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Cat Scratch Disease with Hepato-Splenic Commitment in Immunocompetent Adults

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Abstract

Cat scratch disease (CSD) is an emerging zoonosis caused by *Bartonella henselae*. It can occur atypically including meningitis, neuroretinitis, endocarditis and hepatosplenic involvement, a rare occurrence in immunocompetent adults. Therapeutic management is controversial, supported by case series and retrospective data published literature. Five cases of CSD with hepatosplenic involvement are described. The correct clinical and epidemiological anamnesis allow the diagnostic and avoid the performance of invasive procedures in most cases. The possibility of performing *Bartonella* spp PCR and serology is crucial.

Keywords: Cat-Scratch Disease; Liver Abscess; Splenic Disease; *Bartonella Henselae*

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Introduction

Bartonella henselae infection is an emerging zoonosis with a worldwide distribution, the usual presentation of which is cat scratch disease (SAD) [1]. Its reservoir is the cat, which develops a chronic and asymptomatic infection, more frequent in animals under one year of age [2]. Transmission occurs by the bite, lick, or scratch of cats and by the bite of the flea Ctenocephalides felis, which acts as a vector. The seroprevalence of B. henselae in these animals varies according to the region, being up to 50% [1]. In Buenos Aires it has been reported at 11.9% [3].

GSD occurs frequently in childhood, characterized by regional lymphadenopathy anatomically related to the site of inoculation, which is usually self-limited. In 10-15% of immunocompetent adults it presents in an atypical form including Parinaud's oculoglandular syndrome, neuroretinitis, meningoencephalitis, hepatosplenic lesions, osteomyelitis, endocarditis and fever of unknown origin. In patients with cellular immunity disorders, it can manifest with angioproliferative lesions that involve the liver, spleen, lymph nodes, skin and mucosa, known as bacillary angiomatosis and hepatosplenic peliosis [4]. The different clinical scenarios produced by B. henselae infection pose a diagnostic challenge.

Below, five cases of GSD with hepatosplenic involvement in immunocompetent adults, diagnosed between 2017 and 2019, are reported.

Clinical Cases

Case 1

64-year-old female patient. She consulted for an 8-day fever accompanied by a retro-ocular headache and arthralgia in both wrists. She reported contact with a young cat and flea bites.

Laboratory was performed showing erythrocyte sedimentation rate (ESR) of 75 mm 1st hour, TGO 36 IU / L, TGP 38 IU / L and FAL 347 IU / L. Transthoracic X-ray and echocardiography were performed without pathological findings, and blood cultures were negative. An abdominal ultrasound revealed hepatomegaly with hyperechogenicity and mild splenomegaly with multiple focal hypoechoic lesions of up to 16mm. Serological tests were performed that ruled out HIV, syphilis, brucellosis, Chagas disease, and viral hepatitis. Serology was performed for Bartonella henselae, resulting in positive IgM> 1/20 and IgG> 1/512 with positive peripheral blood PCR. He completed 6 weeks of treatment with rifampicin and azithromycin, observing defervescence at 72 hours and disappearance of splenic lesions on subsequent control ultrasound (Figure 1).

Case 2

21-year-old male patient who consulted for fever and odynophagia of 1 month of evolution, having been evaluated in other centers where he received antibiotics without clinical response. He was referring to young cat licking.

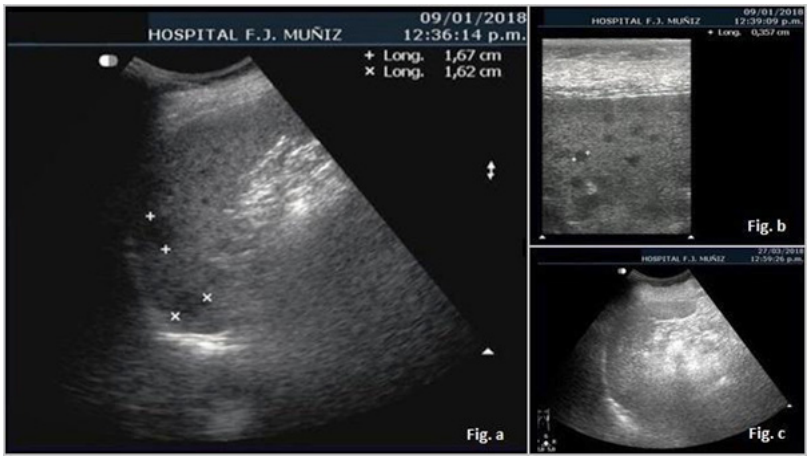

Figure 1: Splenic ultrasound.

In laboratory examination he presented ESR of 40 mm in 1st hour, TGO 26 U / I, TGP 80 U / I and HIV negative ELISA. The physical examination revealed mild abdominal pain. An abdominal ultrasound was performed where 3 hypoechoic images were observed in the liver, the largest of 19 mm, mild splenomegaly with focal hypoechoic images of up to 20 mm and precaval adenopathy of 40 mm. Blood cultures were negative. Serology and PCR were requested for Bartonella henselae, both being negative. Given the strong clinical, imaging, and epidemiological suspicion, empirical treatment with rifampicin and doxycycline was started for 8 weeks. The patient evolved favorably, with defervescence at 48 hours. A new serology was performed for B. henselae after one month, showing seroconversion of IgG. A follow-up ultrasound was requested two months after starting the treatment, verifying disappearance of the lesions.

Case 3

A healthy 48-year-old male patient who reported contact with a young cat. He consulted for fever, submandibular tumor and abdominal pain in the right upper quadrant of one week of evolution. On physical examination, he presented reddish-colored cat scratches on his right hand, 5 cm non-painful, mobile, hard, elastic right submandibular adenopathy, and 3 cm splenomegaly below the costal margin.

In laboratory examination he presented ESR 32 mm / hour, TGO 53 IU / l and TGP 58 IU / l. Abdominal ultrasound was performed, observing a focal and hypoechoic image of the liver of 10 mm with isoechoic adenopathy of 9 mm in the hepatoduodenal ligament and heterogeneous splenomegaly with hypoechoic images smaller than 5mm. In the soft tissue ultrasound he revealed 15 and 16mm lymphadenopathy in the right parotid region.

Blood cultures and serologies for HIV, viral hepatitis, and brucellosis were negative. PCR and serology were performed for Bartonella henselae with a negative result, verifying IgG seroconversion on day 20. He underwent treatment with doxycycline for 6 weeks with defervescence 48 hours after the start of the treatment. Ad-integrum resolution was observed in control ultrasound.

Case 4

48-year-old male patient with no history. He consulted for a 3-week evolution with fever, asthenia, adynamia, profuse sweating, headache and abdominal pain, accompanied by painful epitrochlear and left axillary lymphadenopathy. He reported a puppy cat bite on the left hand 3 months ago. He had consulted another center, where an abdominal ultrasound revealed splenomegaly and began treatment with azithromycin for suspected SAE. He evolved with defervescence 72 hours after it started but continued with constitutional symptoms. Abdominal and soft tissue ultrasound was repeated, showing 163 mm splenomegaly with an 8 mm hypoechoic image, hyperechoic liver, 36 mm left axillary adenopathy and 22 mm left epitrochlear image. No alterations were observed in the laboratory parameters. HIV infection was ruled out and blood cultures were negative.

IgM Bartonella henselae with a titer greater than 1/20 and IgG with a titer greater than 1/516 were requested. Combination treatment with rifampicin, doxycycline, and adjuvant corticosteroids was decided. Due to gastrointestinal intolerance to doxycycline, he completed 3 weeks of treatment with rifampicin and azithromycin with resolution of the clinical picture and ultrasound improvement.

Case 5

29-year-old female patient with a history of contact with a cat, she did not remember having been scratched.

She consulted for fever, headache, asthenia and adynamia of 15 days of evolution. Mild hepatosplenomegaly was noted. A laboratory was performed showing leukocytes 2400 / mm3, Hct 35%, Hb 11.5 g / dl, TGO 201 U / l, TGP 115 U / L, FAL 278 U / l, LDH 1762 U / l and ESR 48 mm / hour. Blood cultures were negative.

An abdominal ultrasound showed homogeneous hepatomegaly, a spleen of 128 mm with hypoechoic images smaller than 4 mm, isoechoic adenopathies of 14.3 mm in the hepatoduodenal ligament and isolated retroperitoneal isoechoic adenopathies, smaller than 12.4 mm. In contrast tomography of the brain, chest, abdomen and pelvis no additional findings were observed.

Serologies for M. pneumoniae, C. pneumoniae, EBV, CMV, HIV, viral hepatitis, and lues were negative.

A liver biopsy was performed with the finding of a minimal lymphocytic infiltrate made up of small cd3 + lymphocytes. Lymphoid B elements were not recognized. No evidence of involvement due to lymphoproliferative disease.

Whole blood PCR for Bartonella henselae was positive, while IgG immunofluorescence was negative. Treatment with azithromycin was started and due to persistent fever on day 10 of treatment, doxycycline was added with good clinical response and normalization of laboratory parameters. A new IgG determination was requested for Bartonella henselae with a positive result, confirming the diagnosis by seroconversion.

In ultrasound control after 2 months, an improvement in hepatosplenomegaly and a decrease in the number of lesions was observed.

Discussion

Atypical SAE is uncommon in adults, most of the reported cases are in the pediatric population and are immunocompromised, while in the immunocompetent adult it may present with hepatosplenic involvement, manifesting as a febrile syndrome with constitutional symptoms and micro abscesses in the liver and spleen. [5,6, and 7] There are few reports of this involvement by B. henselae in the literature. [1,2,5, and 6] In the cases presented, the most frequent signs and symptoms were fever, headache, and abdominal pain; two of the cases were accompanied by regional lymphadenopathy. The presence of hepatosplenic involvement with the presence of micro abscesses, observed in the five cases, was of importance for the clinical suspicion. In the laboratory, an increase in ESR was observed together with a slight increase in liver transaminases in four of the cases.

All patients reported close contact with cats, a fact that highlights the importance of an adequate anamnesis. It is important to define the type of contact with the feline and to include, in addition to the scratches, bites, licks and bites of its fleas as a relevant epidemiological antecedent.

The diagnosis was made through IFI and PCR in blood, without requiring the obtaining of material by biopsies except in one of the cases. The two most widely used serological techniques are ELISA and IFI. Their sensitivity and specificity are variable and can give false positives due to cross-reaction with other species of Bartonella spp, Coxiella burnetti and Chlamydophila pneumoniae [8]. Despite this, it is a useful tool when adding the IgG titer> 1/256, IgM> 1/20 and when analyzing paired samples [9]. Armitano R, et al. (2018) [8], analyzed the IgG and IgM serologies in patients with clinical suspicion, observing that 10% of the cases presented Ig M> 1/20 with negative IgG [8]. This highlights the importance of requesting a new serological sample during convalescence. Molecular biology techniques are more specific, but have a lower sensitivity (43-76%), a fact that agrees with what was observed in our patients [1].

The treatment of SAE is controversial and there are few studies in this regard. In its typical presentation, as it is a self-limited disease, watchful waiting can be maintained, although some authors recommend drainage and antibiotic treatment [10]. Bass JW, et al. (1998) [11], observed that a 5-day course of azithromycin managed to decrease lymph node size, without reducing the duration of symptoms [11]. In a retrospective study that evaluated patients with ocular involvement, the use of doxycycline plus rifampin and corticosteroids showed a better result in posterior visual acuity in moderate and severe cases. The duration of treatment was 4 to 6 weeks in all cases [12]. Although there are no controlled clinical trials on the treatment of hepatosplenic involvement, there is in case reports a preference for combination treatments with rifampin, including gentamicin, trimethoprim-sulfamethoxazole, and fluoroquinolones in pediatric patients, and to doxycycline in adults [6,10].

Defervescence occurred within 72 hours in 4 of the 5 patients, a finding similar to that reported in the literature [6]. This allows the use of therapeutic tests when there are delays or difficulties in diagnostic confirmation. Subsequent control was performed with abdominal ultrasound, finding ad-integrum resolution within 2 months of starting antibiotics in 4 patients.

The diagnosis of SAE requires strong clinical suspicion. It should be considered within the differential diagnoses of febrile syndrome with hepato-splenic involvement. A thorough history of contact with cats including lick, bite and / or flea bites is important. Performing paired serological tests and PCR in peripheral blood allows the diagnosis to be confirmed avoiding the performance of invasive procedures.

Table 1: Clinical and epidemiological characteristics.

	CASE 1	CASE2	CASE 3	CASE 4	CASE 5
Contact with cats	**Flea bite**	**Lick**	**Scratch**	**Bite**	**Close contact**
Time of clinical evolution	8 days	30 days	7 days	21 days	15 days
Abdominal pain	+	+	+	+	-
Palpable lymphadenopathy	-	-	+	+	-
Headache	+	+	+	+	+
Hepatosplenomegaly	+	+	+	+	+
Hypoechoic liver and / or splenic lesions	+	+	+	+	+
VSG	75 mm	40 mm	32 mm	3 mm	48mm
FAL	347 UI/l	Normal	Normal	Normal	278 U/l
TGO / TGP	36/38 UI/l	26/80 UI/l	53/58 UI/l	30/40 UI/l	201/115 U/l
Ig M	> 1/20	It was not done	It was not done	> 1/20	It was not done
Ig G 1st sample	> 1/512	Negative	Negative	>1/512	Negativee
Ig G 2nd sample	It was not done	Positive	Positive	It was not done	Positive
PCR blood	+	-	-	It was not done	+
Treatment	Azithromycin + rifampicin 6 weeks	Doxycycline + rifampicin 8 weeks	Doxycycline 4 weeks	Rifampicin + azithromycin 3 weeks	Azithromycin 10 days, Then azithromycin + doxycycline 6 weeks
Defervescence	72 hrs	48 hrs	48 hrs	72 hrs	72 hrs (of biterapia)
Ultrasound control with improvement of lesions	+	+	+	+	+

+ (present/positive), - (negative/absent)

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Declarations

The authors declare that they have no conflicts of interest of any kind, that the work has been approved by the ethics committee responsible for the workplace and do not declare means of financing the work carried out.

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