Cat-scratch disease, ¿does it always present with lymphadenopathy?: A case report

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Abstract
Cat-scratch disease (CSD) is a zoonotic disease, caused by Bartonella henselae, a gram-negative bacillus, that has a variable clinical presentation and must be suspected in immunocompetent patients or immunocompromised patients with prolonged febrile syndrome of unknown origin that have history of interaction with cats. Diagnosing CSD may be challenging, so clinical suspicion and a thorough clinical interview and workup are essential to come up with a definitive conclusion. Typically, CSD presents with regional lymphadenopathies and subsequent systemic compromise. However, it can present with a unique manifestation such as hepatosplenic compromise. Herein, we present a patient with prolonged febrile syndrome with systemic symptoms and reticuloendothelial compromise.

Key words: Bartonella henselae, cat-scratch disease, hepatosplenic abscesses, prolonged febrile syndrome

Enfermedad por arañazo de gato, ¿siempre se presenta con adenopatías?: A propósito de un caso

Resumen
La enfermedad por arañazo de gato es una zoonosis, ocasionada por la bacteria Bartonella henselae, con presentación clínica variable y se debe sospechar en pacientes inmunocompetentes e inmunocomprometidos con síndrome febril prolongado o sin foco claro que hayan tenido contacto con gatos; esta es una enfermedad infecciosa de difícil diagnóstico por lo que requiere alta sospecha clínica y minuciosa anamnesis. Se presenta de forma común con afectación ganglionar y posterior compromiso sistémico. Sin embargo, se puede encontrar afectación hepatoesplénica como único hallazgo. A continuación, presentamos un caso de un paciente con fiebre prolongada, síntomas sistémicos y afectación reticuloendotelial.

Palabras clave: Bartonella henselae, enfermedad por arañazo de gato, abscesos hepatoeplénicos, síndrome febril prolongado.

Objective
The objective of this report is to remember about the existence of this pathology and the atypical forms of its presentation; encourage clinical suspicion and raise awareness about the importance of having differential diagnoses and the development of a complete medical history when approaching a patient because this fully determines the recovery or development of complications.

Introduction
Cat-scratch disease (CSD) is a zoonotic bacterial disease, generally benign and self-limited that causes chronic lymphadenopathies or a wide variety of clinical manifestations. It is also known as one of the etiologies of prolonged febrile syndrome. CSD can be present in either immunocompetent or immunodeficient patients. It is caused by a non-mobile, facultative anaerobe, gram-negative, intracellular bacillus.
known as *Bartonella henselae* that is really hard to isolate in a bacterial culture. CSD was firstly named in 1950 by Debré et al., and was firstly associated as an infectious etiology in 1983 with the identification of the bacillus in a lymph node biopsy with Warthin-Starry stain.

CSD is present worldwide, reporting approximately 24,000 cases annually in the United States. In Colombia, due to the lack of regular notification, we do not have the exact number of cases per year. It is reported that 87 to 99% of patients diagnosed with CSD have a history of contact with cats. It affects all ages but it is slightly more frequently diagnosed in children (50%)\(^1\,2\,4\).

This zoonotic disease is transmitted to cats through a flea named *Ctenocephalides felis*, that contaminates the cat’s saliva to then be transmitted to human beings through cat bites or scratches, due to its tendency to lick and scratch themselves more than other animals as part of grooming\(^1\).

It mainly affects less than a year-old cats because they are more susceptible of contracting the infection; weather is another important risk factor: hot and humid areas have an increased presence of fleas, so the risk of feline contagion is greater. Horizontal transmission between infected and non-infected cats has not being demonstrated, neither vertical transmission in female cats to their breeding\(^1\).

Clinical presentation can be variable; 80 to 90% of cases typically present with a pustule or papule of a diameter between the range of 0.5 – 1 cm as the primary inoculation lesion, 3 to 8 days after a cat scratch or bite. Around two weeks later, a solitary lymph node appears proximal to the inoculation site and also, other symptoms include headache (14%), anorexia (15%), fever (31%), thoracic transient maculopapular exanthema, nodosum erythema, erythema multiforme (5%) and weight loss (2%)\(^1\,2\,6\).

Atypical clinical manifestations are present in 5 to 20% of cases and are characterized by a wide range of symptoms such as prolonged fever (more than two weeks), persistent malaise, asthenia, adynamia, anorexia and headache with severe systemic symptoms (table 1)\(^1\,2\,6\).

Immunocompromised patients show bone, skin and mainly hepatic compromise more frequently\(^1\,2\). Hepatic involvement is frequent, has been described as peliosis hepatitis, which is a rare vascular condition with proliferation of the sinusoidal hepatic capillaries that results in cystic blood-filled cavities distributed throughout the liver. This is not specific for this entity, the differential diagnoses include infections such as CMV, TB, HIV or liver abscesses\(^6\).

Prospective analyses have shown bartonellosis (B. henselae) as the third etiologic agent of prolonged febrile syndrome of unknown origin, so CSD should always be considered in the differential diagnosis of this entity\(^2\).

Diagnosis is made through clinical interview, in which exposure to feline species should be emphasized. *B. henselae* is difficult to culture due to its slow growing (approximately 21 days), so serologic tests with enzyme immunoassay (EIA) or indirect immunofluorescence assay (IFA) are the most frequently used. Polymerase chain reaction may be used as well; sensitivity of serologic tests is around 95% and specificity, 99%\(^1\,2\,6\).

Lymph node biopsy is not indicated routinely, but should be considered in some cases if symptoms do not resolve or a differential diagnosis should be made (lymphoma or tuberculosis). In those cases, histologic studies, Warthin-Starry stain and PCR for *B. henselae* should be made\(^5\,6\).

**Case report**

This was a 9-year-old female patient, born and raised in Bogotá - Colombia, without relevant past medical history; vaccinations complete for her age. Presents to the emergency room with 1 month history of intermittent fever, that peaks up to 39°C associated with abdominal pain predominantly in the left abdomen, of variable intensity, intermittent, of daily presentation, asthenia, adynamia, hiporexia, weight loss of 8 kg in 1-month, nocturnal diaphoresis and daily bilateral epistaxis. Initial abdominal ultrasound showed multiple hepatic nodules and multiple hypechoic images in the spleen.

She has a history of exposure to a cat that comes into her house daily and two months ago she got bit by it. She denies contact with other animals, she has not traveled recently and has not had contact with chronic coughing patients or patients with respiratory symptoms.

In the physical examination she was hydrated, there weren’t palpable lymph nodes, neither signs of liver or spleen enlargement nor neurologic deficit.

Initial exams showed no abnormalities (Table 2), only a follow-up abdominal ultrasound showed evidence of focal liver lesions and multiple splenic lesions.

Abdominal MRI was performed showing multiple focal lesions in the liver and the spleen with central restricted diffusion and post-contrast rim enhancement. Impression includes possible abscesses of bacterial, mycobacterial, and fungal origin (Figure 1).

Due to these findings, antimicrobial therapy is started using metronidazole and ampicillin-sulbactam. Also, a consultation with a pediatric infectious disease specialist and intervention radiologist is requested.

Serologic tests are performed including HBsAg, IgG and IgM antibodies for Epstein Barr virus, *Toxoplasma spp.* and HIV without positive results; positive IgG and IgM antibodies for Cytomegalovirus were found and negative blood cultures.
Infectious diseases specialist suggested high chance of an infectious origin of the lesions found, so blood PCR for Cytomegalovirus was performed with negative results; due to past medical history of exposure to cats and a cat bite, IgG and IgM antibodies for *Bartonella henselae* and amoebae serologic tests were performed; a biopsy and mycobacterial culture was considered, along with PCR and culture for *M. tuberculosis* and nontuberculous mycobacteria, culture for common germs and fungi, gram stain, KOH and Ziehl-neelsen stain.

*Mycobacterium tuberculosis* and nontuberculous mycobacteria PCR test report was negative; Serologic test for *Bartonella henselae* came out positive with 1/40 IgM antibodies and 1/200 IgG antibodies titers.

A diagnosis of Bartonellosis with hepatic peliosis was made. Treatment with azithromycin rifampicin was started until 14 days of treatment were completed.

Ampicillin-sulbactam and metronidazole were stopped. The patient was discharged after 18 days of hospitalization, with resolution of fever and constitutional symptoms.

**Discussion**

The patient mentioned above debuted with fever of unknown origin and abdominal due to the initial clinical presentation an infectious cause was considered the highest probability, so etiological agents such as HBV, CMV and other hepatotropic viruses were ruled out, as well as amebiasis and mycobacteria. In the interrogation, the patient manifested having been bitten by a cat, therefore, bartonellosis was considered as a possible etiology.

Diagnostic criteria are considered as follows:
- History of exposure to cats, even if there is not an evident inoculation site.
- Negative serologic tests for other lymphadenopathy etiologies, positive PCR, evidence of organ lesions.
- Positive serologic tests for *B. henselae* >1/64 IgG
- Lymph node biopsy with granulomatous inflammation or bacterial finding with Warthin-Starry stain.

Our patient meets the above criteria. 68% of patients with Bartonellosis present with hepatosplenic compromise, typicallly with micro abscesses\(^5\) evident in abdominal ultrasound. IgM and IgG Antibodies titers were positive for B. henselae; 1/40 and 1/200 respectively. Serologic tests for CSD usually show higher IgG titers, around 1/264. That is why a prior *B. henselae* infection was considered. Differences in serologic test prevalence have been found according to the patients' area of residence, being higher in rural areas compared with urban areas (10). A positive IgG test result between 1/64 and 1/200 suggests a possible *B. henselae* infection, uncommon given the short period of IgM synthesis\(^6,11\).

The typical clinical manifestation of CSD is lymphadenopathies. In contrast, our patient only had reticuloendothelial
compromise along with systemic symptoms. This clinical presentation is common in children younger than 14-years-old compared to older patients\textsuperscript{12}.

In most cases, treatment may not be necessary. CSD is usually self-limited around 2 to 4 weeks after symptoms onset and does not need antimicrobial treatment.

In mild cases, symptomatic treatment may be needed as well as treatment with high intracellular concentration drugs such as azithromycin and Clarithromycin for two weeks. Antimicrobial therapy is more effective in severe cases, cases with systemic compromise or patients with immunological diseases\textsuperscript{5,12}. It should be made as well with macrolides along with rifampicin, ciprofloxacin or gentamicin for 4 to 6 weeks\textsuperscript{10}.

Immunocompromised patients and patients with ophthalmologic involvement should get 6 weeks of treatment. If it is a disease relapse, treatment should be made for 6 months\textsuperscript{10}. In patients with persistent systemic involvement, immunodeficiency should be suspected, but these can also occur in immunocompetent patients. Unfortunately, the patient was lost to outpatient follow-up, so no further studies have been possible.

In conclusion, clinical suspicion of CSD is very important in patients with prolonged febrile syndrome, and a thorough clinical interview in which exposure to a cat is present along with hepatosplenic lesions in the initial clinical workup.

**Responsabilidades éticas**

Confidencialidad de los datos. Los autores declaran que los datos tuvieron un manejo ético y confidencial de la información según las normas constitucionales y legales sobre protección de datos personales.

Derecho a la privacidad y consentimiento informado. Los autores declaran que en este artículo no aparecen datos que permitan identificar a ningún paciente. Se solicitó consentimiento informado previo a la redacción del manuscrito.

Declaración de contribución. Todos los autores hicieron parte del análisis e interpretación de los datos, la redacción del artículo y la aprobación de la versión final.

Financiamento. No se obtuvo financiación de ninguna entidad, se realizó con recursos propios.

Conflictos de interés. Los autores declaran que no tienen ningún conflicto de interés, de ninguna índole.

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