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Resolution of Cardiac Symptoms through Preoperative Intravenous Iron Supplementation in a Cancer Patient

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Abstract

Cardiologic assessment was conducted on a 78-year-old male patient scheduled for elective aortic valve surgery who complained of angina and dyspnea that had arisen over the previous few months. Evaluation showed stable coronary artery disease and iron deficiency anemia (hemoglobin, 7.7 g/dL). Colonoscopy revealed a non-stenosing carcinoma of the right colonic flexure that was causing chronic blood loss. The interdisciplinary tumor board of the hospital decided that his need for an extended right hemicolectomy followed by resection of two pulmonary nodules that were suspicious of metastatic lesions had priority over his cardiac surgery. Prior to abdominal surgery, the patient received 4 × 500 mg intravenous iron (Ferric-Carboxymaltose) over 2 weeks, for correction of iron deficiency and optimization of hemoglobin concentration. This treatment led to rapid improvement of his angina and exertion-induced dyspnea. His hemoglobin concentration continued to rise even after completion of the iron supplementation, and reached normal levels before thoracoscopic removal of the lung nodules, which took place 1 month after resection of the colon tumor. The patient remained in good clinical condition without any need for blood transfusions. As follow-up visits showed persistent abatement of angina and dyspnea, aortic valve surgery and other cardiac interventions were no longer deemed necessary.

Keywords

Patient Blood Management, Iron Deficiency, Anesthesia, Anaemia, Heart Failure

1. Introduction

The term patient blood management was coined in 2005, and was defined as an

evidence-based, multidisciplinary approach that is aimed at optimization of the care of patients who might need transfusions and the use of blood products [1]. Preoperative anemia, blood loss, and red cell transfusions have been identified as risk factors in the surgical setting. Muñoz *et al.* showed that these risk factors adversely affect postoperative infection rates, length of hospital stay, and mortality [2]. To avoid these adverse effects, the strategic adoption of patient blood management in surgical practice is widely recommended [3].

Patient blood management rests on three pillars of care: detection and treatment of preoperative anemia; reduction of perioperative blood loss; and harnessing and optimization of the patient-specific physiological reserve of anemia [3]. A bundle of measures is used to achieve these goals, including treatment of any underlying disease, the ideal timing for surgery, adoption of minimally invasive techniques, and immediate correction of coagulopathy, among others.

Bloodless therapeutic modalities, such as the use of erythropoietin (EPO) and intravenous iron supplementation, have moved into the focus now that the risks of unnecessary blood transfusions are increasingly being recognized. Lin *et al.* conducted a systematic review of 39 studies showing that transfusion rates can be significantly reduced by a short preoperative regimen of EPO or a single dose of EPO plus intravenous iron administered in the preoperative or intraoperative period [4]. Litton *et al.* included 72 studies in a meta-analysis according to which intravenous iron therapy is associated with increased hemoglobin levels and reduced risk of the need for red blood cell transfusion [5].

Patient blood management has been demonstrated to be worth the associated efforts. In a retrospective observational trial conducted in a total of 605,046 patients, Leahy *et al.* showed that a health-system wide patient blood management program can improve patient outcomes and reduce product-related costs [6]. The patient outcomes that were assessed in this study included the use of blood products, in-hospital mortality, length of hospital stay, hospital-acquired infections, and acute myocardial infarction or stroke. However, the benefits of patient blood management can be extended beyond just the surgical setting. Here, we describe the case of a patient who experienced significant collateral improvement to his cardiac situation due to preoperative iron supplementation after an unexpected diagnosis of cancer.

2. Case Presentation

A 78-year-old male was admitted to the Cardiology Unit in mid-March 2018 for diagnostic assessment prior to elective aortic valve surgery. He reported signs of coronary artery disease and heart failure, with a history of angina that had built up over the previous few months, and dyspnea triggered by slight exertion. His sociodemographic and anamnestic characteristics are summarized in **Table 1**. Coronary angiography showed stable two-vessel disease, including stenosis of the left anterior descending artery and chronic total occlusion of the right coronary artery. Echocardiographic evaluation revealed intermediate to high-grade

Table 1. Sociodemographic and anamnestic characteristics.

Family History	Medical History	Therapy
Father: Pancreatic carcinoma	Cancer of the rectum 1998	Abdomino-perineal extirpation
Brother: Pancreatic carcinoma	Bladder cancer 2012 G1, pTa	Transurethral resection of the prostate 2012
Son: Prostate gland carcinoma	Adenocarcinoma of the rectum 03/2018 G3 T2 pN0 (0/20), cM0	Right hemicolectomy 04/2018

aortic valve stenosis and grade I-II aortic valve insufficiency. However, his left ventricular function appeared to be preserved, with an ejection fraction of ~60%.

Laboratory tests showed pronounced iron deficiency anemia, with an erythrocyte count of 4.0 T/L, hemoglobin of 8.0 g/dL, and hematocrit of 26.6% (**Figure 1**). His iron levels were low (17 µg/dL; normal range, 80 - 160 µg/dL), as was his transferrin saturation (3%; normal range, 16% - 45%) and serum ferritin levels (6 µg/L; normal range, 50 - 310 µg/dL). This was accompanied by correspondingly high transferrin (359 mg/dL; normal range, 172 - 344 mg/dL) and soluble transferrin receptor (14.24 mg/L; normal range, 2.16 - 4.54 mg/L). As the patient had a history of rectal carcinoma that had been successfully treated approximately 20 years ago, colonoscopy was performed in search of the cause of his anemia. This investigation revealed a nonstenosing malignant tumor of the right colonic flexure, with a size of 4 cm × 5 cm. Staging showed two pulmonary nodules of the right lung that were suspected to be metastatic lesions.

The interdisciplinary tumor board of the hospital agreed on two-stage surgery including extended right hemicolectomy and resection of the pulmonary nodules, while any cardiac intervention was postponed. Optimizing the red blood cell mass was mandatory prior to surgery. To this end, the patient received intravenous iron supplementation on an outpatient basis, which started on April 4, 2018. At that time, his hemoglobin had further declined to 7.7 g/dL (**Figure 1**). The patient was in poor general condition, intolerant to exercise, and suffered shortness of breath even when speaking. However, he showed no edema or other signs of heart failure.

Overall, 2000 mg intravenous iron (Ferric-Carboxymaltose) was administered over 2 weeks, as four sessions with 500 mg in each. One week after the start of treatment, the condition of the patient had improved considerably, and his walking dyspnea was completely resolved. Also, he reported reduction in his angina symptoms.

The last intravenous iron dose was administered on April 19, 2018. Laboratory tests performed on April 18, 2018, revealed markedly improved red blood cell parameters, with an erythrocyte count of 4.8 T/L, hemoglobin of 10.8 g/dL, and hematocrit of 36.0% (**Figure 1**). Surgical resection of the colon tumor was scheduled for April 30, 2018. At the time of his hospital admission on April 29, 2018, his hemoglobin had risen further to 12.1 g/dL (hematocrit, 37.2%), and the patient appeared to be in good clinical condition.

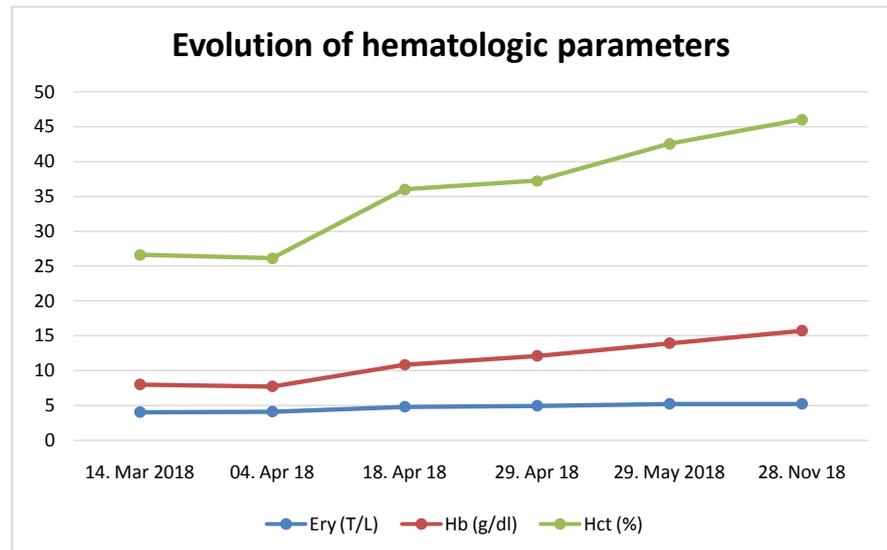


Figure 1. Evolution of the patient erythrocyte counts, hemoglobin and hematocrit levels.

Surgery was performed successfully on the next day. His postoperative hemoglobin concentration never fell below 10.1 g/dL. Histological examination of the colon tumor showed a mucinous adenocarcinoma with a maximum diameter of 3 cm (G3, pT2, PN0 [0/20], M1). The patient was hemodynamically stable throughout the postoperative period, and did not require any blood transfusions. He was discharged on postoperative day 9.

One month after the hemicolectomy, *i.e.*, on May 30, 2018, the lung nodules were resected via video-assisted thoracoscopic surgery. Without having received any further iron supplementation in the meantime, the patient showed normal red blood cell parameters at the preoperative laboratory assessment performed on May 29, 2018 (erythrocyte count, 5.2 T/L; hemoglobin, 13.9 g/dL; hematocrit, 42.5%). He reported being able to climb two flights of stairs and to have extended walks without any angina or dyspnea. Postoperatively, his hemoglobin levels remained above 11.7 g/dL. Neither of the two lung nodules showed signs of malignancy. According to histological evaluation, one nodule was a hamartoma, while the other one was an anthracotic lymph node, which was left *in situ*. The patient was discharged on the third postoperative day. From the oncological point of view, no further interventions were considered necessary, apart from his follow-up visits.

The cardiological evaluation performed a month later, on June 29, 2018, did not indicate the need for cardiac intervention. Echocardiographic assessment still showed moderate aortic stenosis with preserved left ventricular function (ejection fraction, 55% - 60%), but his angina and dyspnea had significantly improved, and the patient did not report any heart-related limitations in his daily life. Follow-up visits were arranged.

Another cardiological evaluation performed on September 25, 2018, described good right and left ventricular function with a left ventricular enddiastolic vo-

lume of 124 ml and an ejection fraction of 57%, and reiterated the patient's satisfaction with his cardiac and general state of health.

On November 28, 2018 the patient had a routine check at the oncological clinic. At this time the Hb value was 15.7 g/dl, and the patient reported again to be able to climb several floors without any limitations due to cardiac symptoms.

In a follow-up check about one year after the first hospital admission, *i.e.* on February 27, 2019, the patient continued to be clinically stable, without indications for cardiac surgery. He reported to perform daily walks of about 1 hours duration.

3. Discussion

Iron deficiency affects up to 50% of heart failure patients and has been associated with poor quality of life, impaired exercise tolerance, and increased mortality [7]. The case presented here shows that intravenous iron supplementation not only rendered the patient operable with respect to his recently detected colon carcinoma, but also effectively improved the cardiac symptoms he had been assessed for in the first place. His anemia and iron deficiency that was due to chronic bleeding from the colon carcinoma had given rise to, or at least greatly enhanced, the clinical signs of coronary artery disease and heart failure. Although the preserved left-ventricular ejection fraction of ~60% indicated a normal cardiac function apart from aortic valve disease scientific publications demonstrated that iron administration on the one hand positively impacts mitochondrial function by improving substrate utilization and myocardial bioenergetics [8] and on the other hand reverses the reduced contractility and relaxation of cardiomyocytes caused by iron deficiency [9].

In addition randomized, placebo-controlled clinical studies in patients with heart failure reduced ejection fraction (FAIR-HF, CONFIRM-HF, EFFECT-HF) have revealed a consistent benefit on self-reported Patient Global Assessment (PGA), NYHA class and a beneficial effect on peak oxygen uptake (peak VO_2), irrespective of the presence of baseline anemia [10] [11] [12]. Further results showed that, compared to placebo, iron substitution led to significant improvement in patient's exercise capacity as measured by the distance of the 6-minute walking test (6MWT) and it was associated with a positive impact on quality of life. Therefore, recent guidelines from the European Society of Cardiology for the treatment of heart failure recommend intravenous iron supplementation for symptomatic iron deficiency patients with the aim to improve quality of life and to increase exercise capacity [13].

In the case presented here a significant subjective improvement of cardiac symptoms like angina symptoms and complete resolution of walking dyspnea were reported only one week after the first intravenous iron infusion of 500 mg. Since such a significant symptomatic improvement is unlikely to be caused by improvement of anemia alone in such a short time period, we postulate the beneficial effect of iron substitution on myocardial bioenergetics and contractil-

ity of cardiomyocytes to be at least partially accountable for these effects. In the present case the resolution of cardiac symptoms even led to cancelation of aortic valve surgery and other cardiac interventions.

Given this comparatively simple solution to a serious medical condition, it appears advisable to pay increased attention to iron deficiency parameters and hemoglobin levels in patients with cardiac symptoms; *i.e.*, dyspnea or angina. This applies particularly to the setting of coronary artery disease. The scientific literature recommends higher hemoglobin levels for patients with coronary artery disease than for those without [14] [15].

Intravenous iron supplementation is an effective means to treat iron deficiency and iron deficiency anemia without the risks of a blood transfusion. In addition, as is shown by this case, it can have rapid and long-lasting benefits on cardiac function. Whether these beneficial effects are related to the increase in hemoglobin or might also be due to other effects of the iron on the heart remains to be determined. However, already 1 week after the initiation of treatment, the patient experienced marked symptom reduction, and his hemoglobin improved in a reliable manner. The right hemicolectomy was considered urgent and was performed even before the target hemoglobin level of at least 13 g/dL had been achieved. Nevertheless, his blood counts continued to improve after a transient surgery-related decrease, and reached normal levels at the time of the video-assisted thoracoscopic surgery, although the patient had not received any further iron supplementation after the initial administration of 2 g. Of note, the iron supplementation was not associated with any reported or observed adverse reaction.

This favorable course of events enabled the patient to undergo repeated surgery without being compromised by the initially diagnosed anemia. He was stable from the cardiopulmonary point of view throughout the postoperative periods, and he was discharged in good clinical condition. All of the subsequent laboratory tests revealed regular red blood cell counts. Meanwhile, the initial plans for aortic valve surgery were suspended, which also applied to any intention to perform coronary intervention in the long run, including stent implantation or coronary artery bypass grafting.

4. Conclusion

In conclusion, the case discussed here shows that anemia and iron deficiency should be considered as a potential cause of cardiac symptoms that can be brought about or augmented by the mere reduction in oxygen carriers and negative impact on myocardial bioenergetics. Intravenous iron administration offers benefits in terms of restoring erythrocyte counts, with potentially fast and sustained effects on cardiac function.

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Conflicts of Interest

A.G. is Medical Director of Vifor Pharma Austria.

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Incidence of Ostomies in Tertiary Care Teaching Institution

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Abstract

A retrospective observational study was conducted at Saveetha medical college and hospital, over 2 years, from January 2017-January 2019. A total of 29 patients with ostomies were included in this study. Information regarding the types and indications of the ostomies were collected from the hospital records. The collected data were analyzed using Microsoft Excel, and represented by tables and charts. Majority of patients were the males and the predominant age group was 51 - 60 years old. The objective of the present study was to classify ostomies based on organs and to analyze the aetiology for creating those ostomies.

Keywords

Ostomies, Ileostomy, Jejunostomy, Colostomy, Indications, Malignancy

1. Introduction

Ostomies or stomas are a lifesaving procedure in which surgically an opening is created on the abdominal wall. Stoma comes from a Greek word meaning “opening” or “mouth”. In World War One, mortality rate of 60% for primary repair of colonic injuries dropped to 30% in World War Two due to introduction of colostomy. In 1710, Littre of Paris was the first to make a ventral colostomy for a baby with imperforate anus. An ileostomy was first done in 1912 for ulcerative colitis but was widely used only after Brooke did his everted ileostomy in 1952. Stomas are used to divert faecal matter away from distal bowel for the distal anastomoses to heal or to relieve obstruction in emergency situation. Though it is a lifesaving procedure, carries significant number of complications which are associated with decreased quality of life and increased economic health burden. Complications are divided into early (up to 30 days after surgery)

and late (more than 30 days after surgery).

The most common types of ostomy connect either small intestine (ileostomy or jejunostomy) or large intestine (colostomy) to abdominal wall. Other ostomies that are not very common are gastrostomy, ureterostomy, cystostomy and urethrostomy. It could be permanent or temporary. Temporary ones can be closed without a major laparotomy when it is no longer required. Major indications of ileostomy include diffused bowel injury carcinoma colon, carcinoma rectum, and inflammatory bowel disease. Colostomy is employed in colonic obstruction primarily due to cancer of distal colon or rectum, anorectal carcinoma, rectovaginal fistula and perforation with peritonitis. Jejunostomy is done mostly in carcinoma of stomach or upper gastrointestinal tract carcinomas like hypopharynx, oesophagus [1]. In this study, an attempt was made to identify common ostomies and their indications in a tertiary care setup.

2. Aims and Objectives

The purpose of the present study was to classify ostomies based on organs and to analyse the aetiology for creation of ostomy in surgical patients.

3. Methods and Materials

This is a retrospective observational study conducted at Saveetha Medical College and Hospital, over two years, from January 2017-January 2019. All patients with ostomies were included. Hospital records were perused to collect data. The data analysis was done in Microsoft Excel. The Institutional Review Board of Saveetha Medical College and Hospital has given approval for the project.

Inclusion criteria:

- All patients with a newly created stoma (in this admission).
- We included both gastrointestinal and genitourinary stomas.
- All stomas irrespective of indication was included in the study.

Exclusion criteria:

- We excluded stomas in patient operated elsewhere.
- We excluded patients undergoing revision of existing stomas.

4. Results

In the present study there were 29 patients who had ostomies over a period of two years. There were 9 females and 20 males (**Figure 1**) ranging from 21 to 80 years of age, commonest age group for ostomies was 51 to 60 years (**Figure 2**).

There were 6 cases of ileostomy, 6 cases of colostomy, 13 cases of feeding jejunostomy, 2 cases of gastrostomy, 1 case of ureterostomy and 1 case of urethrostomy (**Figure 3**).

Most common indications for these ostomies were malignancy (75.90%), trauma (6.90%) and others (17.20%). Others included small bowel gangrene (2 persons), duodenal perforation (1 person) and urology causes like urethral stricture (1 person) and neurogenic bladder (1 person) [**Table 1**].

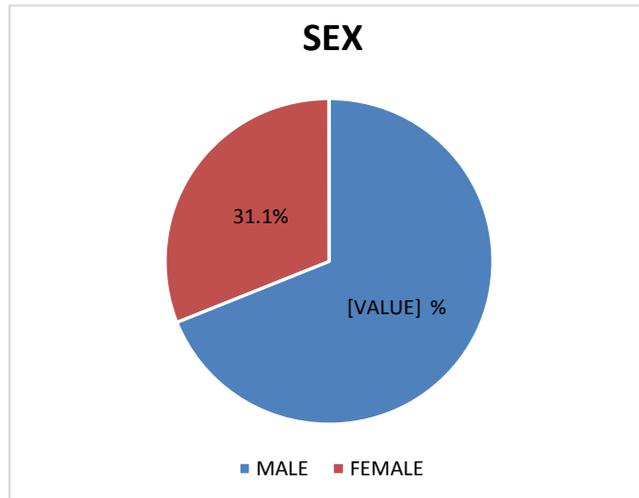


Figure 1. Shows gender distribution of ostomies.

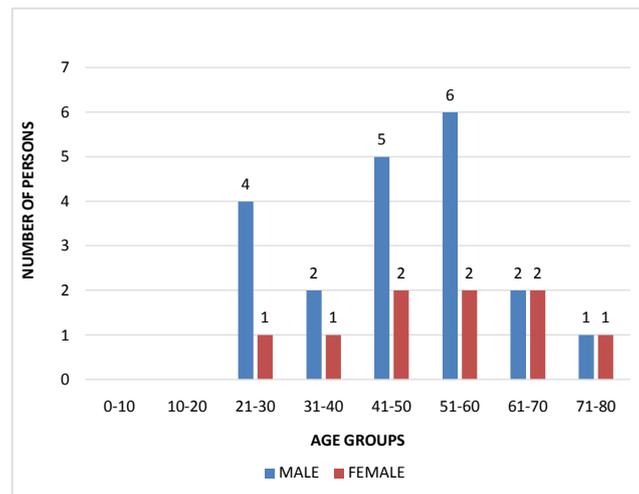


Figure 2. Shows age distribution of ostomies.

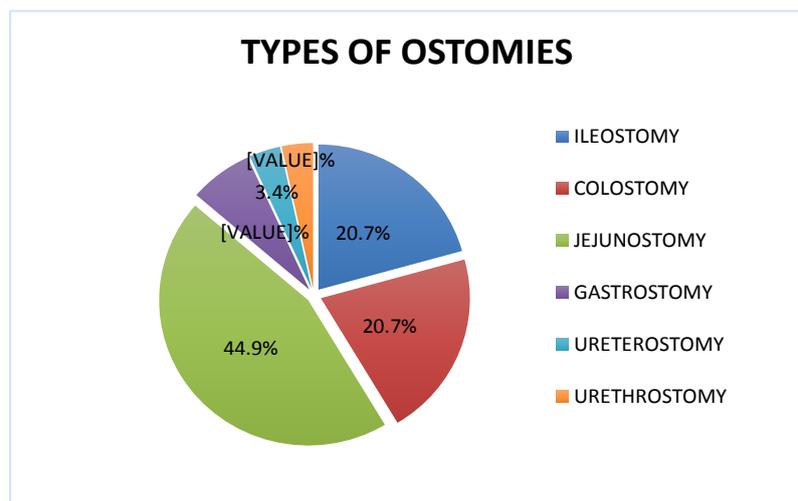


Figure 3. Shows the different types of ostomies.

Table 1. Shows the indications of ostomies.

Indications	No of persons	Percentage
Malignancy	22	75.90%
Trauma	2	6.90%
Others	5	17.20%

Though the commonest age group for ostomies was 51 - 60 years, malignancy was common in the age group of 40 to 50 years (**Figure 4**). Trauma was common in the age group of 21 to 30 years.

Of the 29 ostomies done, 22 were for malignancy. The indications for ostomies amongst the malignancy were carcinoma of stomach (6 cases), rectum (5 cases), colon (5 cases), hypopharynx (3 cases) and oesophagus (3 cases) [**Figure 5**].

5. Discussion

There were only sporadic records of ostomy surgery before 1700s. All through the 18th century, accepted treatment of bowel perforation was to close any open abdominal wound and “trust in the best”. This treatment plan was associated with high death rates. Most stomas were really fistulas that grew spontaneously following bowel perforation. One specialist noticed the relationship between spontaneous fistula formation and patient survival and expressed in his journal that perhaps surgeons should “take an exercise from natural force” and build arranged stomas in such cases. In the year 1706 a battlefield wound resulted in a prolapsed colostomy and it was the first ever stoma recorded. In 1793, an imaginative surgeon did colostomy on a 3-day old baby with an imperforate anus. The surgical procedure was effective and the patient lived to the age of 45 years. Ileostomy was relatively an advanced procedure and was first performed in nineteenth century for a patient with a blocking lesion in the ascending colon [2]. (**Figure 6**) As far as the recent advances go, the pouching system that we know today is a disposable product made of skin friendly, water repellent, cloth like material covering film laminates.

Ileostomy or colostomy is an artificial opening made in the small intestine or large intestine to divert faeces and flatus outside the abdomen, where it passes into an external outpouching system. Depending on the cause for which diversion has been made a stoma may be temporary or permanent. An ileostomy is usually placed in right iliac fossa and the effluent is usually liquid. End colostomy is usually sited in left iliac fossa, whereas a transverse colostomy is brought out in right hypochondrium and the effluent is solid. Ileostomy patients are more likely to develop fluid and electrolyte imbalance. The types of ileostomy are loop and end ileostomy. In loop ileostomy, a loop of small intestine is pulled out through the cut in the abdomen. This section of intestine is opened and stitched to the skin to form a stoma. In these cases, the stoma will have two openings, although, one may not be able to see both. One opening is active through

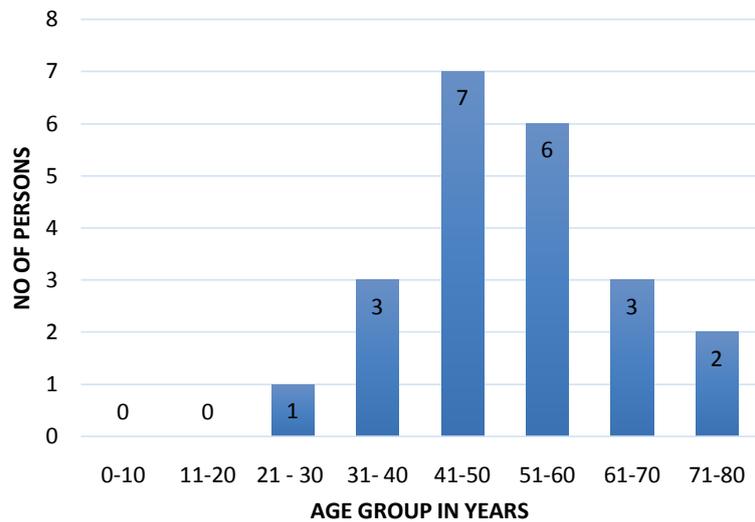


Figure 4. The distribution of malignancy in different age groups.

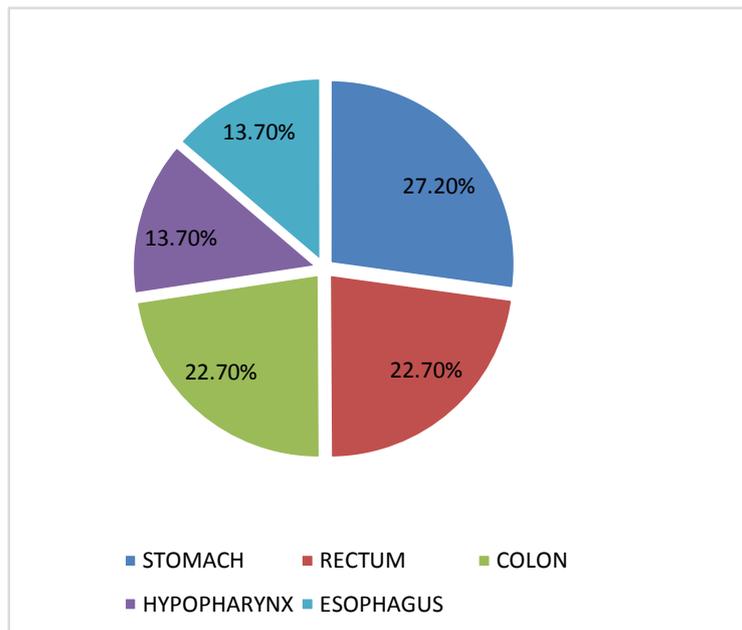


Figure 5. Indications for ostomies in malignancy.

which waste products leave the body and the other one is connected to the inactive part of bowel. The loop ileostomy is usually temporary and can be reversed during second surgery at a later date. It's often used for defunctioning a low rectal anastomosis after anterior resection of rectum or an ileoanal pouch. The advantage of loop ileostomy over a loop colostomy are bowel can be brought to surface easily and the absence of odour [3].

In an end ileostomy the whole of colon is removed through an incision in the abdomen. Then, the end of ileum is brought out of the abdomen through a smaller incision and stitched on to skin to form a stoma. Over time, the stitches dissolve and the stoma heal on to the skin. This type of ileostomy is usually but



Figure 6. Colostomy.

not always, permanent. It's done in cases where total proctocolectomy is done like Ulcerative colitis, Crohn's disease, Familial polyposis coli. It can be done even after subtotal colectomy without anastomosis, where it can be later reversed [3].

The different types of colostomy are loop, end and double barrel colostomy. In loop colostomy, a loop of bowel is pulled out onto abdomen and held in place with an external device. The intestine is then sutured to the abdomen and two openings are made in one stoma. One opening for stool and the other for mucus. This type of colostomy is usually used in emergencies and is a temporary stoma. End colostomy is formed after an abdominoperineal excision of the rectum for rectal cancer or as a part of Hartmann's procedure, bringing the divided colon through right iliac fossa incision. The colonic margin is then sutured to the adjoining skin. Colostomy in Hartmann's procedure following a large bowel resection, the distal bowel is closed and left in situ and the proximal end is brought out as an end colostomy. It's done for emergency resection as in volvulus or diverticular perforation [4].

Double barrel colostomy, the bowel is cut and both ends are brought out onto the abdomen. Only proximal stoma is functioning. The colon is divided so that both ends can be brought separately to the surface with a skin bridge intervening. Temporary colostomy indications are distal bowel obstruction, defunction a low rectal anastomosis, following traumatic injury to rectum or colon, fulminant colitis. Permanent colostomy indication is rectal carcinoma excision, where end colostomy is done.

Stomal complications are quite common. A complicated stoma can cause social, domestic as well as psychological problems. On occasion these complications need surgical revision. Sometimes this can be done with an incision immediately around the stoma, but on occasion reopening of abdomen and freeing up the stoma is required. Early complications are those occurring in first postoperative month. It can be local skin problems like skin irritation and excoriation, stoma retraction, bleeding, parastomal abscess, complete necrosis and metabolic disturbances. Late complications appear after first postoperative month. Those are stenosis, prolapse and parastomal hernias. Skin irritation is due to poor stoma siting. It is a result of chemical dermatitis or frequent appliance changes or

fungal irritation by candida albicans or may be even due to abscess [4].

In the study done by QA Ahmed et al thirty-five stomas out of eighty-five developed stoma related complications. Skin excoriation and ulceration were most common, it was more common in ileostomy than colostomy. Painful skin with ulceration makes it difficult to apply the ostomy bag and cause problems in handling the effluent. Local skin problems are quite common and can be avoided by early application of stomahesive methyl cellulose paste with proper sized bag. Treatment includes Zinc oxide paste and keep it dry if the ulcer heals.

Most of the complications are due to lack of experience and surgery done in emergency. A surgeon whose is trained, experienced and observes all technical details usually give good results. Complications need to be avoided as increase in their rates can give rise to economic burden to both patients and health sector. Moreover, reduction of complications can have a positive effect on the quality of life of the patients.

Jejunostomy and gastrostomy are one of the methods of enteral feeding. Gastrostomy is now used for enteral feeding purpose only. It is done when feeding is required for more than one month. Indications are oesophageal cancer, pharyngeal carcinoma, trauma, sepsis, head and neck surgeries and severe malnutrition.

Types of gastrostomy:

- Based on duration of use which is temporary or permanent.
- Based on lining which is mucus lined (permanent) and serosa lined (temporary).
- Based on technique:
 - a) Stamm temporary gastrostomy: After opening the abdomen, anterior wall of stomach is opened. Feeding tube is placed in position. Two layers of purse string sutures are put around the tube. Wound is closed.
 - b) Percutaneous endoscopic gastrostomy-now becoming common method.
 - c) Janeway's mucus lined permanent gastrostomy is done by making a tunnel in stomach wall.

Problems in gastrostomy:

- a) Tube related like leakage, malposition, displacement, blockage, breakage, erosion of skin infection.
- b) Gastrointestinal complications like aspiration and pneumonia, diarrhoea, bloating, abdominal cramps, nausea, vomiting, and constipation.
- c) Metabolic or biochemical complications like electrolyte disorders, vitamin, mineral, trace element deficiencies and drug interactions.
- d) Infective, it could be exogenous or endogenous.

Jejunostomy for enteral nutrition is becoming more popular because of its comfort, easy to do, can be kept for long time, lesser complications than gastrostomy. Indications are same as gastrostomy. Types are Witzel jejunostomy in which site of jejunostomy is 30 cm from duodenojejunal junction and Needle jejunostomy by using catheter of small gauge.

When created urinary stomas are created, the urine does not go to the blad-

der. The urine is rerouted through opening on the abdomen created by a surgeon. Ureterostomy is a urinary stoma in which ureter is attached to skin's surface through a small opening in the abdomen. Indications include bladder cancer, spinal cord injury, malfunction of bladder.

In the present survey the number of ostomies over a period of two years were less (twenty-nine cases) compared to the study done by QA Ahmed et al where the number cases were eighty-five. In this study, we found that 68.9% of the study population were males which correlated with study done by QA Ahmed *et al.* who had 73% of the study population as males. While the maximum clustering of cases in this analysis was in the age group of 51 - 60 years, whereas in the study done by QA Ahmed et al the commonest age group for ostomies was 21 - 30 years.

In the present study the commonest ostomy done was feeding jejunostomy, followed by equal number of cases of ileostomy and colostomy (20.7%) but in the study done by QA Ahmed et al colostomy was common. According to this survey the commonest indication for the ostomies were advanced malignancy which was in contrast to study done by QA Ahmed et al in which main indications were intestinal tuberculosis and enteric perforation.

6. Conclusion

Males were two times more likely to have a stoma than females. Maximum clustering of cases was in age group 51 - 60 years. The most common type of ostomy in our study was feeding jejunostomy, however, it was followed by equal number of cases of ileostomy and colostomy. The commonest indication for creating a stoma was malignancy in our study.

Limitations of the Study

The study duration is short, the sample size is small and hence we are unable to provide data about complications and follow up at this moment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Endometriosis Misdiagnosed as a Metastatic Ovarian Tumour

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Abstract

Endometriosis is a debilitating problem with pain in the short term and high risk of infertility later. It is an oestrogen-dependent condition found in about 10% of women of reproductive age, about 1/3 of infertile women and as high as 80% of women with chronic pelvic pain. The condition is not well understood and thus associated with misdiagnosis and delayed diagnosis. Higher rates of misdiagnosis occur in blacks and this is especially for pelvic tumors-fibroids and ovarian tumors. We present here the case of a 30-year-old nullipara, who had an umbilical nodule (Sister Mary Joseph's) and was found on imaging to have a pelvic tumor which was suspected to be an ovarian cancer. Diagnostic laparoscopy during the menstrual phase however revealed endometriosis in early stage. Misdiagnosis of endometriosis has potential to distort the course of the disease and endanger fertility prospects; early laparoscopic evaluation of patients with unclear pelvic pathologies would help to prevent this occurrence.

Keywords

Diagnosis, Endometriosis, Pelvis, Tumour, Treatment, Imaging

1. Introduction

Endometriosis is often symptomatic when present, causing debilitating illness in many cases. It is the occurrence of endometrium-like glands and stroma outside the uterine cavity [1].

Endometriosis affects about 10% of women of reproductive age 15 - 49 years.

It has been implicated as one of the top three causes of female infertility [2].

Endometriosis can also be described as a disease of theories as the cause and course has been explained by findings that suggest various theories [1] [2] [3]. Endometriosis was thought to be rare among black populations; evolving knowledge however continued to unravel this myth. Misdiagnosed endometriosis is a recognized factor in treatment delays and worsening conditions, leading to infertility and chronic pelvic pain, especially in blacks [2]. Endometriomas have been misdiagnosed for pelvic tumors mainly; fibroids and malignant ovarian tumors [2]. Endometrioma being misdiagnosed for a metastatic tumor is a rare occurrence.

We present here the case of a 30-year-old nullipara, who had a peri-umbilical nodule (Sister Mary Joseph's) and was found on imaging to have a pelvic tumor which was suspected to be a metastatic ovarian cancer. Laparoscopy during the menstrual phase, together with tissue histology however revealed endometriosis with tubal masses.

2. Case Report

A 30-year-old single nullipara, presented to the gynae clinic with one year history of lower abdominal pain which had become worse and continuous in the 2 months preceding her presentation to the hospital. She had significant weight loss but no history of cough, haemoptysis, abnormal uterine bleeding, or bleeding from other body orifices. She had used a non-steroidal anti-inflammatory drug (Diclofenac tablets) for 1 year and at the time of presentation; she had an upper gastrointestinal tract endoscopy done which showed that she had developed gastritis.

Examination revealed a young woman, with significant weight loss, but no pallor or lymph node enlargement. There was a nodular firm, non-tender 2 cm diameter spherical growth occupying the right half of the umbilicus. There was mild suprapubic tenderness and ascites was demonstrable by shifting dullness. She had a pinhole cervical os and a boggy, soft, tender Pouch of Douglas (POD), and a tender firm mass within it (**Figure 1** & **Figure 2**).

There was no adnexal or cervical motion tenderness. An assessment of a metastatic ovarian tumor was made. Ultrasound scanning (USS) and Computerized tomography (CT) revealed a huge ovarian mass completely obliterating the POD with suspected metastasis to the anterior abdominal wall (**Figure 3**).

The CA-125 level was <3.5 MIU/ml, while her CEA was <3.5 MIU/ml both were normal for laboratory reference range. Serum quantitative β -HCG assay was <50 miu/ml.

She was scheduled for laparoscopy, but shortly before the procedure she started menstruating with associated severe dysmenorrhea. Before laparoscopy, she had pelvic examination under anaesthesia, which revealed a cervical external os diameter \approx 3 mm, with scanty bleeding from the cervical os. Operative findings included haemoperitoneum with a covering layer of clearer peritoneal fluid, which upon suctioning revealed a bulky uterus with two huge tubal masses

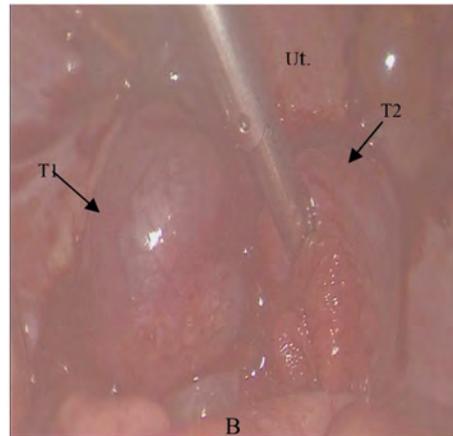


Figure 1. Tubal masses (T) in the posterior cul de sac mimicking a malignant ovarian tumor (Ut. = uterus, B = bowel).

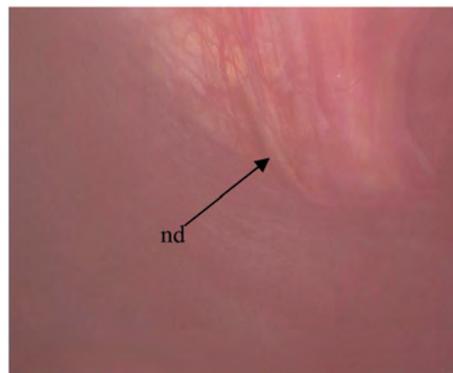


Figure 2. Laparoscopic view of the peritoneal surface of the umbilical nodule (nd).



Figure 3. CT scan view showing the Mass in the POD and the umbilical nodule (nd).

(mid-tubal diameter \approx 6 cm each), posterior to the uterus and filling up the POD, there was continuous efflux of fresh blood from the dilated fimbrial ostia. The ovaries were covered by the tubal masses, they looked grossly normal, but had transparent haemorrhagic cysts on their surfaces. The peritoneal surface of the umbilicus had a well circumscribed 2 cm diameter nodular growth; which together with the cysts on the ovaries were excised for histology. Peritoneal fluid was also obtained for cytology and mycobacterial assay. The cervical external os was then dilated, to allow outflow of menstrum. The ascitic fluid cytology revealed reactive mesothelial cells with no evidence of atypical or malignant cells seen. It was also negative for acid fast bacilli.

Histological sections of the ovarian cystic mass and umbilical nodules showed islands of endometrial glands and endometrial stroma (**Figure 4**).

The glands contained a single layer of tall columnar cells and there were no foci of atypia or malignancy, features adjudged as consistent with endometriosis. She was commenced on dydrogesterone and her dysmenorrhea and pelvic pain had significantly reduced. Repeat ultrasonography done one month and repeated two months later confirmed absence of any pelvic tumors.

3. Discussion

Continuous epigastric pain made this patient first present to the gastroenterologist where endoscopic findings confirmed a probable sequela of analgesic abuse. The benefit of long term use of non-selective NSAIDs, for treatment of endometriosis, is limited by their adverse effects on the gastrointestinal tract [4]. This finding may also explain her weight loss from anorexia as patients with gastric ulcers typically have pain exacerbations after meals [5].

The huge tubal masses observed at laparoscopy, the demonstration of retrograde menstruation and the histologic confirmation of peritoneal endometriotic

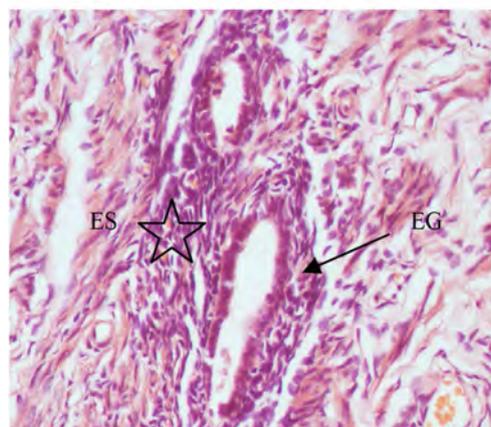


Figure 4. Photomicrograph of the ovarian cystic mass showing islands of endometrial glands EG (arrow) and endometrial stroma ES (asterisk) consistent with endometriosis of the ovary. (Haematoxylin and eosin stains, $\times 400$.)

deposits largely clarify the diagnosis of endometriosis. Laparoscopy done in the menstrual phase of the cycle afforded us this opportunity. There is currently no evidence in support of menstruation being an absolute contraindication to elective laparoscopy. It has however been recommended that laparoscopic resection of peritoneal endometriosis, should be avoided during the luteal phase because of the high recurrence rate observed when compared to other phases of the menstrual cycle [6].

The contiguous location of the ovary to the uterine tubes in the pelvis makes recognition of these organs in disease-states difficult. The cul de sac uterine tubal masses in this patient were misdiagnosed on ultrasound scanning and CT for a malignant ovarian tumor. Normal ovarian tissue with minor thin walled cysts on their surfaces which were excised and confirmed with histology suggested early stage endometriomas. Ovarian endometriomas have been demonstrated in histopathological specimens to start initially as extra-ovarian cysts with ectopic endometrium lining the surface of the cortex, which later gets invaginated to form an intra-ovarian pseudocyst [3].

The nodular umbilical growth in this patient was painless and had never bled, although it had increased in size over 12 months. This finding raised suspicion of malignancy as it has been reported in literature that 88% of umbilical malignancies originate outside the umbilicus [7]. The histologic finding of benign fibrocollagenous tissues however put our suspicions to rest and supports earlier reports that 60% of umbilical nodules are benign [8]. Ovarian and endometrial cancer reportedly account for 28% of Sister Mary Joseph's nodules [9]. Endometriosis has not been clearly shown in systematic reviews to increase the risk of ovarian cancer. However when ovarian cancer develops, the clear cell and endometrioid histologic types appear more likely [10] [11].

Intraoperative cervical dilatation significantly reduced the size of the tubal masses before the end of laparoscopy. Ultrasound scanning done during subsequent menstruations confirmed that the pelvic masses were no longer present. It had been reported that significantly more retrograde menstruation occurred with cervical external os diameter < 4.5 mm [12].

4. Conclusion

Misdiagnosis of endometriosis has potential to distort the course of the disease and endanger fertility prospects; early laparoscopic evaluation of patients with unclear pelvic pathologies would help to prevent this occurrence.

Ethical Consideration

The patient gave a written informed consent permitting the authors to publish this case report, while ensuring that her identity is not mentioned.

Authors' Contributions

IJO performed the initial clinical assessment and the laparoscopy together with

AMA. AMA performed the histopathology and prepared the histopathological report, while ONK coordinated the radio-diagnosis. The initial draft of the manuscript was written by IJO with assistance from AMA. All authors read and approved the manuscript for publication.

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Conflicts of Interest

The authors declare that there is no competing interest relating to this case report.

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Recurrent Hypoglycaemia in a Diabetic Patient Presented a Gastric Cancer: Think about Paraneoplastic Syndrome

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Abstract

The hypoglycaemia paraneoplastic is uncommon in diabetic patients. Our aim was to report a case of paraneoplastic hypoglycaemia discovered after the diagnosis of gastric adenocarcinoma in a diabetic patient. A 65 years old man, was hospitalized for the management of acute digestive haemorrhage. In his medical history, he had diabetes since 20 years. He was alcoholic weaned for 3 years and had an unexplored repetitive epigastralgia. During his hospitalization, the exploration of acute digestive haemorrhage found a gastric adenocarcinoma with hepatic metastasis. At the 4th day of his hospitalization, he presented a hypoglycaemic coma with capillary blood glucose at 0.36 g/L. The patient was conscious after the infusion of Hypertonic Glucose Solution (HGS) 10%. After 3 days, the recurrent hypoglycaemia occurred and we intermittently treated by infusion of glucose solution 10%. The measurements of insulin level and C-peptide weren't performed because they didn't exist in the city. So, the notion of cancer and the recurrent hypoglycaemia even if we stopped the oral antidiabetic therapy make us think of a paraneoplastic syndrome. The chemotherapy associated with corticosteroid therapy is the standard treatment of the hypoglycaemia paraneoplastic but the patient refused the chemotherapy and we couldn't use the corticosteroid therapy because of digestive haemorrhage. At the end of his hospitalization, he still had hypoglycaemia treated by infusion of glucose solution 10%. In the absence of means of diagnosis, we should think of paraneoplastic syndrome in front of recurrent hypoglycaemia and cancer in the diabetic patient.

Keywords

Extrapancreatic Tumors, Gastric Carcinoma, Hypoglycaemia, Paraneoplastic Syndrome

1. Introduction

In the diabetic patient treated by insulin or hypoglycaemic sulfamide, the hypoglycaemia is one common acute complication but it is rare in the context of paraneoplastic syndrome. The cause of this syndrome is either an insulinoma or extrapancreatic cancers. In the 45% of cases, the extra-pancreatic cancer comes from the mesenchymal tissue in the 45% of cases and rarely, it comes from the epithelial tissue [1] [2] [3] [4]. The paraneoplastic hypoglycaemia is due to the secretion of a precursor of high molecular weight of “Insulin-like Growth Factor-2” (IGF-2) or “big IGF-2”; this precursor mimics the effects of insulin [5] [6] [7]. In the diabetic patients, the causes of hypoglycaemia must be sought to differentiate the reactive hypoglycaemia and the organic hypoglycaemia like the paraneoplastic hypoglycaemia [8]. Indeed, this one can be under diagnosed in case of tumoral pathologies. Sometimes, it is the premature sign of some cancers [9] [10] [11]. Our aim was to report a case of paraneoplastic hypoglycaemia discovered after the diagnosis of gastric adenocarcinoma in the diabetic patient. An informed consent was obtained from the patient to report this case.

2. Case History

A 65 years old man, state employee retired, was hospitalized at the department of oncology and polyvalent medicine of the University Center Hospital of Antanambao Toliara, in the south of Madagascar for the management of acute digestive haemorrhage.

In his medical history, he had diabetes since 20 years treated by oral antidiabetic (glibenclamide). His treatment was taken irregularly and was stopped since a few months after a discomfort. He was chronic alcoholic who has been weaned for 3 years. He had a repetition epigastralgia not exploring and a repetition discomfort since a few months. In his eating habits, he took cassava 2 times a day and rice once a day.

At the admission, he was conscious, his hemodynamic state was stable. His general state was deteriorated and he presented a cutaneo-mucosal pallor. The abdomen was flexible; there was an epigastric pain without portal hypertension signs. There were blackish stools at the digital rectal examination

He was fasted and his treatment was composed of red blood cell transfusion, plasma transfusion, parenteral alimentation and medicaments to eradicate *Helicobacter pylori* (amoxicillin, omeprazole, clarythromycin during 14 days).

After he underwent a digestive endoscopy and we found a bloody bulging mass at the fundus of stomach. We practiced a biopsy of mass and the histologi-

cal examination found a gastric adenocarcinoma.

The evolution of digestive haemorrhage was favourable on the 2nd day of his admission. So, he begun a semisolid food (soft diet) and we definitively stopped his antidiabetic treatment.

On the 4th day, the patient presented cold sweats followed by loss of consciousness. The diagnosis of hypoglycaemic coma was immediately withheld, with a capillary blood glucose level of 0.36 g/L.

An infusion of hypertonic glucose serum 10% instantly normalized its state of consciousness.

After 3 days, a fasting capillary blood glucose checking revealed hypoglycaemia at 0.42 g/L, confirmed by the plasma glucose measurement. Thus, a discontinuous infusion of GHS 10% was systematically introduced. Despite this, episodes of hypoglycaemia were still observed. **Figure 1** shows the kinetics of fasting capillary glycaemia over time during routine infusion of 10% GHS.

The other blood tests showed a good renal function with a creatinine clearance: 110 mL/min/1.73 m² by MDRD formula (Reference value: 120 mL/min/1.73 m² +/- 20 mL/min/1.73 m²); a good hepatic function with AST 30 IU/L (Reference value: 7 - 40 IU/L), ALT 25 IU/L (Reference value: 5 - 35 IU/L), GGT 40 IU/L (Reference value: 15 - 55 IU/L), and total bilirubin 8 µmol/L (Reference value: 3 - 22 µmol/L); a microcytic anemia at 9 g/dL (Reference value of hemoglobin: 14 - 18 g/dL) after transfusion of 3 blood bags and a glycated hemoglobin at 6.2% (Reference value: ≤ 7%). Dosages of insulinemia and peptide C were not achieved because of their unavailability.

Regarding the extension assessment, an abdominal ultrasound showed hepatic nodules suspected of malignancy. The chest X-ray showed no metastases. So, it was therefore stage IV gastric adenocarcinoma. Thus, palliative chemotherapy has been indicated. After the announcement of the diagnosis and prognosis, the patient refused the proposed treatment. We then opted for a best supportive care. At the end of hospitalization, the patient had again presented signs of hypoglycaemia, motivating an outpatient infusion of glucose serums.

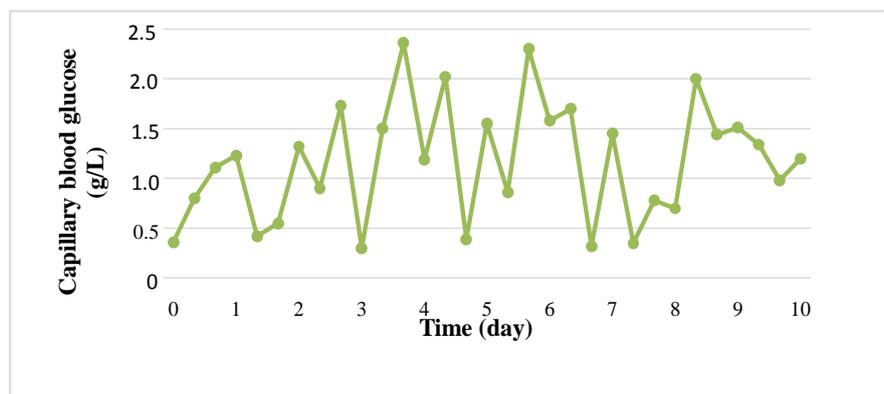


Figure 1. Kinetics of fasting capillary glycaemia over time during routine infusion of 10% GHS.

3. Discussion

Numerous studies have been conducted on hypoglycaemia in Madagascar, both in Antananarivo and Toliara. But they are mostly focused on hypoglycaemia caused by alcohol [12] [13], leaving aside paraneoplastic hypoglycaemia. Alcohol is known to induce immediate hypoglycaemia [14]. Despite the history of chronic alcoholism in our patient, hypoglycaemia of ethyl origin has been ruled out since alcohol has already been weaned since several years.

Paraneoplastic hypoglycaemia is a rare condition. It is linked to a pancreatic or extrapancreatic tumor. Mesenchymal and hepatic tumours are the most frequently reported in the literature [15] [16] [17]. Those of the digestive tract remain rare [18] [19] [20]. However, the stomach is the most common location in the gastrointestinal tract in 67% of cases [10] [19] [21]. Like our case, a gastric carcinoma is discovered after a digestive bleeding and hypoglycaemia.

Regarding the circumstances of discovery, to our knowledge there are few studies on the correlation between digestive bleeding and cancer of the digestive tract in Madagascar. A study carried out in the reference center of the Joseph Raseta Befelatanana University Hospital shows that gastric cancer represents only 2.73% of the causes of upper gastrointestinal bleeding. These are mainly related to duodenal ulcer, which accounts for 31.50% of cases [22]. Some atypical cases of digestive cancers have also been reported [23] [24]. Gastric adenocarcinoma frequently affects men, aged 60 and over, smoking and having a history of *Helicobacter pylori* infection. Digestive haemorrhage is manifested in the majority of cases in the advanced stage of the disease [25]. Our patient with melena was diagnosed with metastatic gastric adenocarcinoma. So, we should explore every digestive bleeding to seeking a cancer cause like a gastric cancer.

The hypoglycaemia is the most common acute complication of diabetes. It is most often of iatrogenic origin [26]. The sulfamids are the most incriminated. In fact, the risk of hypoglycaemia due to their use is related to their plasma half-life and their binding to their receptors. For glibenclamide, still widely used in Africa but less and less in developed countries [27], its half-life is 4 to 11 hours and its binding to its receptors is strong and durable, explaining the frequent occurrence of hypoglycaemia. The hypoglycaemia is more frequent and severe in the elderly and/or with renal insufficiency [28]. Our patient took glibenclamide but already stopped for several months before his hospitalization. So, the cause of his hypoglycaemia has no relation with the drug intake. A study carried out on diabetic patients admitted for severe hypoglycaemia in the Joseph Raseta Befelatanana University Hospital shows that 21.33% of the patients had hypoglycaemia due to renal failure, 13.33% due to fasting and 10.67% due to taking antidiabetic drugs. But for 26.67% of cases, the causes were not specified [29]. Tumour causes including extrapancreatic could have been found, contributing to better management of hypoglycaemia. Further research into the exact cause of hypoglycaemia is necessary to avoid missing the diagnosis of a serious pathology. In the context of cancer, the hypoglycaemia should be suggestive of a paraneoplastic origin.

Indeed, the clinical manifestations of hypoglycaemia are of two types: neuroglycopenic and neurovegetative. The signs of neuroglycopenia correspond to a deficiency of glucose of the central nervous system and appear for a threshold of blood glucose lower than 0.50 g/l. They can result in confusion, behavioral problems, drowsiness, visual disturbances, transient motor deficiency, seizure and loss of consciousness. On the other hand, neurovegetative symptoms are related to stimulation of the autonomic nervous system by central hypothalamic activation, which is itself caused by hypoglycaemia, as soon as blood glucose falls below 0.55 g/l. Sweating, cravings and paresthesia are cholinergic signs, whereas anxiety, palpitation and tremor correspond to adrenergic manifestations [1] [21] [30].

The presence of hypoglycaemia with collapse of insulinemia, peptide C and IGF-1, associated with an increase in IGF-2: IGF-1 ratio, leads to extrapancreatic tumour origin [9] [10] [21]. While an elevation of insulinemia, C-peptide leads to insulinoma [31]. In our case, these biological assessments were not available in our city. Blood samples must be taken to the capital for on-site examination or sent abroad. So the cost remains exorbitant for the majority of Malagasy people, who have no social cover or income sufficient to perform this kind of biological exam knowing that the average income of the Malagasy population is 348 USD per inhabitant per year according to a survey carried out in 2007 [32]. Thus, in our case, the diagnosis was directed to a paraneoplastic syndrome in view of the recurrent characteristics of hypoglycaemia in the absence of favourable factors, in particular the stopping of the oral antidiabetic, and the discovery of a gastric cancer.

Corticosteroid therapy, such as prednisolone at 2 mg/kg/day, is the basic treatment for paraneoplastic hypoglycaemia associated with tumour-specific therapy [7] [21]. In our case, the patient presented a recurrent hypoglycaemia because he refused chemotherapy and the corticotherapy was not conceivable because he had a gastrointestinal haemorrhage although this one is stopped after a well conducted treatment.

4. Conclusion

In the context of cancers in diabetic patients, a paraneoplastic syndrome must be evoked in front of recurrent hypoglycaemia. It is still difficult to confirm in our country, given the lack of adequate technical platforms. A multidisciplinary collaboration between oncologists, endocrinologists and resuscitators would better support this entity.

Conflicts of Interests

The authors declare no conflicts of interest regarding the publication of this paper.

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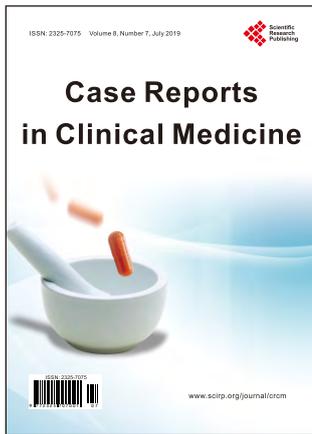
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