CASE REPORT

A case of rheumatic valvular heart disease and autoimmune gastritis

Cátia Costa, David Durão, Marisa Peres, Margarida Leal

Hospital Santarém, Santarém,
Portugal

Correspondence to

Dr Cátia Costa,
ccatiasofia@sapo.pt

Accepted 6 December 2014

SUMMARY

We present a case of a 50-year-old female patient with a history of depressive disorder and anaemia (attributed to menorrhagias). She was admitted to the cardiology department with symptoms of fatigue on moderate exertion for several months, with worsening in the month before hospitalisation. Echocardiography revealed a severe mitral stenosis of rheumatic aetiology. Laboratory tests showed microcytic and hypochromic anaemia, reduced iron stores and vitamin B₁₂ levels, and positive serum antiparietal cells autoantibodies. Endoscopy showed focal areas of erythema in the stomach, corresponding histologically to chronic atrophic gastritis. In this context, two distinct clinical entities were diagnosed in the same patient: severe rheumatic mitral stenosis and autoimmune gastritis. The patient was started on vitamin B₁₂ and iron supplementation and underwent surgical correction of the valvular disease. There was symptomatic improvement in her signs of fatigue.

BACKGROUND

There is a great variety of autoimmune diseases and their pathophysiological mechanisms have been extensively studied in recent years. Although rheumatic heart disease is becoming less prevalent in developed countries, it still represents a major public health problem in many regions of the world. However, autoimmune gastritis is associated with high morbidity but its real prevalence is unknown. It is characterised by the presence of autoantibodies directed against intrinsic factors as well as parietal cells, which damage the gastric mucosa.

Although there are no cases described in the literature of coexistent rheumatic mitral stenosis and autoimmune gastritis, both result from an autoimmune process. This paper describes for the first time a case with both entities and raises the question of whether it was just a coincidence.

This case also illustrates the importance of clinicians being aware of insidious onset anaemias as they may constitute a treatable condition that can reduce the cardiac burden.

CASE PRESENTATION

The authors present a case of a 50-year-old female patient with a history of anaemia attributed to menorrhagias and a depressive disorder. She had also several episodes of tonsillitis during her childhood. The patient was hospitalised in the cardiology department with symptoms of fatigue on moderate exertion for several months, with worsening in the month before hospitalisation. At physical examination, discoloured skin and mucous membranes were noted

with no other abnormalities of the skin or appendages; on cardiac auscultation, rhythmic S1 and S2 were found as well as a diastolic murmur at the cardiac apex, best heard with the patient in a left lateral decubitus position. The remaining physical evaluation, including gynaecological and neurological examination, showed no other relevant findings.

INVESTIGATIONS

During hospitalisation, several examinations were performed.

- ▶ A 12-lead ECG, showing sinus rhythm with a heart rate of 75 bpm, normal electrical axis and criteria for dilated left atrium.
- ▶ A transoesophageal echocardiography, which revealed thickening of the mitral valve with commissural fusion and calcification (figure 1A).

Figure 1 (A) Echocardiography revealing a thickening of mitral valve leaflets, with fusion and calcification of the commissures. (B) Echocardiography showing maximum and mean transvalvular mitral gradients of 26 and 14 mm Hg, respectively, and a functional area of 1 cm², compatible with severe mitral stenosis.

CrossMark

To cite: Costa C, Durão D, Peres M, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-207578

Maximum and mean transvalvular gradients were 26 and 14 mm Hg, respectively, with an estimated functional area of 1 cm² (figure 1B); these findings were compatible with severe mitral stenosis of rheumatic aetiology. Mild regurgitation was also present. Biventricular function was preserved with normal-sized ventricles. The left atrium was dilated. There was also a moderate tricuspid regurgitation, with an estimated systolic pulmonary artery pressure of 50 mm Hg;

- ▶ Laboratory tests, which showed a microcytic and hypochromic anaemia (haemoglobin 9.1 g/dL), reduced iron stores and vitamin B₁₂ levels, and positive serum antiparietal cells auto-antibodies. The determination of anti-intrinsic factor auto-antibodies was negative. The peripheral blood smear revealed the presence of anisocytosis and teardrop-shaped cells.
- ▶ An upper gastrointestinal endoscopy, which showed areas of erythema in the gastric body, histologically confirmed to correspond to chronic atrophic gastritis (figure 2).
- ▶ A pelvic ultrasound, in the context of menorrhagias, which showed no pathological changes in the uterus or attachments.

DIFFERENTIAL DIAGNOSIS

- ▶ In this context, two distinct clinical entities were diagnosed: a severe rheumatic mitral stenosis and an autoimmune gastritis.
- ▶ Anaemia of a multifactorial aetiology was also present, due to iron and vitamin B₁₂ deficiency.

TREATMENT

Treatment was started with parenteral vitamin B₁₂ and iron supplementation, and the patient was referred for surgical correction of the valvular stenosis.

OUTCOME AND FOLLOW-UP

There was an improvement of serum iron, vitamin B₁₂ and haemoglobin levels and the patient underwent surgical correction of valvular disease without incidence.

Clear symptomatic improvement of the symptoms of fatigue was observed.

DISCUSSION

Rheumatic fever is currently considered a major cause of mitral stenosis, however, it is becoming less prevalent in developed

countries.¹ This decline is explained by the use of penicillin as primary and secondary prophylaxis as well as by the progressive improvement in living and sanitation conditions, and consequent decrease in the prevalence of infections transmitted by group A *Streptococcus*.^{1 2}

Rheumatic fever is more frequent in women.¹ It results from an autoimmune process that develops after pharyngeal infections by group A *Streptococcus*.¹ In the heart, the mitral valve is the most affected structure, with leaflet thickening, fusion of the commissures and shortening of the chordae.

The aetiopathogenesis of rheumatic heart disease is still not fully understood. Several genes appear to be involved in the development of rheumatic fever and rheumatic heart disease, with contributions from innate and adaptive immunity.³ The molecules involved in innate and acquired immune responses are encoded by genes of which the polymorphisms have been associated with rheumatic fever and rheumatic heart disease.³

Most pathogens that enter the body are initially recognised by the innate immune system, a non-specific defence system, which recognises a limited number of specific patterns shared by groups of pathogens. This activation of the innate immune system leads to the production of proinflammatory cytokines and molecules, which act as signals in the activation of the adaptive immune system.³ The latter system includes antigen-presenting cells that express on their surface molecules of the human leucocyte antigens (HLA) of the major histocompatibility complex (MHC) system, allowing the presentation of antigens to T lymphocytes. These molecules, encoded by genes located on chromosome 6, are subdivided into classes: class I (HLA A, B and C) and class II (such as HLA DR, DQ and DP).³ Several studies point to an association of the rheumatic disease with different alleles of the HLA system, in particular class II molecules and those encoded by DR and DQ genes.^{3 4}

For the development of the disease, the molecular mimicry between streptococcal antigen (M protein) and human proteins including myosin, tropomyosin, keratin, laminin and vimentin, among others, seems to be fundamental. This similarity plays a central role in the pathogenesis through stimulation of autoreactive T cells, which trigger valvular injury.³ Several studies show that autoantibodies reactive against *streptococcal* antigens and human proteins bind to the endothelium resulting in an inflammation process with valvular lesions and cellular infiltration. Cytokines, produced during the process of activation of the immune system, appear to be crucial in perpetuating the inflammatory process and valvular injury, and polymorphisms in genes encoding molecules such as tumour necrosis factor α , transforming growth factor β , interleukin 1 and interleukin 10, among others, have already been identified.³

On the other hand, autoimmune atrophic gastritis is characterised by atrophy of the body and fundus of the stomach in the presence of autoantibodies directed against intrinsic factor as well as parietal cells.⁵ This leads to hypo-achlorhydria and, over time, to vitamin B₁₂ deficiency and anaemia, an end stage of the process known as pernicious anaemia.⁵

Data on the epidemiology of autoimmune gastritis is sparse because most studies refer to the prevalence of pernicious anaemia, which has been reported to be as high as 1.9% in individuals over 60 years.⁵ However, some studies suggest that autoimmune gastritis is probably more prevalent than expected.⁵

Several authors have suggested the possible role of *Helicobacter pylori* infection in the pathogenesis of autoimmune atrophic gastritis and pernicious anaemia.⁶ The central mechanism seems to be the capability of *H. pylori* to induce a process of autoimmunity through mimicry between antigens of the

Figure 2 Biopsied lesions of the gastric body during gastrointestinal endoscopy coloured with H&E (2×10 magnification), showing chronic active gastritis with moderate mucosal atrophy and intestinal metaplasia.

bacteria and the H⁺/K⁺-ATPase pump, which would induce a cross-activation of autoreactive T and B cells.^{6 7} It is believed that genetic susceptibility may play a crucial role in losing immune tolerance.⁶ Thus, the HLA system seems to have a preponderant role at this stage of presentation of antigens to T lymphocytes, triggering an inappropriate activation in genetically susceptible individuals.^{6 7} Various findings support the belief that infection by *H. pylori* can be replaced by an autoimmune process directed by autoreactive CD4 T cells that recognise the H⁺/K⁺-ATPase pump and *H. pylori* antigens, ending in irreversible destruction of the gastric mucosa.⁶ The HLA-DR

system (class II of the MHC) has been most commonly associated with pernicious anaemia, with various alleles being identified in different world populations.⁶

This paper describes a case where the two clinical entities coexist, raising the question of whether it was just a coincidence. Nowadays, the association between autoimmune gastritis and other autoimmune disorders, such as autoimmune thyroid disease, type 1 diabetes and vitiligo, has been recognised. Nevertheless, there have been no cases reported in the literature of an association between autoimmune gastritis and rheumatic heart disease.

This case also illustrates an important decompensation factor of heart disease: anaemia of multifactorial aetiology, which was most likely due to menorrhagia (resulting in iron deficiency) and probably exacerbated by impaired iron and vitamin B₁₂ absorption due to autoimmune gastritis. It constitutes a treatable condition that can reduce the cardiac burden.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Carabello B. Modern management of mitral stenosis. *Circulation* 2005;112:432–7.
- 2 Carapetis J. Rheumatic heart disease in developing countries. *N Engl J Med* 2007;357:439–41.
- 3 Guilherme L, Kohler K, Postol E, et al. Genes, autoimmunity and pathogenesis of rheumatic heart disease. *Ann Pediatr Cardiol* 2011;4:13–21.
- 4 Bajoria D, Menon T. The HLA class II associations with rheumatic heart disease in south Indian patients: a preliminary study. *J Clin Diagn Res* 2013;7:302–4.
- 5 Miceli E, Lenti M, Padula D, et al. Common features of patients with autoimmune atrophic gastritis. *Clin Gastroenterol Hepatol* 2012;10:812–14.
- 6 Lahner E, Annibale B. Pernicious anemia: new insights from a gastroenterological point of view. *World J Gastroenterol* 2009;15:5121–8.
- 7 Andres E, Serraj K. Optimal management of pernicious anemia. *J Blood Med* 2012;3:97–103.

Learning points

- There are no reported cases in the literature of coexistent rheumatic mitral stenosis and autoimmune gastritis. This paper describes, for the first time, a case with both entities, leaving the question unanswered of whether it was just a coincidence.
- Rheumatic fever and autoimmune gastritis have aetiopathogenic autoimmune mechanisms. Several studies point to an association with different alleles of the human leucocyte antigen (HLA) system, in particular class II. The molecular mechanism by which the HLA class II system seems to confer susceptibility to autoimmune diseases is yet to be elucidated.
- This case also illustrates the importance of the awareness of clinicians to the diagnosis of insidious onset anaemias such as those due to iron, vitamin B₁₂ or folate deficiency, as they constitute treatable conditions that can reduce the cardiac burden.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow