Pleural and extradural spinal involvement in a patient with systemic bartonellosis

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ABSTRACT

Bartonella henselae is a gram-negative pleomorphic fastidious bacillus that predominantly affects the pediatric population. Its best-known clinical manifestation is cat scratch disease (CSD), which is initiated by inoculation of the bacterium through feline saliva, its main reservoir.

The clinical spectrum of *Bartonella henselae* infections is broad; fever with lymphadenopathy is the most frequent presentation, usually self-limited. Despite the availability of specific serological tests, a delay in diagnosis is common, especially in cases with unusual manifestations.

This paper aims to describe an atypical form of systemic bartonellosis with lymph node, pleural and extradural spinal involvement in a pediatric patient.

Keywords: Bartonella henselae; cat scratch disease; fever of unknown origin; pediatrics.

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INTRODUCTION

Bartonella henselae (BH) is a pleomorphic, fastidious, gram-negative bacillus that primarily affects children. The typical clinical presentation is cat scratch disease (CSD), which begins with inoculation of the bacterium present in feline saliva through biting or scratching. Cats are the main reservoir and acquire it from the flea *Ctenocephalides felis*.^{1,2} Subsequently, a brownish-red papule appears at the site of contact, accompanied by lymphadenopathy in 85-90% of cases, with a tendency towards self-limited resolution.³ Cervical and axillary lymphadenopathy are the most common forms constitutional symptoms such as fever, asthenia, nausea, and abdominal pain⁴ are frequent.

The clinical spectrum of Bartonella henselae infections is vast and includes osteomyelitis, optic neuritis, oculoglandular syndrome of Parinaud, encephalitis, endocarditis, and hepatosplenic disease. In immunocompromised patients, severe systemic disease may develop after infection, termed bacillary angiomatosis.⁵

We present the case of a pediatric patient who developed atypical bartonellosis with lymph node, pleural and extradural spinal involvement.

CLINICAL CASE

A 6-year-old female patient, previously healthy, attended a tertiary care center for a medical history of 10 days of evolution characterized by fever, pain, and a tumor on the anterior aspect of the right thigh. She was undergoing treatment with cephalexin on the ninth day, as indicated in another institution. He reported sporadic contact with cats. On admission, the patient was evaluated in good general condition, febrile (38 °C) with spontaneous pain in the anterior aspect of the right thigh, intensity 8/10. She associated a painful dorsal tumor on palpation, rigid and elastic at the level of D6, with no

other noteworthy data on physical examination. Admission weight was 22.5 kg (PC 75-90).

On admission, the patient had elevated acutephase reactants, with a C-reactive protein (CRP) level of 33.7 mg/L, an erythrocyte sedimentation rate (ESR) of 76 mm/h, and leukocytosis with 11,770 white blood cells, predominantly neutrophils. Blood cultures were negative, and both the chest X-ray and abdominal ultrasound had normal results. The inguinal Doppler ultrasound revealed an oval-shaped lymph node with a homogeneous echostructure, exhibiting a marked increase in vascularization on color Doppler examination, with the most significant dimension measuring 16 mm in its short axis and increased echogenicity of the surrounding subcutaneous cellular tissue. Muscular planes had no alterations.

With a diagnosis of lymph node adenitis, treatment was started with clindamycin 30 mg/ kg/day and ceftriaxone 80 mg/kg/day. The girl remained febrile, with 3-4 daily fever registers, showing no improvement in the described lesions. As a differential diagnosis of prolonged fever and adenitis with poor response to treatment, a tuberculosis work-up was initiated, which was negative (gastric lavage, purified protein derivative [PPD], and chest X-ray reported normal); associated immunodeficiencies were evaluated with negative serology for human immunodeficiency virus (HIV) and determination of immunoglobulins and lymphocyte populations within normal parameters. Additionally, determinations were performed to evaluate the trends of reactants and hemograms (Table 1). To rule out any impact on target organs, an echocardiogram and fundus examination were performed, which revealed normal results.

On the seventh day of hospitalization, the patient was admitted to the hospital.

The result of IgG BH serology (IFA)

TABLE 1. Evolution of laboratory parameters during hospitalization with a decrease in reactants after surgery

	Admission	Day 6	Pre-drainage	Post-drainage	At discharge (day 42)
White blood cells 10 ⁹ /L	11 770	15 950	13 100	8970	6040
Neutrophils %	52	63	68	44	35
Lymphocytes (%)	33	23	22	39	47
Hemoglobin g/dL	11	11	10.3	10.5	10.9
Platelets 10%L	329	339	469	485	390
CRP mg/L	33.72	70.89	71.57	21.84	1.77

CRP: C-reactive protein.

was positive with a titer greater than 1:512. Azithromycin 10 mg/kg/day was added to the treatment.

Given the persistence of fever and intermittent pain at the T5-T6 level on day 20 of intravenous antibiotic treatment, spinal magnetic resonance imaging (MRI) was requested. It showed in the right paraspinal plane, dorsal to T5 to T8 tissue, with heterogeneous signal, iso-hyperintense to IV contrast, in T1, T2, and STIR sequences, with extension to the spinal canal through the neuroforamen at T7-T8 and the homolateral hemithorax. At the paraspinal level, it showed an isointense collection to CSF. In the intracanal location, it presented a granulomatous aspect, with an extradural location that displaced and compressed the dural sac, resulting in a slight reduction in the diameter of the medullary cord. In the intrapleural segment, small granulomatous collections were evidenced (Figure 1).

Given the poor clinical evolution and the persistence of both lesions, a multidisciplinary decision was made between the Clinical, Infectious Diseases, General Surgery, and Neurosurgery Departments to drain the inquinal lesion first, as it was easier to treat. During the procedure, abscessed adenopathy was evidenced in the right thigh. A culture was taken (with no microorganism growth), and the pathological anatomy described a granulomatous infiltrate with areas of central necrosis and palisaiding histiocytes. Negative stains: Grocott technique and Ziehl Nielsen technique. CD68 immunohistochemistry: granular cytoplasmic positive in histiocytes. Highlight granulomas CD20: membrane positive in B lymphocytes. Non-contributory Warthin Starry technique (nonspecific background marking).

After drainage of the lesion, the patient became afebrile and experienced a marked



FIGURE 1. Magnetic resonance imaging of the thoracic spine (T2 sequence with gadolinium)



A. Sagittal view. An extradural paraspinal lesion is observed from T5 to T8, presenting an isointense signal to cerebrospinal fluid (red arrow), with a granulomatous appearance.

B. Sagittal section. There is a pleural lesion with a granulomatous aspect, characterized by small internal collections (green arrow). The adjacent parts present diffuse borders with a hyperintense signal.

C. Axial section at the level of T7. The right vertebral pedicle and its posterior arch have a heterogeneous hyperintense signal (red arrow). There is a pleural lesion with a granulomatous aspect, characterized by small internal collections (green arrow). The adjacent parts present diffuse borders with a hyperintense signal.

improvement in acute-phase reactants. The patient remained expectant regarding the extradural and pleural collections, as there were no signs of spinal cord compression or respiratory compromise. She underwent a total of 42 days of treatment with intravenous ceftriaxone, and after drainage, trimethoprim-sulfamethoxazole was added to the treatment, and hospital discharge was granted. In the last control, one month after completing oral antibiotic therapy (she received 60 days of antibiotic treatment), a new MRI was performed, which showed total resolution of the paraspinal and intrathecal collections, as well as the inflammatory changes previously described in studies. Figure 2 highlights the main milestones of the clinical case.

FIGURE 2. Timeline

DISCUSSION

The Bartonella henselae serotype is responsible for the highest percentage of bartonellosis. Although contact with felines is relevant, the absence of such contact does not rule out the pathology. The pathogenic characteristics of human infection vary substantially according to the immunologic status of the host. CSD in immunocompetent individuals is typically self-limiting, characterized by fever and lymphadenopathy proximal to the site of inoculation. The systemic manifestation of bartonellosis comprises 2-10% of cases and may or may not be accompanied by lymphadenopathy.² The most frequent symptom is a prolonged fever,

Admission Fever of 10 days' duration, with pain and a tumor on the right thigh.	First studies CBC with elevated APR. Abdominal ultrasound: NL. Altered inguinal Doppler ultrasound. First diagnosis: lymph node adenitis. Start ceftriaxone, clindamycin, empirical.	Second phase of studies Persists febrile. Extension of studies with TBC, HIV serology, determination of GAME, and lymphocyte populations. Serology IgG <i>Bartonella</i> <i>henselae</i> . Start azithromycin.	Second phase of imaging studies Access to the MRI study is evaluated for pleural and extramedullary involvement.	Multidisciplinary meeting Admission to the operating room is decided to collect a sample from the thigh. Clinical improvement of the patient. TMS is started.	Discharge Hospital discharge with indication for TMS.	Follow-up She complied with TMS treatment for 60 days. Control with MRI in the second month of control: no inflammatory processes are evidenced.
Admission	Day 1	Day 4	Day 16	Day 22	Day 42 Day 42	Day 134 discharge

PR: acute phase reactants; NL: within normal limits; TBC: tuberculosis; HIV: human immunodeficiency virus; GAME: gamma globulins G, A, M, and E; IgG: immunoglobulin G; MRI: magnetic resonance imaging; TMS: trimethoprim sulfamethoxazole.

often accompanied by other symptoms such as myalgias, arthralgias, and malaise. The organs involved include the eyes, reticuloendothelial system, bones, heart, lungs, and skin. The expected histopathological findings vary according to the disease and the host. The typical pathologic anatomy of CSD lymphadenopathy reports irregular necrotic granulomatous changes with stellate microabscesses. However, a recent pathologic study of molecularly confirmed cases of CSD by PCR showed that only 57% had microabscesses, while 92% had necrotic granulomas. Both characteristics coincide with the anatomopathological report of our patient.^{1,6} Given the high prevalence of tuberculosis in our country, this differential diagnosis should always be taken into account in patients with prolonged fever associated with adenopathies.⁷ During the physical examination, it is essential to examine the skin in search of animal bites or scratches that may help us to guide the diagnosis.⁸

Specific diagnosis is made by serology or polymerase chain reaction. Most available serological tests have a sensitivity of 88-95% and a specificity of 97-99%. IgG BH titers >1:512 are indicative of recent infection, even in the absence of positive IgM. IgG titers <1:64 can be maintained for extended periods (up to 6 months following cure of the disease).⁴ The reported patient met IgG serologies greater than 1:512 dilution. Cultures of the material obtained from the drainage had no germ rescue, likely due to antibiotic treatment.

Treatment depends on the presentation. According to the guidelines established by the U.S. Centers for Disease Control and Prevention, antibiotics may not be necessary for the treatment of GSD because it is self-limiting. However, antibiotic therapy is suggested for atypical presentations. A pediatric study by Scolfaro et al, describes that administration of macrolides or a combination antibiotic therapy regimen for 2 to 3 weeks resulted in rapid clinical improvement. Commonly recommended antibiotics include macrolides (such as erythromycin, azithromycin, and clarithromycin), fluoroquinolones (such as ciprofloxacin), trimethoprim-sulfamethoxazole and doxycycline.9 Rifampicin and gentamicin showed utility in the treatment of hepatosplenic presentation in children, as indicated by the research of Arisov et al.¹⁰

To date, no randomized controlled studies have evaluated the effectiveness of treatment in atypical forms or estimated the duration of treatment. It is crucial to consider prescribing azithromycin to patients with extensive lymphadenopathy or to shorten the course of the disease.¹¹

Regarding the surgical resolution of thigh involvement, the literature suggests that an excisional biopsy can be performed if lymphadenopathy persists or if the diagnosis remains unclear, even in patients who have already received antibiotic treatment.¹² Individuals who develop disseminated disease are the the candidates for the initial antimicrobial therapy.^{13,14}

It is essential to conduct further studies comparing the proposed therapeutics to enhance the progression of the cases. Systemic bartonellosis should be included in the pediatrician's differential diagnosis repertoire for accurate detection and treatment.

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