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Case Report

Infective endocarditis due to *Bartonella bacilliformis* associated with systemic vasculitis: a case report

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Abstract

Infective endocarditis due to *Bartonella bacilliformis* is rare. A 64-year-old woman, without previous heart disease, presented with 6 weeks of fever, myalgias, and arthralgias. A systolic murmur was heard on the tricuspid area upon examination, and an echocardiogram showed endocardial lesions in the right atrium. *Bartonella bacilliformis* was isolated in blood cultures, defining the diagnosis of infective endocarditis using Duke's criteria. Subsequently, the patient developed clinical and laboratory features compatible with antineutrophil cytoplasmic antibody-associated vasculitis. This case presents an uncommon complication of *B. bacilliformis* infection associated with the development of systemic vasculitis.

Keywords: Infective endocarditis. *Bartonella bacilliformis*. Systemic vasculitis.

INTRODUCTION

Infective endocarditis (IE) is an infection of the endocardial surface that usually occurs in patients with previous anatomical abnormalities, such as rheumatic heart disease, congenital malformations, prosthetic valves, and intracardiac devices. *Staphylococcus* and *Streptococcus* spp. are the most commonly identified microorganisms in blood cultures. However, in some cases, conventional cultures are negative due to previous antibiotic use or because some fastidious microorganisms require isolation in special media, such as infections by the HACEK group (*Haemophilus* spp., *Aggregatibacter* spp., *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* spp.) and *Brucella* spp. Additionally, a few *Bartonella* spp. have been identified as causes of endocarditis, with *Bartonella quintana* and *Bartonella henselae* being the most common[1]. *Bartonella bacilliformis*, the etiologic agent of Carrion's disease (CD), has also been reported as a cause of endocarditis in a pediatric patient with a history of right ventricular-coronary artery fistula[2]. Infections can trigger vasculitis through various direct (e.g., endothelium infection) or indirect (e.g., molecular mimicry) pathways. Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of vasculitides that predominantly affect small vessels and cause systemic manifestations. AAV has three major variants: microscopic polyangiitis (MPA), granulomatosis with polyangiitis [(GPA), previously Wegener's granulomatosis], and eosinophilic granulomatosis with polyangiitis [(EGPA), previously Churg-Strauss syndrome]. Several microorganisms that trigger systemic vasculitis have been described, including *Staphylococcus aureus* nasal carriage, which has been related to GPA and *B. henselae* with Henoch-Schönlein purpura[3,4]. Here, we present the case of a woman diagnosed with *B. bacilliformis* endocarditis associated with systemic vasculitis.

CASE REPORT

A 64-year-old woman, with a past medical history of idiopathic pulmonary fibrosis and hypothyroidism, presented with 6 weeks of intermittent fever, myalgias, and arthralgias. She reported a previous course of antibiotics for an unspecified infection without presenting any improvement. On physical examination, she was febrile at 39°C and had hypothyroid facies and mesosystolic murmur on the tricuspid area. The rest of the examination was unremarkable. Ancillary testing revealed normocytic, normochromic anemia (11.1g/dl), 9.26 × 10^3 leukocytes/µl, lymphopenia (0.84 × 10^3 lymphocytes/µl), neutrophilia (7.72 × 10^3 neutrophils/µl), 0.09 × 10^3 eosinophils/µl, thyroid-stimulating hormone level of 22.7µUI/ml, total bilirubin of 0.30mg/dl, and creatinine of 0.82mg/dl. Initial blood and urine cultures were negative. An electrocardiogram revealed no abnormalities, but the transthoracic echocardiogram showed a perivalvular lesion in the right atrium, suggestive of vegetation. The patient was admitted to the Cardiology ward with the probable diagnosis of atrial myxoma vs IE.

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Transesophageal echocardiography (TEE) revealed two masses, 10 × 18mm and 5 × 10mm, on the lateral wall of the right atrium (**Figure 1**). The patient was transferred to the Infectious Diseases ward, where tests were performed, including repeated aerobic and anaerobic blood cultures, peripheral smear for malaria, serology testing for *Brucella* and *Salmonella*, bone marrow culture, and enzyme-linked immunosorbent assay (ELISA) test for human immunodeficiency virus, all of which resulting negative. The erythrocyte sedimentation rate, rheumatoid factor, and C-reactive protein were elevated (94mm/h, 24.2IU/ml, and 8.31mg/dl, respectively), and the complement values were normal (C3, 157mg/dl and C4, 18mg/dl). Due to persistent fever of 39°C, worsening anemia (8.9g/dl), and a history of a recent travel to Tarapoto, a jungle region in San Martín, Peru, where CD cases were recently reported, blood samples were sent to the Institute de Medicina Tropical *Daniel Alcides Carrión* in Lima to rule out CD. The samples revealed negative blood smears (Giemsa stain) but positive blood cultures for *B. bacilliformis* in Columbia agar (growth at 15 days of incubation). The definitive diagnosis of IE due to *B. bacilliformis* was made using modified Duke's criteria. Treatment with intravenous (IV) ciprofloxacin (400mg/12h) was initiated, but changed to IV ceftriaxone (2g/24h) shortly after, due to lack of clinical improvement.

Despite this therapeutic modification, the patient had persistent anemia and intermittent fever and presented progressive weight loss, paresthesia in extremities, muscular weakness, livedo reticularis, and macular exanthema in the abdomen, dorsum, and lower limbs. Moreover, acute kidney injury (AKI) with creatinine of 1.69mg/dl, proteinuria (0.5g/24h), and the absence of hematuria were noticed. For this reason, Rheumatology evaluated the case and recommended electromyography, which was conclusive for mononeuritis multiplex; immunological markers were positive for p-ANCA (by ELISA). Renal biopsy revealed tubulointerstitial inflammation to predominance of mononuclear cells and moderate-severe thickening of juxtaglomerular and interlobular vessels. Due to the persistence of symptoms, two *Bartonella* blood cultures were repeated and, again, resulted positive (growth at 20 days and 17 days of incubation). A few coccobacilli were also reported in the blood smear. Furthermore, a follow-up TEE showed growth of the intracardiac masses (**Figure 2**), prompting a change from ceftriaxone monotherapy to a combination therapy of IV ciprofloxacin (200mg/12h), gentamicin (4mg/kg per 24h), and oral (PO) rifampicin (10mg/kg per 24h). The aminoglycoside was changed later to PO azithromycin (500mg/24h) due to worsening renal function. Additionally, surgical treatment was considered, but the patient did not consent to the procedure. The fever, anemia, and lymphopenia progressively resolved, but the weakness and paresthesias persisted. A multidisciplinary team decided to initiate PO prednisone (20mg/24h) for AAV, based on the symptomatology and immunological and electromyographic findings. The patient was discharged afebrile, with progressive clinical improvement and negative blood cultures for *B. bacilliformis* after 10 weeks of antibiotic treatment. On outpatient evaluation, a follow-up TEE showed absence of vegetations, prednisone dose was reduced to 5mg/day, and PO azathioprine (50mg/24h) was added, resulting in resolution of myalgias and paresthesias.

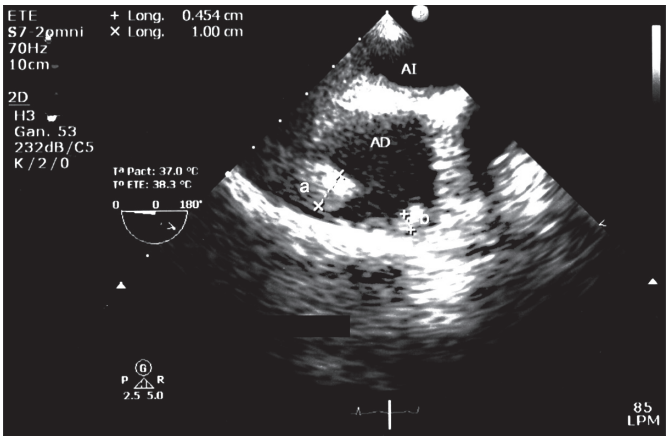

FIGURE 1 - Transesophageal echocardiogram: masses on the lateral wall of the right atrium, measuring (a) 10 × 18mm and (b) 5 × 10mm on admission. **AI:** left atrium; **AD**: right atrium.

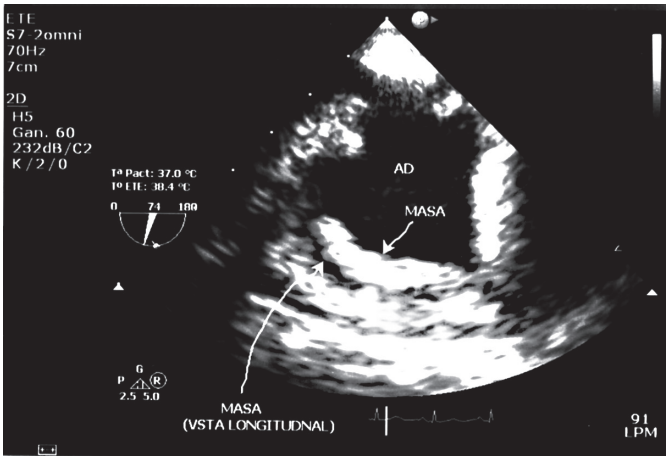

FIGURE 2 - Transesophageal echocardiogram: longitudinal mass located on the lateral wall of the right atrium, measuring 32 × 12mm at 3 weeks of the initial antibiotic regimen administered to the patient. **AD:** right atrium; **MASA**: atrial mass.

DISCUSSION

Carrion's disease is a metaxenic disease endemic in Colombia, Ecuador, and Peru, caused by *B. bacilliformis* and transmitted by the bite of female *Lutzomyia* sand flies. This biphasic disease consists of an acute form, known as Oroya fever, and a chronic phase, denominated Peruvian wart[5]. Infectious and noninfectious complications occur in 70% of patients in the acute phase, such as neurological, hematologic, and cardiovascular alterations, including cardiac failure, pericarditis, and myocarditis[6]. To our knowledge, only one case of endocarditis caused by this bacterium was reported in a pediatric patient with underlying cardiac disease[2]. We diagnosed *B. bacilliformis* endocarditis based on modified Duke's criteria[1], considering as major criteria the persistence of positive cultures for *B. bacilliformis* and the presence of intracardiac lesions on TEE in the absence of any other anatomical explanation. Persistent bacteremia due to *B. bacilliformis* has been described in up to 54% of patients with Peruvian wart living in endemic areas, from where there are no reports of endocarditis[5]. Our

patient had a recent and short epidemiological exposure to a new endemic area in the Peruvian jungle, which could explain her different outcome[7]. The patient initially received a regimen based on our current guidelines for treating acute *B. bacilliformis* infection; however, due to the lack of clinical and microbiological responses, we designed a combined therapy based on published antibiotic susceptibility testing of this microorganism[8,9]. A recent local study showed that 26% of evaluated strains of *B. bacilliformis* in patients with CD were resistant to ciprofloxacin, which could explain the initial treatment failure in our patient[10]. This study and our case may indicate the need to revise current Peruvian guidelines, which recommend the use of ciprofloxacin as first-line therapy for Oroya fever.

Additionally, the patient showed clinical features compatible with AAV. We considered the case as MPA due to clinical findings (livedo reticularis, low weight, myalgias, arthralgias, paresthesias), AKI, presence of positive p-ANCA, mononeuritis multiplex, absence of granulomas, asthma, and peripheral eosinophilia. Several infections, including IE, cause positive ANCA tests by indirect immunofluorescence but negative ELISA testing. Our patient presented with positive p-ANCA (by ELISA); thus, this finding was most probable because of an AAV[1,11]. Glomerulonephritis is the most frequent histological finding in this type of vasculitis; however, some cases may consist of interstitial nephritis without glomerular involvement, as shown in this patient[12]. Endocarditis can cause renal injury through several pathways, such as cortical necrosis and renal infarction (e.g., septic embolism), and due to antibiotic use (e.g., interstitial nephritis), but the most frequent finding is immune complex-mediated glomerulonephritis, characterized by AKI, hypocomplementemia, hematuria, and prominent endocapillary proliferation, among others. The absence of most of these characteristics in our patient made this diagnosis less probable[1].

In conclusion, this case report considers *B. bacilliformis* as a potential etiologic agent of IE in patients with conventional negative blood cultures and previous epidemiological exposure to an endemic area, and as a possible trigger for developing systemic vasculitis.

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Conflict of interest

The authors declare that there is no conflict of interest.

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