Cat scratch disease in a child with sickle cell anemia

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Abstract

Objective: Cat-Scratch Disease (CSD) manifests as a painful regional lymphadenopathy, occurring after cat scratch or bite, being transmitted by the bacterium Bartonella henselae. The diagnosis is given by the biopsy or puncture of affected lymph nodes, which must be submitted to histopathology, serology or PCR (preferable). Case report: an 8 years old male child presented progressive, painful, right supraclavicular adenomegaly, in the absence of systemic symptoms. He reports prior contact with domestic cat. Cervical and supraclavicular USG showed nodular images corresponding to lymph nodes. HIV, toxoplasmosis, EBV, CMV, Bartonella henselae and VDRL serologies were negative. The patient underwent a biopsy of supraclavicular lymph node, which suggested CSD as the primary diagnosis. We opted for the outpatient treatment with azithromycin. He was re-evaluated after two weeks, and there was regression of symptoms. Discussion: This case illustrates a typical evolution of CSD, in which a scholar was seized by subacute cervical lymphadenopathy with positive epidemiological history and negative serology for Bartonella. The serologic testing excluded other causes of lymphadenopathies more common in this age group. The good general condition despite the pronounced adenomegaly without signs of toxemia, is characteristic of CSD. Conclusion: The lack of more accurate laboratory tests, the difficulty in cultivating the pathogen and the need for histopathology hinder the quick diagnosis of CSD and contribute to the non-recognition of this disease. Bartonella henselae research should be considered in tracking lymphadenopathy, especially if subacute evolution as in this patient.

Keywords: anemia, sickle cell, cat-scratch disease, lymphadenitis, primary treatment.
INTRODUCTION

Cat scratch disease (CSD) is a relatively common disease in the United States, representing the leading cause of infant chronic (duration equal or longer than three weeks) lymphadenopathy.

There is no CSD incidence estimation for the Brazilian population, although the increased presence of domestic cats in homes indicates growing indexes. In Brazil, few cases have been reported, probably due not to a low incidence, but because diagnostic tests for this disease are not included in differential diagnostic panels for several other clinic syndromes\(^3\,^4\). Therefore, it is of great importance to understand CSD various forms of clinical manifestations to further assess its real incidence in the Brazilian population.

Bartonella henselae bacteria is the primary etiological agent for CSD. Young cats (less than 12 months old) are the largest infection source because they are often asymptomatic. Furthermore, it is speculated that these bacilli bacteria are part of the feline oral microbiome, which is transferred to their claws through licking.

Bartonella has been isolated from fleas and it has been shown that the disease it causes is transmitted intraspecifically from cat to cat, but not interspecifically from cat to humans. About 95% of CSD patients have previous history of cat scratch, 4% of dog bite or scratch, and 1% has previous history of contact with these animals\(^4\).

CSD, which is also known as bartonellosis, manifests as a regional and painful lymphadenomegaly of sub-acute duration after the cat bite or scratch. In some cases, a generalized adenopathy occurs. Three to five days after the scratch or bite, an ephemeral papule appears, subsequently it evolves to a pustule and then to a crust. These lesions are associated with localized and painful adenopathy, that eventually suppurates, in lymph nodes responsible for the drainage of the scratched region.

General symptoms such as fever and anorexia are frequent, and if the disease is not identified and treated, the lymphadenopathy can persist for months. Encephalitis, meningitis, hepatitis, and disseminated infections are rare forms of this disease\(^1\,^4\).

In this study we report a clinical case of a pediatric patient diagnosed for CSD, and discuss issues concerning its epidemiology, differential diagnostic tests, and treatment.

CASE REPORT

J.W.G. F, a 7 years and 10 months old male patient, presented progressive tumoration process in the right supraclavicular region, painful upon palpation only, associated with weight loss, absence of fever, and worsening of the clinical state. Patient had no previous history of infections, diseases, or vaccination before nodule emergence. Appetite was unaffected, but there was agitation during sleep.

After tumoration discovery, patient was submitted to medical evaluation with requisition of cervical and right supraclavicular ultrasound imaging. Multiple ultrasound images from both regions evidenced hypoechoic nodules of varying sizes; the largest nodule had 2 cm, which matching lymphadenomegaly criteria. In the view of tumoration progression, patient was hospitalized at the Pediatrics Infirmary from the University Hospital affiliated to the Federal University of Juiz de Fora.

The child also presented history of prematurity and low birth weight, and suffered from sickle cell anemia diagnosed during newborn screening, with basal hemoglobin levels of 8 g/dL. At the time of this study, he was taking folic acid at 5 mg/day and hydroxyurea at 500 mg/day. Patient never had allergies and surgeries but he had multiple hospitalizations previously due to pain crises, in addition to three episodes of urinary tract infection. Patient reported contact with dog, horse and parrot, besides previous contact with a domestic cat. He did not report previous trips and his vaccines were up to date.

On physical examination, patient had a weight of 19.9 kg (z score 0/-2) and a height of 117 cm (z score 0/-2). He was in good general condition, hydrated, and had a healthy skin tone. Patient showed lymph nodes of fibroelastic consistency, mobile and painless in the submandibular, anterior cervical, bilateral axillary and bilateral inguinal regions, in addition to the right supraclavicular lymphadenomegaly of approximately 3 cm, that was painful and mobile. In the cardiac auscultation, rhythm was regular in two periods, with normal sound intensity and early systolic murmur (+ +/6 +). Liver was palpable at 2 cm from the right costal margin while spleen was not palpable.

Remainder of the physical examination without abnormalities.

Laboratory tests results are shown on Table 1. Some of the abnormalities found that matches chronic hemolytic anemia included increase of indirect bilirubin, lactic dehydrogenase, and reticulocytes count, in addition to red blood cells morphological alterations.

New ultrasound examination revealed multiple cervical lymph nodes, which were reactive, bilateral, and more exuberant to the right, suggesting a systemic disease. Furthermore, abdominal ultrasonogram showed a reactive mesenteric lymph node. Serological results performed as differential diagnostic tests are shown on Table 2.

Patient was submitted to the excision biopsy of the right supraclavicular lymph node, which histological analysis revealed a granulomatous pattern lesion composed of small epithelioid granulomas with the presence of rare multinucleated giant cells and a minor focus of necrosis (Figure 1).

Specific fungi and BAAR staining tests were negative, suggesting CSD as the main diagnostic hypothesis. Although Bartonella henselae serological result was negative, pathological examination suggested cat scratch disease. Thus, we started an ambulatory treatment with azithromycin for five days, at 10 mg/kg on the first day and 5 mg/kg on the...
Table 1: Results of the laboratory tests on the date of the hospitalization.

| Test               | Result               | Test               | Result       |
|--------------------|----------------------|--------------------|--------------|
| Hematimetry        | 2.13 millions/mm³    | ESR 1st hour       | 36 s         |
| MCV                | 94.1 fL              | ESR 2nd hour       | 62 s         |
| MCH                | 34.9 pg              | Sodium             | 136 mEq/L    |
| MCHC               | 37.0 g/dL            | Potassium          | 4.2 mEq/L    |
| RDW                | 16.7 %               | Total calcium      | 8.4 mg/dL    |
| Hemoglobin         | 8.03 g/dL            | Ionic calcium      | 4.09 mg/dL   |
| Hematocrit         | 29.7 %               | Magnesium          | 2.1 mg/dL    |
| Leucocytes         | 12100 /mm³           | Phosphorus         | 4.4 mg/dL    |
| Banded neutrophils | 4 %                  | Ureia              | 12 mg/dL     |
| Segmented neutrophils | 44 %               | Creatinine         | 0.4 mg/dL    |
| Eosinophils        | 8 %                  | Total protein      | 8.1 g/dL     |
| Monocytes          | 8 %                  | Albumin            | 4.1 g/dL     |
| Lymphocytes        | 34 %                 | GOT                | 52 U/L       |
| Platelets          | 481000 /mm³          | GPT                | 30 U/L       |
| Reticulocytes      | 11 %                 | Total Bilirubin    | 1.9 mg/dL    |
| Lactic dehydrogenase | 1016 U/L          | Direct Bilirubin   | 0.4 mg/dL    |
|                    |                      | Indirect Bilirubin | 1.5 mg/dL    |

MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; RDW: red blood cell distribution width (anisocytosis index); ESR: erythrocyte sedimentation rate; GOT: glutamic oxaloacetic transaminase; GPT: glutamate-pyruvate transaminase.

Table 2: Serological tests results performed as differential diagnostic tests.

| Test                  | Result   | Interpretation   |
|-----------------------|----------|------------------|
| Cytomegalovirus       | IgG > 250 | reactive         |
|                       | IgM 0.4  | non-reactive     |
| Toxoplasmosis         | IgG 0.02 | non-reactive     |
|                       | IgM 0.06 | non-reactive     |
| Epstein-Barr Virus    | IgG 208.0| non-reactive     |
|                       | IgM      | non-reactive     |
| Anti-HIV I and II     | IgG 0.2  | non-reactive     |
|                       | IgM      | non-reactive     |
| Bartonella henselae   | IgG Less than 1/5 | negative |
|                       | IgM Less than 1/320 | negative |
| VDRL                  | -        | non-reactive     |
| Paracoccidioidomycosis| -        | non-reactive     |

following four days. Two weeks later, patient was evaluated and presented almost complete involution of the cervical lymphadenomagaly, besides a good general condition.

DISCUSSION

This case illustrates a typical progression of CSD, in which an infant student presented cervical lymphadenomagaly with subacute duration and positive epidemiological history, but *Bartonella henselae* negative serology. Serological screening excluded other adenitis causes, which are more common in this age group. CSD diagnose investigation followed some exclusion criteria, since this hypothesis was suggested based on its prolonged progression.

Diagnosis are performed based on clinical and epidemiological data, as well as microbiological tests as Gram stain and cultures of secretion collected either from lymph node puncture guided by ultrasound imaging, or from externalized secretions from suppurred lymph nodes. Unfortunately, *Bartonella* has a poor growth yields in routine culture methods. The criteria proposed by Margileth for matching clinical manifestations are also very useful for the CSD diagnosis (Chart 1)\(^5,6\). In the case reported here, there was a history of contact with a cat, although there were no reports of scratches or bite. In this situation the diagnosis depends on a high levels of suspicion. Clinically, several signs and symptoms matched with CSD. The fact that the patient was doing well, despite the pronounced lymphadenomagaly, and showed no toxemia signs was also typical of CSD.

Usually, CSD patients are under the age 20 (80% of cases), and are mostly males. A week or two after the cat scratch there is an incubation period of three to 30 days, and then, at the site of inoculation, one or more erythematous papules appear usually in exposed areas. These papules rapidly progress into vesiculopustular lesions.
was found without signs of local phlogosis. Systemic signs were not observed, and lymphadenomegaly granuloma giant cells, resulting in the typical palisading necrotizing abscess, forming a halo of epithelioid cells with rare Langhans are increased, neutrophils become fragmented, and there migrating from the cortex to the medulla. Then, necrotic foci agglomerates appear first below the subcapsular sinus, accumulation of amorphous intercellular proteinaceous material. Lymph node architecture, in addition to macrophages activity and alterations consist of follicular hyperplasia with slight distortion of lymph nodes alterations, they are not pathognomonic. Early exclude other etiologies. Despite the consistency of histological necrotizing lymphadenitis and lymphomas. Serological studies, tuberculosis, lymphogranuloma venereum, tularemia, Kikuchi bacterial suppurative lymphadenitis, fungal lymphadenitis, days to five weeks, and are directly related to suppuration of such as anorexia, nausea, chills, adynamia and moderate fever occur in 60% of cases. Febrile episodes last from three days to five weeks, and are directly related to suppuration of ganglions. In the case herein reported, primary lesion and systemic signs were not observed, and lymphadenomegaly was found without signs of local phlogosis.

Biopsy is one useful method to diagnose CSD and to exclude other etiologies. Despite the consistency of histological lymph nodes alterations, they are not pathognomonic. Early alterations consist of follicular hyperplasia with slight distortion of lymph node architecture, in addition to macrophages activity and accumulation of amorphous intercellular proteinaceous material.

Microabscesses with focal necrosis and neutrophils agglomerates appear first below the subcapsular sinus, migrating from the cortex to the medulla. Then, necrotic foci are increased, neutrophils become fragmented, and there is fibrin accumulation. Finally, macrophages surround the abscess, forming a halo of epithelioid cells with rare Langhans giant cells, resulting in the typical palisading necrotizing granuloma. Histological differential diagnostic tests include other bacterial suppurative lymphadenitis, fungal lymphadenitis, tuberculosis, lymphogranuloma venereum, tularemia, Kikuchi necrotizing lymphadenitis and lymphomas. Serological studies, specific Bartonella stainings and molecular studies may be needed to distinguish these conditions.

The choice treatment is azithromycin administration for five days. Although the disease is self-limiting, the antibiotic reduces the symptoms and the risk of its progression to more severe forms.

The patient whose case was reported here suffered from sickle cell anemia, a chronic condition with high morbidity, which main acute complications are vaso-occlusion crises. To our knowledge, there are no CSD cases in sickle cell disease patients reported in the literature. Nonetheless, since CSD is an infection disease, it could be used in differential diagnostic tests as an alternative cause of fever and pain crises in these patients. This possibility increases the importance of early CSD diagnosis and treatment.

CONCLUSION

In sum, the lack of additional more accurate tests, the pathogen cultivation low yields under routine conditions, and the need of histopathological studies difficult CSD diagnosis, contributing to the unawareness about this disease. This case illustrates the importance of Bartonella henselae agent in lymphadenomegaly etiology. The search for B. henselae should be considered in the diagnostic screen tests, especially when disease duration is subacute, as it was in the case reported in this study.

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