosis. Tuberculosis of the spine is a diagnostic impasse notably in immunodeficient patients for the clinician.

Keywords

Tuberculosis, Spinal, Vertebrae, M. Tuberculosis, Pott's Disease

1. Introduction

Pott's disease, also known as tuberculous spondylitis, is one of the oldest demonstrated diseases of humankind. Bone and soft-tissue tuberculosis accounts for approximately 10% - 15% of the extrapulmonary tuberculosis cases and between 1% and 2% of the total cases. Tuberculous spondylitis is the most common form of musculoskeletal tuberculosis, comprising 40% - 50% of all patients [1] [2] [3] [4]. Spinal tuberculosis may be a diagnostic and a therapeutic challenge for the clinician. Firstly, the symptoms and the laboratory findings are nonspecific that may lead to a significant delay in diagnosis. Secondly, neural involvement occurs in approximately half of the patients causing irreversible damage if not promptly and adequately treated [2] [5]. Immunosuppression may be a significant risk factor for tuberculosis. The mechanism for increased susceptibility to infection in these patients is the alteration of chemotactic, phagositic, and bactericidal activity of the polymorphonuclear leukocytes. However, the role of immunosuppression for the development and outcome of spinal tuberculosis has not been determined.

Spinal tuberculosis which occurs in approximately in one percent of the patients with tuberculosis is still associated with significant morbidity and mortality [1]. In this retrospective study, we evaluated the clinical and diagnostic features of thirty-six patients with spinal tuberculosis. Diagnostic difficulties encountered for the identification of spinal tuberculosis and effect of immunosuppression on the clinical aspects of spinal tuberculosis were also assessed.

2. Patients and Methods

Our study group consisted of 36 Caucasian patients who were diagnosed with spinal tuberculosis at the Internal Medicine Department of Cerrahpasa Medical Faculty between January 1990 and June 2016. Patient data regarding the clinical features, laboratory, radiologic, and therapeutic findings were obtained from files of the patients seen at the Internal Medicine and Neurosurgery Departments for thoracolumbar symptoms. All patients had complete blood count, serum biochemistry, urine analysis, ESR, CRP, tuberculine test, chest X-ray, ECG, computed tomography, and magnetic resonance imaging. Sputum culture was done in 20, FOB with bronchial lavage culture was carried out in 26, and tissue culture was performed in 30 patients.

Patient characteristics are shown in Table 1. All patients received anti-tuberculous treatment. The patients were followed-up for at least a minimum of six years as out patients after treatment.

Table 1. Characteristics of the patients.

	Absent n (%)	Present n (%)
History of pulmonary tuberculosis	26 (72%)	10 (28%)
Active pulmonary tuberculosis	24 (66.6%)	12 (33.4%)
Tuberculosis vaccination	4 (11%)	32 (89%)
İmmunosuppression	20 (55.6%)	22 (44.4%)
Symptoms	13 (36%)	23 (64%)

3. Results

Twenty two of the patients (61.7%) were male and the mean age was 46.2 ± 14.8 years. Four patients (11.4%) had cervical, three (7%) had both cervical and thoracal, eighteen (52.9%) had thoracal, eight (24%) had lumbar, and three (8%) had sacral involvement. Twelve (33.3%) subjects had a prior history of pulmonary tuberculosis. Eight patients (24%) had diabetes mellitus. The mean duration of diabetes was 9.4 ± 3.2 years. Six (16%) patients were using steroid treatment at the time of diagnosis for an average of 4 months. Two (5%) patients used azathioprine and methotrexate. The mean steroid dose was 24.8 ± 14.6 mg methylprednisolone (minimum dose: 10 mg and maximum dose 32 mg) per day. A total of 16 patients were under immunosuppression during the sutudy. The most frequent (64%) symptom was back pain. Fever was present in 42%, malaise in 38%, night sweats in 28%, weight loss in 24% of the patients while 36% were asymptomatic.

Mean ERS and CRP were 86.2 ± 24.8 mm/h and 72.4 ± 20.6 mg/L. The mean tuberculin induration was 14.6 ± 5.4 mm while it was negative in 16 (44.4%) patients. Radiologic evidence of current lung tuberculosis was observed in 12 (33.3%) patients while fibrotic or calcific parenchymal radiologic lesions associated with previous infection were detected in 10 (27.7%) subjects. Plain radiography revealed features of spinal tuberculosis in 14 (38.8%) patients. Sputum culture was positive only in one patient while bronchial lavage culture grew m. tuberculosis in 8 (22.2%) patients. MRI was the most useful diagnostic tool that revealed pathologic findings of spinal tuberculosis in 72.2% and CT showed diagnostic lesions in 33.3% of the patients.

Two patients (5.8%) had iliopsoas abcess. Computed tomography (CT) guided needle aspiration biopsy was performed in 30 patients (83.3%) and 9 of these (30.0%) had a histopathological diagnosis while 21 (70.0%) were culture positive. Smear positivity of the needle aspiration material for acid-fast bacilli was obtained in 32% of cases while culture positivity was present in 72% of our cases. Histologic studies confirmed the diagnosis of spinal tuberculosis in 64% of the patients. The most common cytological finding was epithelioid cell granulomas observed in 82% of the patients. Lymphocytic infiltration was noted in 78% and granular necrotic background was present in 70%, and scattered multinucleated and Langhans' giant cells were seen in 62% of the cases. CT guided needle aspiration biopsy provided the final diagnosis in 86% of the patients when both microbiology and pathology results were assessed together. In the remaining 8 (22.2%) patients with clinically and radiologically suspected tuberculosis, the diagnosis was confirmed with response to antituberculous treatment. MRI was performed in 30 (83.3%) patients and 80% of these cases had compatible MRI findings with vertebral tuberculosis.

All patients received antituberculous treatment with at least four drugs for a minimum of twelve months. The antitubeculous treatment regimen consisted of SM 1.0 g/day, and PRZ 20 mg/kg for two months with INH 5 mg/kg, RIF 10 mg/kg, and ETM 25 mg/kg. The mean duration of treatment was between 12 and 18 months. The clinical and laboratory features of the patients are shown in Table 2. Two patients were immobilized for two months and received concomitant rehabilitation therapy. All patients improved without a neurological deficit or complication.

Table 2. Clinical features of the patients.

	Absent n (%)	Present n (%)
Positive tuberculine test	16 (44.4%)	20 (55.6%)
Radiologic features of previous pulmonary tuberculosis	26 (72. 2%)	10 (27.8%)
Radiologic features of current pulmonary tuberculosis	25 (69.4%)	11 (30.6%)
Positive vertebral radiography findings	24 (66.6%)	12 (33.4%)
Positive spinal CT findings	14 (38.8%)	22 (61.2%)
Positive spinal MR findings	6 (20%)	20 (80.0%)
Sputum culture (+)*	18 (90.0%)	2 (10.0%)
Bronchial lavage culture (+)**	22 (84.6%)	4 (15.4%)
Tissue culture (+)***	9 (30.0%)	21 (70.0%)
Tissue histopathology (+)***	10 (33.3%)	20 (66.7%)

Performed in: *20 patients, **26 patients, ***30 patients.

4. Discussion

Tuberculosis of the spine is an uncommon form tuberculosis occuring in fewer than 1% of the patients with tuberculosis. Systemic symptoms and clinical findings usually arise late in the course of infection after significant spinal destruction has occured [1] [2] [3] [4]. Therefore, the diagnosis is a challenge for the clinician. In our study, we found that neither patient history, nor physical examination, or the laboratory findings were specific and sensitive for the diagnosis. We have observed that only the radiologic findings pointed out to the final diagnosis. But on the other hand, the presence of similar radiologic findings in malignant, metastatic, or fungal spinal involvement was the vulnerable point for plain radiography and CT. MRI examination was the most effective imaging study for spinal tuberculosis. The final diagnosis was only confirmed by the isolation of acid-fast-bacilli (AFB) in smear or culture from the lesion site.

Constitutional symptoms fever, weight loss, and night sweats were present in approximately 40% of the cases. Local back pain was the earliest and the most common symptom of spinal tuberculosis. Back pain occurred in 64% of the patients. Chronic back pain as the only symptom is observed in 61% of cases of spinal tuberculosis while the patient symptom profile was compatible with the findings of Pertuiset, Le Page, and Cormican *et al.* [3] [6] [7] [8]. Symptoms or history were not reliable or helpful for the immediate diagnosis of spinal tuberculosis in our study. Systemic symptoms and back pain were usually manifestations of advanced disease. Lumbar pain revealed mechanical destruction. Diagnosis of spinal involvement was not suspected in patients without tuberculosis history, evidence of radiologic findings of previous, or current pulmonary tuberculosis.

Erythrocyte sedimentation rate (ESR) is generally raised many folds and may be markedly elevated over 100 mm/hr in the majority of patients with spinal tuberculosis [1] [3] [7]. Of the laboratory findings ERS and CRP were the most useful parameters in our study showing current inflammation. Although ERS and CRP were helpful, they were not sensitive or specific enough for accurate diagnosis. Tuberculine test results are

positive in 84% - 95% of patients with Pott's disease who are not infected with HIV [3] [6] [7]. PPD was only positive in 55.6% of our patients. Tuberculin test was not highly useful because its diagnostic accuracy was low in our patient group which is probably related to the high incidence of immunodeficient patients. The laboratory results were not reliable for pointing out to spinal tuberculosis.

The progression of spinal tuberculosis is usually slow and insidious with an average disease duration ranging from 4 to 11 months. Patients are admitted only when there is severe pain, marked deformity, or neurological symptoms [9] [10] [11]. In these patients, vertebral radiography still remains the cornerstone of spinal imaging. It often provides enough information for diagnosis and treatment of spinal tuberculosis. The plain radiograph may describe changes consistent with spine tuberculosis in up to 99% of the cases. The characteristic radiographic findings include rarefaction of the vertebral end plates, loss of disk height, osseous destruction, new-bone formation and soft-tissue abscess [9] [12] [13] [14]. Plain radiography and CT scan revealed destructive or inflammatory changes that occured late in the course of the disease. The main disadvantage of plain radiograph or CT was that they generally were normal in the early stages of the disease and only revealed manifestations of advanced spinal tuberculosis. Vertebral radiography with CT still remained the cornerstone of spinal imaging but it was not neither specific nor sensitive for early diagnosis. Using different pulse sequences, MRI revealed a better differentiation for soft tissue inflammatory and destructive lesions. MRI was efficient for demonstrating the features of spinal tuberculosis and appeared to be the most crucial step for the assessment of spinal tuberculosis that lead the clinician to final diagnosis. MRI was the most effective imaging study for demonstrating spinal tuberculosis. Chest X-ray and lung CT revealed revealed fibrotic or calcific lesions of pulmonary tuberculosis in a minority of patients. Current lesions of active pulmonary tuberculosis were also rare in our patients.

Spinal tuberculosis can present with atypical features resembling neoplastic or infectious lesions that necessitate the exclusion of such etiologies. The golden standart was CT guided needle aspiration biopsy which provided the final diagnosis in 86% of the patients. Smear positivity for acid-fast bacilli was low (32%) while culture positivity was obtained in 70% of our patients. Positive smear and culture results were lower compared to other studies [7] [9] [11] [12] [13] [15]. Histologic studies confirmed the diagnosis in approximately two thirds of our patients. As with respiratory tuberculosis, culture may not be the gold standard for diagnosing spinal tuberculosis because mycobacterial bacilli may not be readily detected from lung or extrapulmonary sites. Therefore, diagnosis of spinal tuberculosis must be made on ground of clinical manifestations and radiology when bacteriology and pathology are negative or equivocal.

Because microbiologic studies may remain negative, histopathologic examination can be significant. In smear and culture negative patients, presence of granulomatous inflammation and caseification necrosis in the biopsy specimes was compatible with the final diagnosis which was confirmed with a positive antituberculous treatment response, retrospectively. Gross pathologic findings including exudative granulation tissue with interspersed abscesses was crucial for diagnosis. Coalescence of abscesses resulting in

areas of caseating necrosis strongly supported the diagnosis of tuberculosis. Histopathologic examination may be the final step in the diagnostic pathway of spinal tuberculosis cases even it is not diagnostic on its own. In patients with compatible pathologic findings, retrospective evaluation of antituberculous treatment response after neoplastic and other infectious etiologies have been excluded, may be the best diagnostic approach in equivocal cases of spinal tuberculosis.

The small sample size warrants a more comprehensive study to confirm these findings. Further research with more heterogenous patient features is needed to describe the clinical findings of spinal tuberculosis. The second limitation is the presence of advanced disease with fibrotic tissue changes, thereby obscuring a positive culture result in such patients. The high ratio of immunosuppressed patients may be considered as the third limitation because the defective immune system may have a negative role on patient symptoms, tuberculin test results, and even on radiologic findings thereby beclouding or delaying the final diagnosis. The fourth limitation may be the inadequacy for discriminating acute and chronic cases since the diagnosis is much more difficult clinically for chronic cases.

5. Conclusion

Spinal tuberculosis is a major diagnostic challenge for the clinican. Although history and current symptoms are important, they are not reliable for diagnosis, especially in the immunodeficient patients. Tuberculine test is not useful because of the high incidence of false negative results that may lead to erroneous or delayed diagnostic outcomes in states of immunosuppression. Other laboratory results are neither specific nor sensitive for diagnosis and only may indicate current inflammation. Chest X-ray or CT may reveal pathologic findings of old tuberculosis infection that may lead to diagnosis but they are equivocal for final diagnosis. Plain vertebral radiography and CT may be helpful as the initial non-invasive diagnostic work-up of patients but their sensitivity is low. MRI is the most efficient diagnostic tool for demonstrating the features of spinal tuberculosis and appears to be the most crucial step for the assessment of spinal tuberculosis that may strongly indicate the final diagnosis. Clinicians should bear in mind that spinal tuberculosis can present with atypical features resembling neoplastic or infectious lesions that necessitate the exclusion of such etiologies. The patients may present with symptoms that do not point out to spinal disease or may be totally asymptomatic. Pott's disease appears as a diagnostic dilemma especially in immunodeficient patients since neither the patient history, the symptoms, nor the laboratory findings are sensitive or specific.

Conflict of Interests

There are no conflicts of interest to declare.

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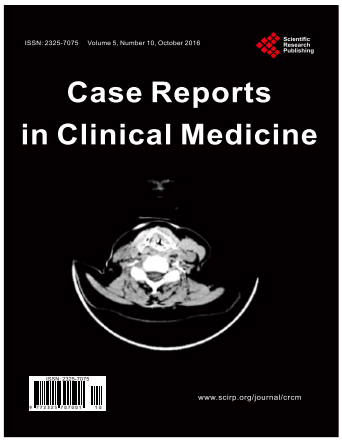

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