Case report

Fatal bacillary angiomatosis mimicking an infiltrative vascular tumour in the immune restoration phase of an HIV-infected patient

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Bacillary angiomatosis mainly affects the HIV-infected population. Information is limited on the evolution of bacillary angiomatosis during immune restoration following initiation of HAART. We report an unusual case of fatal Bartonella quintana bacillary angiomatosis occurring in an HIV-infected man during the immune restoration phase.

Introduction

Bacillary angiomatosis (BA) is a proliferative vascular disease caused by Bartonella quintana and Bartonella henselae that was first described in severely immunosuppressed HIV-infected patients [1]. Currently available HAART increases and maintains high CD4+ T-cell counts, thereby preventing most opportunistic infections. Nonetheless, when HAART is started in severely immunosuppressed patients, paradoxical worsening of a concomitant or subclinical infection can occur in the so-called immune reconstitution inflammatory syndrome (IRIS) [2,3]. We report the case of an HIV-positive man with Bartonella quintana BA that dramatically worsened in the phase of immune restoration after initiation of HAART.

Case report

A 44-year-old man was admitted to investigate a large laterocervical mass. He was an active smoker and former intravenous drug user, and had compensated chronic HCV infection; 6 months previously, he had presented with a toxic syndrome and laterocervical lymphadenopathies. At that time, he was diagnosed with HIV infection (CD4+ T-cell count 18 cells/mm³ and plasma HIV-1 viral load 325,000 copies/ml) and lymph node tuberculosis was suspected, although Ziehl–Neelsen (ZN) stain and culture for Mycobacterium tuberculosis from lymph node puncture material were negative. Tuberculostatic treatment was started, with an apparently good initial clinical response; 1 month later, the patient developed cytomegalovirus polyradiculopathy. Ganciclovir and antiretroviral therapy (abacavir, lamivudine and lopinavir plus ritonavir) were then started. Soon after, the cervical adenopathies increased in size. Thoracoabdominal computed tomography (CT) study and bone marrow analysis excluded lymphoproliferative neoplasm, and the clinical picture was interpreted as IRIS associated with tuberculosis. Corticosteroid treatment was added to the antiretroviral and antituberculosis therapies.

After 4 months, the patient was admitted again because of progressive growth of a laterocervical mass. The large, hard and painful mass had a cutaneous fistula and produced oropharyngeal dysphagia (Figure 1A). CD4+ T-cell count at that time was 33 cells/mm³ (3%), and viral load was below the detection limit. The cervical mass was punctured and hematic fluid was obtained. Standard bacterial cultures and ZN staining were negative, and cytologic study showed haemorrhagic material with no signs of malignancy. Local CT study depicted an infiltrative mass (craniocaudal and anteroposterior diameters of 15 and 9 cm, respectively) affecting the cervical soft tissue and vessels (Figure 1B). CT-guided biopsy of the mass resulted in severe bleeding that required application of a compressive bandage and blood transfusion; hence, further diagnostic punctures were contraindicated. Histological examination of the biopsy specimen showed granulation tissue and...
thrombosis in middle-sized blood vessels, with no evidence of malignant disease; periodic acid-Schiff (PAS) and ZN staining disclosed no microorganisms.

Arteriography was performed to define the vascularization of the mass and attempt selective artery embolization. The lesion was highly vascularized, mainly from the left external carotid artery (in the upper portion of the mass) and the left subclavian artery (in the lower external portion), and from the left vertebral artery. Because of this great vascularization, embolization was not feasible.

The patient experienced a fatal clinical evolution: extrinsic compression of the upper airway progressed, he did not respond to anti-inflammatory treatment (intravenous corticosteroids), and he died 25 days after admission due to respiratory failure. A post-mortem study was performed.

Macroscopic inspection at autopsy showed a large left laterocervical supraclavicular mass with a cutaneous fistula running deeply through the soft tissue to the peritracheal region. Histological examination documented vascular proliferation involving the subcutaneous soft tissue and lymph nodes, with extension to the peritracheal tissues. The vascular tissue was comprised of individual capillaries with occasional thrombosis and some anastomoses. ZN and PAS staining showed no microorganisms, and Warthin–Starry staining was inconclusive, disclosing only a few bacterial colonies on the skin surface. Further study by electron microscopy showed numerous extracellular microorganisms in association with fibrous long-spacing collagen, which were identified as *Bartonella* spp [4]. Blood was extracted, and isolation and purification of genomic DNA was carried out using the Qiagen DNA blood Mini Kit (Qiagen, Hilden, Germany) following the manufacturer’s instructions. The sample was analysed by PCR combined with reverse blot hybridization, which simultaneously targeted 16S rRNA and the 16-23S rRNA intergenic spacer of *Bartonella* [5]. *Bartonella quintana* was identified and later confirmed by *gltA* amplification and sequence analysis, as described previously, showing 100% similarity (GenBank accession number Z70014) [5]. Serological testing to detect *Bartonella* infection was not performed.

**Discussion**

*Bartonella* species are fastidious, gram-negative rods that are difficult to grow in conventional cultures. Therefore, the diagnosis of *Bartonella* infection is challenging and usually based on serological testing, specific tissue stains (for example, Warthin–Starry) and molecular assays (for example, PCR) [6]. In nature, *Bartonella* has a complex life cycle, involving reservoir hosts and various arthropod vectors, such as lice and fleas [7]. The broad spectrum of infections caused by *Bartonella* spp. includes characteristic clinical manifestations, such as BA and cat scratch disease, and presentations that are less specific, such as chronic bacteremia, endocarditis and meningoencephalitis [6,7].
BA is a proliferative vascular disease caused by *Bartonella quintana* or *Bartonella henselae*. It mainly affects the skin and lymph nodes, but can also involve several deep-seated organs such as liver and spleen [7]. HIV-infected persons, particularly those with CD4+ T-cell counts <200 cells/ul, are at risk for infection by *Bartonella* spp. In this population, the infection can persist for long periods and produce clinical relapses, but locally aggressive or atypical disease causing death, as occurred in the case presented, is uncommon [1,8].

IRIS developing after HAART initiation produces acute or exaggerated local inflammatory reactions and has been associated with paradoxical worsening of concurrent diseases, expression of subclinical pathologies, and atypical presentation of some illnesses. IRIS usually appears some days or weeks following the start of HAART, but can also be seen several months later. It has been well-described in association with some HIV-related diseases, such as tuberculosis, cryptococcal meningitis, and progressive multifocal leukoencephalopathy [2,3]. To the best of our knowledge, a relationship between BA and immune restoration after HAART initiation has only been reported in a single case, in which bacillary splenitis occurred during the immune restoration phase [9].

Our patient exhibited gradual, locally aggressive progression of cervical BA that resulted in death due to extrinsic upper airway compression. Concurrent neoplasm or tuberculosis with *Bartonella* infection has been described in lymph node biopsy samples [10]. However, the fact that *Mycobacterium tuberculosis* was not identified in the first or subsequent samples and the presence of *Bartonella* at the last hospital admission suggest that *Bartonella* infection had been the cause of lymph node enlargement since the onset of disease. Along this line, it is possible that the initial improvement with antituberculosis therapy was related to the known activity of rifampin against *Bartonella* [11]. The manifestation of BA as angiomatous skin lesions is well-described, but to our knowledge, it is unusual for this infection to mimic an infiltrative, vascular tumour [12]. The timing of worsening of the cervical mass (4 months after HAART initiation) in the presence of a strong viral response to HAART and a small increase in CD4+ T-cell count (probably due to corticosteroid therapy), support the presence of an immune restoration syndrome. Overall, we believe that the unusual presentation of BA in this case and the common difficulty in diagnosing *Bartonella* infection are likely related to the patient’s fatal outcome.

In conclusion, we present a fulminant presentation of BA as a manifestation of IRIS in a patient in whom undiagnosed *Bartonella quintana* nodal disease was likely present since the onset. Physicians should be aware that new, severe clinical presentations of opportunistic infections can emerge in the context of immune restoration. In this particular situation, development of an aggressive vascular tumour should include BA in the differential diagnosis.

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**Disclosure statement**

The authors declare no competing interests.

**References**