

Churg-Strauss Syndrome Revealed by Acute Coronary Artery Disease: A Case Report*

Maurice Estivals^{1#}, Marc Périé², Daniel Colombier³, Bruno Farah⁴

¹Department of Pulmonology, Hôpital du Pays d'Autan, Castres, France

²Department of Cardiology, CHT G. Bourret, Nouméa, New Caledonia

³Department of Radiology, Clinique Pasteur, Toulouse, France

⁴Department of Interventional Cardiology, Clinique Pasteur, Toulouse, France

Email: #m-estivals@chic-cm.fr

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ABSTRACT

Churg-Strauss syndrome (CSS) is a very rare small-vessel vasculitis. Clinical features include asthma, rhinitis and/or sinusitis, and peripheral eosinophilia. Although cardiac findings are observed in 50% of cases, coronary artery disease is rarely reported and even more rarely suggestive. The value of cardiac MRI for these patients is discussed here. A 52-year-old non-smoker male without family antecedents of cardiovascular disease presented with worsening of atypical asthma that developed 10 months earlier. A month before, he had been admitted to the ICU because of respiratory distress and cardiogenic shock with chest pain. The angiogram revealed stenosis of the three main coronary arteries requiring the placement of several stents. Follow-up cardiac assessments showed good results. General impairment, unstable asthma associated with rhinitis, and eosinophilia suggested a systemic disease. The diagnosis of CSS was established considering that five criteria of the American College of Rheumatology were found. Prednisolone was prescribed at 1 mg/kg/day, which completely suppressed all symptoms and eosinophilia. Cardiac MRI was performed two months later and revealed a good control of myocardial lesions characterized by fibrosis beneath the anterior endocardium and the median septum. Immunosuppressive treatment was then administered together with corticosteroid therapy. These results suggest that acute coronary artery disease can reveal CSS in some cases. Here, the patient's cardiac assessment was normal apart from the acute episode, and cardiac MRI helped detect signs of myocarditis and establish a prognosis of CSS.

Keywords: Vasculitis; Churg-Strauss Syndrome; Acute Coronary Artery Disease; Eosinophilia; Cardiac MRI

1. Introduction

According to the Chapel Hill classification, Churg-Strauss syndrome (CSS) is a necrotizing vasculitis of small-to-medium-sized vessels. It is a rare disease, with 0.5 - 6.8 million cases per year. Physiologically, it is characterized by eosinophilia, an inflammatory disease, and by the presence of neutrophilic polynuclear anticytoplasmic antibodies in 35% - 50% of patients. Symptoms include asthma, rhinitis, sinus polyposis and mononeuritis multiplex. Cardiac findings are observed in about 50% - 60% of cases in the form of pericarditis, myocarditis or ischemic cardiopathy. These play an important role in prognosis, as they are responsible for 48% of deaths. Ischemic events are rare, and are rarely suggestive.

2. Case Report

A 52-year-old non-smoker male was admitted to the Emergency Department in February 2009 with cardiogenic shock occurring in the context of acute coronary syndrome (ACS). An electrocardiogram revealed a lower branch ST elevation with extensive lesion beneath the anterior endocardium. Prior to this, the patient had suffered from moderate persistent asthma for 10 months and had been treated with a combination of fluticasone 250 mg/salmeterol (two puffs/day).

Emergency coronary angiography revealed occlusion of the right coronary artery and the medial left anterior descending (LAD) artery. Nitrates could not be used locally due to the initial cardiogenic shock. Stents were placed on the LAD artery. However, iterative obstructions led to multiple stenting of the LAD and the circumflex arteries with several resuscitations due to cardiac arrest.

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#Corresponding author.

The patient was then transferred to intensive care with mechanical ventilation for 48 hours and placement of an intra-aortic balloon pump for three days. He was then sent to Sydney for a coronary angiography and intracoronary ultrasound analysis. The right coronary artery was found to have been initially occluded but was completely cleared by the local injection of nitrates. No atheroma was found in the left network, which led to a diagnosis of coronary artery spasms in a healthy arterial network in a man without family history of cardiovascular disease.

Peripheral eosinophilia of 2000 polynuclear eosinophils was found. Suspected, but unproven, parasitosis was treated with albendazole.

Three weeks after returning from Australia, the patient was admitted to the Department of Pulmonology due to an episode exacerbated asthma. He showed signs of chronic rhinitis with occasionally purulent rhinorrhea linked to heartburn-associated hyposmia. He reported a weight loss of 7 kg in the past year, although his weight had remained stable since the coronary event. On pulmonary examination, he had diffuse wheezing and a prolonged expiratory phase without stridor. The cardiovascular examination was normal. ENT examination confirmed a mild rhinorrhea associated with posterior discharge. Late-onset asthma associated with ENT findings, possible gastroesophageal reflux (GER) and peripheral eosinophilia suggested a systemic disease. Laboratory analyses revealed pronounced peripheral eosinophilia with 16,900 polynuclear eosinophils, *i.e.*, 68.6% of a total sample of 24.6×10^3 leucocytes.

Chest CT (**Figure 1**) revealed the presence of lingular infiltrates. No mediastinal adenopathy, pleural effusion or pericardial reaction was found. Sliding hiatus hernia was also found.

Facial CT (**Figure 2**) confirmed sinusitis, mainly affecting the frontal and maxillary areas associated with chronic sinusitis.

Macroscopic bronchoscopic findings were normal without vocal chord anomaly but with a marked inflammation of the larynx. Bronchoalveolar lavage (BAL) revealed eosinophilic alveolitis (560 white elements per mm^3 including 49% of eosinophils).

At the bacteriological, virological and mycological levels, the BAL fluid was sterile.

Histologic examination of bronchial biopsies did not find abnormal cells but confirmed a marked extravascular eosinophilia of the superficial chorion.

Immunological tests (CAN, ANCA, rheumatoid factors, quantitation of immunoglobulins, and IgE dosage), parasitic serology, aspergillus-specific IgE and allergy tests were all negative.

Parasitological stool tests yielded negative results three times.

PHmetry and esogastric fibroscopy confirmed the pre-

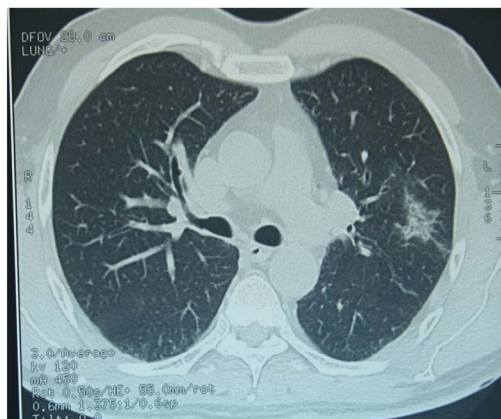


Figure 1. Chest CT. Appearance of isolated infiltrate of the left upper lobe, bilateral bronchial syndrome.

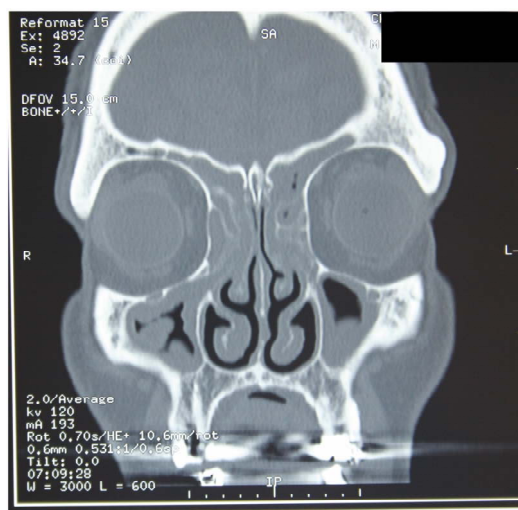


Figure 2. Sinus CT. Appearance of frontal and bilateral chronic maxillary sinusitis.

sence of GER. The electrocardiogram showed a sinus rhythm without changes in repolarization.

The echocardiogram performed six weeks after the initial episode revealed normal left ventricular function and cardiac rhythm.

CSS diagnosis was established due to the fact that Lanham's three criteria were met. In addition, Churg-Strauss vasculitis could explain the significant coronary artery disease, in the absence any other cardiovascular risk factors.

Oral corticosteroid therapy was administered, starting with a dosage of 1 mg/kg/day of prednisolone, together with GER treatment and disease modifying inhaled therapy (formoterol 48 $\mu\text{g}/\text{day}$ and budesonide 1600 mg/day) for asthma.

Rapid and complete suppression of the cough and ENT symptoms (rhinorrhea and dysphonia) was observed. After four weeks, a return to the previous weight was noted, the asthma remained under control and the level of

eosinophils returned to normal.

In April 2009, two months after the initial ACS, a thorough cardiac checkup was performed. The patient was found to be free of all symptoms of coronary disease, and the electrocardiogram revealed normal results. The coronal CT showed satisfactory stent permeability without any sign of restenosis, in addition to a normal coronary network. No parietal irregularity or calcification was observed.

On cardiac magnetic resonance imaging (MRI), the left ventricle (LV) was not dilated (LVEDV: 130 ml, indexed 75 ml/m²) and no thinning of the myocardial wall was found on T1 sequences. There was no vascular dysfunction or pericardial discharge or thickening. A clear subendocardial hypersignal was observed in the medial septum and the anterior median areas on T2 STIR sequences, suggesting an edema.

Finally, diffuse abnormalities of delayed subendocardial enhancement that did not correspond to coronary systematization of the median anterior, median inferior and lateral walls were found. These showed at some points a nodular character, particularly on the inferior-medial wall.

The global and segmental function of the LV was maintained with an LV ejection fraction (LVEF) of 63% (minor axis), 55% (four cavities) and 56% (two cavities).

The perfusion was heterogeneous with a slight defect in the median septal wall, suggesting microcirculatory issues (**Figure 3**). It was concluded that the T2 sequence anomalies and delayed enhancement were compatible with myocardial injury within the scope of vasculitis and probably associated with sub-endocardial fibrosis (**Figures 4 and 5**). LV function was maintained with LVEF at around 60%.

Considering the myocardial injury observed on the MRI, a decision was made to start immunosuppressive treatment in association with corticosteroid therapy (azathioprine 2 mg/kg/day).

3. Discussion

CSS is characterized by necrotizing vasculitis, which affects both small and medium-sized blood vessels at the pulmonary and systemic levels, and is associated with intra- and extravascular granuloma, eosinophilia, and infiltration of eosinophils at the tissue level in asthmatic patients who often suffer from rhinitis or chronic sinusitis [1]. It is a rare condition (0.5 to 6.8/106 per year). The diagnostic criteria were established by Lanham [2] at the Hammersmith Hospital in London.

Here, the diagnosis of CSS was established because three of the criteria of this classification with a sensitivity and specificity of 95% were found [2]. It should be noted that although ENT and asthmatic symptoms were present, the allergy results were negative and IgE levels were

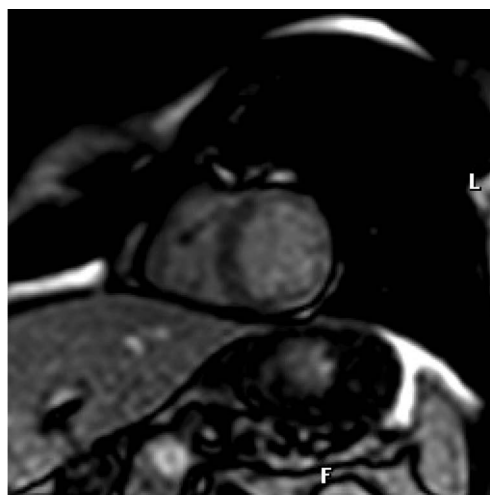


Figure 3. Cardiac MRI. Short axis perfusion. First-pass perfusion sequence after bolus intravenous injection of Gadolinium. Hyposignal in the anterior-septal wall suggesting microcirculatory issues.



Figure 4. Cardiac MRI. DES 2 cav. 2. Delayed enhancement sequence 10 min after intravenous injection of Gadolinium in slices, two cavities long axis. Subendocardial contrast enhancement in two distinct areas: anterior-medial and inferior-medial. A pseudo-nodular enhancement can be observed in the latter.

normal. Asthma was moderated with normal respiratory function under disease modifying treatment; it was never corticoid dependent and was not treated with leukotriene inhibitors. Other possible diagnoses were eliminated (Carrington's disease, Loeffler's syndrome, allergic bronchopulmonary aspergillosis, Wegener's granulomatosis, Hodgkin's lymphoma and drug-induced eosinophilic pneumonia).

We did not consider here the possibility that treatment with inhaled substances could have caused CSS [3], as peripheral eosinophilia was not available at treatment onset.

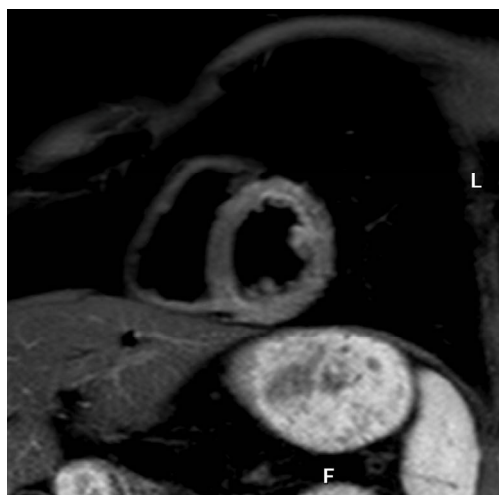


Figure 5. Cardiac MRI. T2 STIR short axis. Weighted “black blood” T2 sequence with fat saturation. Subendocardial hypersignal in the anterior-septal and inferior areas suggesting myocardial edema.

Our patient had an ANCA-negative phenotype, and showed evidence of pulmonary infiltrates on CT images, but no pleural effusion; bronchial biopsies revealed marked extravascular eosinophilia on the superficial chorion. According to the French Vasculitis Study Group criteria [4], he was at risk of suffering a cardiac event.

Cardiac findings are present in about 50% of cases of CSS [1,5] and are responsible for almost half of CSS deaths [6]; they are sometimes difficult to identify. The most frequent cardiac symptoms are pericarditis and myocarditis. Vascular problems and heart failure due to LV dysfunction have also been described [7-10]. Several studies have confirmed the benefits of cardiac MRI in the early diagnosis of cardiac disease [5,11,12], while other diagnostic techniques do not yield useful results.

Cardiac localizations are more frequent in the ANCA-negative phenotype [4,5,12] as was the case in our observation. In the series published by Neumann *et al.* [5], 22 out of 49 patients showed clinical signs of cardiac disease, ANCA were often negative and elevated eosinophilia was often found. A total of 50% of patients had LV dysfunction, 73% had vascular leakages and 41% had pericarditis. Endomyocardial lesions were detected by MRI in 59% of patients who then had a less favorable diagnosis.

LV function was initially normal apart from the acute episode, and there was no vascular injury or pericardial effusion. The coronary angiography revealed a coronary network free from atheroma and restenosis, and permeable stents. There were no unfavorable symptom and initial treatment solely based on corticosteroid therapy seemed justified, as in the case reported by Wagner *et al.* [7].

The detection of cardiac injury by MRI had an impact

on treatment, as cardiomyopathy plays a role in four of five factors that determine poor prognosis for CSS, namely: age over 65 years, severe gastrointestinal injury, renal failure with elevated serum creatinine levels ($>150 \mu\text{m/L}$), and heart disease [5,12-14].

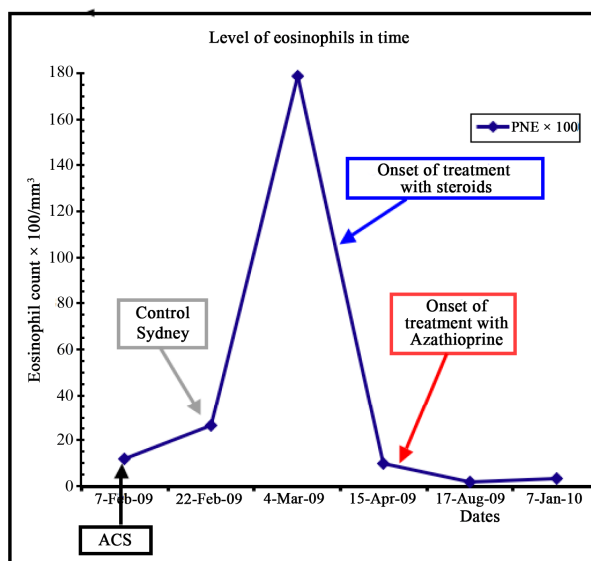
However, due to the low number of cases described, it seems premature to intensify CSS treatment based solely on MRI results from asymptomatic patients [12].

Here, the patient had a favorable prognosis in terms of ENT involvement, but a poor prognosis in terms of heart disease [14]. Therefore, immunosuppressive treatment was started.

Acute coronary events have been poorly reported in the literature [7,9,10,15]. They rarely suggest CSS and no case of multiple stenting could be found in the literature. The mechanisms mentioned are coronary spasms, which are possibly favored more by the toxicity of eosinophils or by myocardial granulomas than by the localization of vasculitis at the level of the coronary arteries [15,16]. In the case reported by Wagner *et al.*, the patient’s history suggested undiagnosed CSS. His phenotype was ANCA negative, with very high initial eosinophilia Tanaka *et al.* [12] reported a case of ACS due to a vasospasm with significant eosinophilia ($>5000/\text{mm}^3$) and ANCA-negative phenotype [15]. The authors suggested a link between coronary vasospasm due to CSS and eosinophilia. It is interesting to note that in the case reported here, eosinophilia was not found during the ACS. Significant eosinophilia was only found a month after the event (Figure 6).

What, then, is the mechanism of vasospasm?

The overall prognosis for patients with CSS remains favorable (79% alive at 10 years) [13]. Heart disease is



ACS = Acute Coronary Syndrome

Figure 6. Level of eosinophils in time.

responsible for almost 50% of deaths [6], so intensive initial treatment is recommended.

Two years after initial diagnosis, the patient remains treated with azathioprine and small doses of corticosteroids (5 mg/day of prednisone). There has been no relapse at the cardiovascular level, but respiratory function remains below normal (LVEF = 3.4 liters at 100% of theoretical values, Tiffeneau = 73%, and mean peak expiratory flow 25/75 at 2.73 liters so 73% of theoretical values). The level of eosinophils was at 680/mm³.

In conclusion, CSS can be accompanied and revealed by ACS. The mechanism of ACS in the healthy coronary network is a vasospasm that seems independent of the coronary localization of the vasculitis, although its origins remain uncertain. In such cases, cardiac MRI should be systematically performed to identify myocardial injuries that can be useful for the prognosis. This will ensure early start of immunosuppressive therapy.

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