Leukocytoclastic Vasculitis, Erythema Nodosum and Large Cervical Lymphadenopathy Associated with Bartonella Henselae Infection in an Adolescent

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Abstract

Typical Cat Scratch Disease (CSD) usually presents with isolated mild lymphadenopathy. An atypical case of this disease is reported with large cervical lymphadenopathy associated with recurrent leukocytoclastic vasculitis and erythema nodosum. This unusual presentation of cat scratch disease suggests that systemic manifestations of this infection can occur in immunocompetent individuals and that long antibiotic treatment for prolonged large cervical lymphadenopathy may be needed.

Key words: Leukocytoclastic vasculitis, erythema nodosum, lymphadenopathy, Bartonella henselae

Introduction

Cat Scratch Disease (CSD) is generally a self-limited, regional lymphadenopathy after contact with a cat, but a wide spectrum of other clinical manifestations can occur [1]. We report the case of an adolescent girl with different dermatologic manifestations along with lymphadenopathy as a result of an exaggerated immune response to Bartonella antigens. Although typical cat scratch disease is a self-limited illness and shows no benefit with antibiotic therapy, in atypical forms a prolonged antibiotic therapy may be required.

Case Report

A previously healthy 13-year-old girl visited the emergency room because of repeated episodes of purpuric lesions in the lower limbs which were suggestive of Henoch-Schölein purpura (HSP). After 3 months from the onset of the skin lesions and coincident with the third episode, a biopsy was performed showing leukocytoclastic vasculitis (Fig. 1). Three months later, the girl was admitted because of new skin lesions, which were consistent with erythema nodosum lesions on the anterior surface of both legs and large cervical lymphad-
enopathy without fever. She was born in Ecuador and had lived in Spain since the age of 9 years. She had a dog in the house, but no cats. At admission, the physical examination revealed large bilateral cervical lymphadenopathy (4 cm), without hepatomegaly or splenomegaly (Fig. 2). The laboratory test showed an increased erythrocyte sedimentation rate (77 mm/hour) and normal C reactive protein (3.3 mg/L). The total leukocyte count was 8.810 (neutrophil 6.120), hemoglobin 11.8 g/dl, and platelets were 180.000. C3 and C4 were normal. Serum angiotensin converting enzyme was normal. Polyclonal hypergammaglobulinemia was observed (IgG 2660, IgA 205, IgM 132 mg/dl). ANA was negative. Serologies were negative for toxoplasmosis, HIV, HCV, and brucella. CMV and Epstein Barr serology showed past infection (VEB IgG VCA positive and EBNA positive). Bartonella Henselae IgM was negative, and IgG positive (1/64). Pharyngeal culture was negative. Protein purified derivate (PPD) was negative. Chest x-ray and abdominal ultrasonography were normal. Cervical ultrasonography showed non-specific enlargement lymphadenopathies of 3 cm in diameter. Fine-needle aspiration biopsy from the enlarged cervical node yielded chronic lymphadenitis. Bacterial culture of the sample was negative. Polymerase Chain Reaction (PCR) of Bartonella and PCR of Mycobacterium in the material were negative. A second serology for Bartonella henselae, one month later of the first one, showed seroconversion with an increase in titers of IgG from 1/64 to 1/256. Treatment was started with azithromycin at a dose of 10 mg/kg during 5 days, with persistence of enlargement of lymphadenopathies during 4 months. Because of no recovery, a cervical lymphadenopathy was excised for histology. A fragment of a 3 x 1.5 x 1cm enlarged lymph node with a white capsule was obtained. Microscopic study showed non-necrotizing granulomas. A longer course of azithromycin treatment was given for 3 months. In the last visit, cervical lymphadenopathy was normal in size and erythema nodosum disappeared, as well as laboratory parameters (with no clinical recurrences) and normal laboratory parameters, including immunoglobulins, one year later.

Discussion

This case illustrates possible dermatologic manifestations associated with cat scratch disease. The first manifestation of this disease concerned purpuric lesions in the lower limbs resembling Shölein-Henoch disease, confirmed as leukocytoclastic vasculitis by biopsy that was done due to the long du-
ration of the lesions and recurrence. Bartonella infection has been described as a possible triggering infection agent leading to Sholien-Henoch disease, although there are controversial data in the literature [2]. Leukocytoclastic vasculitis is generally regarded as a hypersensitivity reaction to infection, drugs, malignancy, and other triggers. In our case the leukocytoclastic vasculitis occurred before seroconversion of Bartonella, so we cannot be sure that these lesions are a consequence of the Bartonella infection.

After the presentation of these dermatologic lesions, large cervical lymphadenopathy was observed, with laboratory findings of an increased erythrocyte sedimentation rate and hypergammaglobulinemia with positive serology for Bartonella henselae. Since the pathology of the lymphadenopathy yielded non-necrotizing granulomas, a broad differential diagnosis was made including other infectious agents, such as toxoplasma, brucellosis, and atypical mycobacteria, and non-infectious disease, such as hematological and solid-organ malignancies that were all ruled out [3]. The typical pathology of cat scratch disease usually shows granuloma with central necrosis, multinucleated giant cells, and microabscesses. In our case the histology was nonspecific of cat scratch disease. PCR for Bartonella henselae was performed with a negative result. PCR results may be dependent on the duration of the illness and are positive during the first 6 weeks. In our case, PCR was carried out at six weeks of the beginning of the disease, which might explain the negative result [4]. The diagnosis of CSD is based on a combination of clinical, epidemiological, serological and histological data, so an algorithm for diagnosis has been proposed with the results of the biopsy [5]. The serology of CSD is interpreted as positive when enzyme immunoassay or indirect fluorescent antibody assay titers are higher than 1/64 for Bartonella henselae or a fourfold rise in titer between the acute and convalescent sera is observed. In our case there was a seroconversion with an increase in titers from IgG 1/64 to 1/256 after a 4-week interval. Early serologic and molecular testing for CSD in children may preclude performing unnecessary interventions [6]. Although CSD is usually described with a history of contact with kittens, we present a case in which contact with a dog was observed. Domestic dogs as well as cats may serve as a reservoir of B. henselae [7]. CSD is a common cause of chronic lymphadenopathy in children, with the lymph node enlargement usually spontaneously resolving within 9 weeks, but rarely lasting up to 12 months; therefore, surgical treatment is unnecessary and it may indicate and provide a confirmatory diagnosis or help to rule out other potentially severe conditions.

Another interesting finding in our patient was erythema nodosum. Erythema nodosum has been previously described in adolescent patients with lymphadenopathies in association with CSD, like our case. This may represent a delayed hypersensitivity reaction to CSD antigens. In one published case of erythema nodosum and lymphadenopathy, the treatment was prolonged with antibiotics along with surgical drainage until the resolution, as in our case [8]. We do not know what the spontaneous outcome would have been in our case, but no improvement was observed in the first 4 months. Only after the prolonged antibiotic treatment for 3 months had a gradual improvement been observed with complete disappearance of the dermatologic lesions, resolution of the lymphadenopathy enlargement, and no recurrences after one year of following. In addition, all laboratory values had become normal at the last visit.

CSD in an immunocompetent patient is generally self-limited, but antimicrobial agents are used for the treatment of acutely or severely ill patients with systemic symptoms. Trimethoprim-sulfamethoxazole, rifampicin, erythromycin, clarithromycin, azithromycin, doxycycline, ciprofloxacin, and gentamicin are among the active agents. Azithromycin therapy provided clinical benefit in achieving appreciable reduction of the affected lymph nodes during treatment [9]. No corticosteroids were used, which has been suggested for some patients with long-lasting CSD [10].

In the study of a child with large lymphadenopathies, leukocytoclastic vasculitis and erythema nodosum, the etiology of Bartonella henselae must be investigated. The selection and duration of the antibiotics remain unknown and should be individualized, but prolonged treatment may be beneficial. In atypical cases of CSD, a prolonged course of antibiotics may be indicated. The selection and duration of the antibiotics remain unknown and should be individualized. CSD patients have been described with a history of contact with kittens,
although dogs can also transmit the disease. Nowadays, there is a widening spectrum of Bartonella henselae infection manifestations, due to the improvement in diagnostic techniques. A high index of suspicion of CSD is necessary in atypical cases in order to prevent the eventual complications of the disease.

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**References**