

Cat Scratch Disease in kidney transplant receptors: is it a rare or underdiagnosed pathology?

Doença da Arranhadura do Gato em transplantados de rim: patologia rara ou subdiagnosticada?

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ABSTRACT

Cat Scratch Disease (CSD) is an infectious disorder which appears after cat scratching particularly in children and adolescents. *Bartonella henselae* is the etiologic agent more frequently involved. There are only a few recent reports demonstrating the disease after transplantation, although the illness is not infrequent in immunologically competent people. Indeed CSD in transplant receptors has only been recently emphasized in the literature and it was concluded that fever and lymphadenopathy in patients who had been exposed to cats should prompt clinicians to maintain a suspicion for the infection. In this report CSD infecting a renal transplanted adolescent complaining of headache, blurred vision and fever, presenting a cat scratching lesion in the right arm, with a bilateral painful cervical lymphadenopathy was related. He also presented indirect immunofluorescence identifying that the two subtype's titles of *Bartonella-henselae* and *quintana*- were elevated. Treatment with doxycycline e rifampicin was introduced and the patient became asymptomatic in about 3 weeks.

Keywords: adolescent; health care (public health); immunosuppression.

RESUMO

A Doença da Arranhadura do Gato (DAG) é uma desordem infecciosa que surge após a arranhadura do animal, especialmente em crianças e adolescentes. *Bartonella henselae* é o agente etiológico mais frequentemente envolvido. Há somente poucos relatos recentes demonstrando a doença após transplante renal, embora a mesma não seja infrequente em pessoas imunologicamente competentes. Na verdade, DAG em receptores de transplantes tem sido somente recentemente enfatizada na literatura e concluiu-se que a presença de febre e linfadenopatias em pacientes que estiveram expostos a contato com o animal deveriam sinalizar os clínicos a manter suspeita da infecção. Neste relato de DAG, é exposto o caso de um adolescente transplantado de rim queixando-se de cefaleia, visão borrosa e febre, apresentando cicatriz de arranhadura no braço direito, com linfadenopatia cervical bilateral dolorosa. Também apresentava imunofluorescência indireta identificando que os dois subtipos de *Bartonella-henselae* e a *quintana*- estavam elevadas. Tratamento com doxiciclina e rifampicina foi iniciado e o paciente tornou-se assintomático em cerca de três semanas.

Palavras-chave: adolescente; avaliação de processos (cuidados de saúde); imunossupressão.

CASE REPORT

A 16 year-old boy was born with a posterior urethral valve, vesico-urethral reflux and a severe bilateral renal dysplasia. He was submitted to a gastrocystoplasty and a bladder catheterization was intermittently performed. He had initiated on CAPD in the first year of life, being submitted to cadaveric renal transplantations with 5 and 12 years-old. Currently he is being

submitted to treatment with cyclosporine 50 mg BID, mofetil-mycophenolate 500 mg TID and prednisone 5 mg/day. Four years after the second transplantation he was admitted to the Hospital with a bilateral cervical lymphadenopathy beginning 7 days before, complaining of headache, blurred vision in the right eye and fever (38°-39 °C) since the day before. When admitted he presented a scratching cat lesion in the right arm,

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1 cm left cervical and 2 cm right supraclavicular lymphadenopathy, both very painful to palpation. Liver was about 3 cm below right costal board and the spleen was also palpable.

Urine and blood cultures were negative. EB virus, toxoplasmosis, cytomegalovirus, fungi and tuberculosis were also non-reagents. Liver function tests were within normal limits and the sedimentation rate was 32 mm. Indirect *Bartonella* IgM immunofluorescence was < 1:20 (normal < 1:16) and IgG 1:256 (normal < 1:64). Indirect immunofluorescence to identify the subtypes of *Bartonella* species was done. *Bartonella henselae* title was 1:2048 and *Bartonella quintana* equals 1:1024, both elevated. An abdominal CT showed increased liver size and splenomegaly, with no focal parenchymal lesions. Patient was evaluated by an ophthalmologist. Posterior uveitis in both eyes with papilledema and right eye hemorrhages were seen in the retinography (Figure 1). A supraclavicular lymph node biopsy demonstrated a pyogenic necrotizing adenitis, suggestive of CSD (Figure 2). Warthin-Starry method allowed visualizing the pleomorphic bacilli (Figure 3). Treatment with doxycycline e rifampicin was introduced and fever decreased 14 days after, headache disappeared nine days later and hepatospleno - lymphadenomegaly were not found at physical examination 2 months afterwards. Antibiotic therapy was maintained during 6 months.

DISCUSSION

Cat Scratch Disease (CSD) is an infectious disorder which appears after cat scratching particularly in children or young adults.¹ *Bartonella henselae* is the etiologic agent more frequently involved.² In immunologically competent individuals the disease is benign and self-limited.³ It has also been recognized in AIDS patients,⁴ but there are only a few reports demonstrating the disease after kidney

Figure 1. Retinography: Posterior uveitis in both eyes with papilledema and right eye hemorrhages.

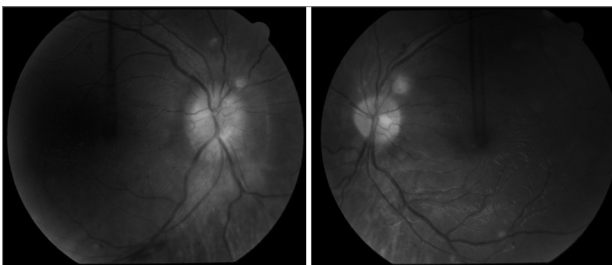


Figure 2. Supraclavicular lymph node biopsy demonstrated a suppurative necrotizing adenitis, suggestive of CSD.

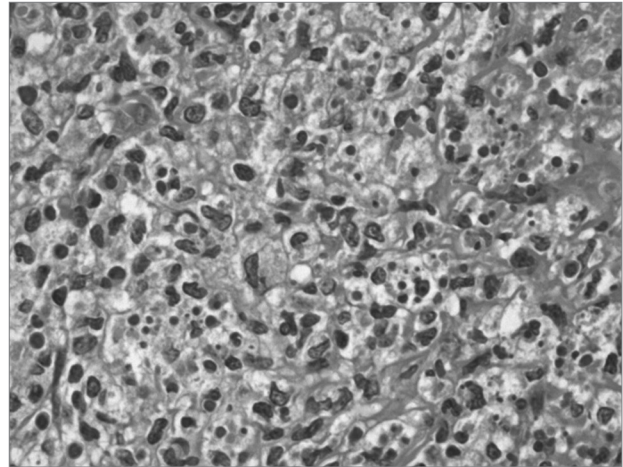
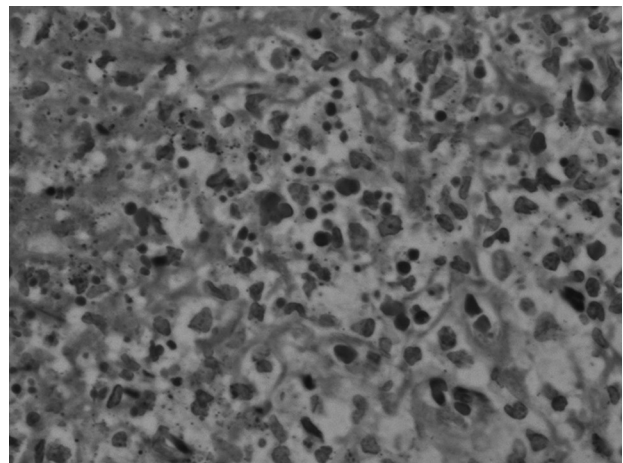


Figure 3. Supraclavicular lymph node biopsy using the Warthin-Starry method allowed visualizing the pleomorphic bacilli.



transplantation. Indeed the issue has been recently emphasized in the literature and it was concluded that fever and lymphadenopathy in patients who had been exposed to cats should prompt clinicians to maintain a suspicion for *B. henselae* infection.^{2,5} In this report CSD infecting a renal transplanted adolescent is presented.

Parinaud, in 1931, was the first to describe conjunctival inflammation with lymphadenopathy after contact with an animal. Debré was the first to observe the occurrence of a regional lymphadenopathy after a cat scratch.⁶ *Bartonella henselae* or more rarely *Bartonella quintana* were identified as the causal agents of the disease in 1992.⁷

The illness occurs more frequently in the autumn and at the beginning of the winter.⁸ Lymphadenomegaly is the most common manifestation and appears two weeks after the inoculation and almost 15% of the lymph

nodes were found to be suppuratives. About 30% of the patients had fever above 38.5 °C, headache and malaise. Lymphadenopathy localization depends on the site of inoculation. The most common affected sites are axilla, epitrochlea, neck, supraclavicular and submandibular areas.⁹ In the first few weeks of disease sedimentation rate is usually increased.¹ Acute renal transplantation rejection reaction was also associated with CSD.¹⁰

Ocular manifestations include neuroretinitis which is a syndrome presenting decreased visual acuity producing optical nerve edema associated with macular exudates. Funduscopy alterations may result from vasculitis through direct vessels invasion by the bacteria.¹¹ Those presenting neuroretinitis usually had fever, malaise and unilateral blurred vision.¹² Ophthalmologic examination usually discloses a unilateral involvement with diminished visual accuracy and afferent papillary defect. Retinal abnormalities may include hemorrhages, cotton wool exudates, multiple retina lesions and exudates.

Differential diagnosis must include toxoplasmosis, malignant diseases-lymphoma and metastasis, granulomatous disease, tuberculosis, sarcoidosis and other infectious disease-pyogenic abscess and fungal infections.

CSD diagnosis has been based in the following findings: (A) Cat contact with a scratching lesion; (B) Negative serum tests for other causes of adenopathy, *Bartonella* positive Polymerase Chain Reaction and liver- splenic lesions in the CT. (C) *Bartonella henselae* positive serology (Elisa or Indirect Immunofluorescence) with a titer equal or greater than 1: 64 and (D) a biopsy showing granulomatous inflammation consistent with CSD or with a positive Warthin-Starrry coloration for the bacilli.¹ The reported patient presented all the required diagnosis criteria.

As previously related a rare significant cross reaction occurred for IgG between *B. henselae* and *B. quintana* specimens, as occurred in the reported patient.¹³ However, serology still remains the most widely used method for the diagnosis of CSD because culture and isolation are difficult to perform and are not yet easily available. Using indirect immunofluorescence, an IgG titer above normal limits- as occurred in our patient- must be considered positive for CSD.¹⁴

Histopathology of the involved lymph node demonstrated a lymphoid hyperplasia with acellular and necrotic centers, peripheral histiocytes and lymphocytes around them suggestive of CSD and the positive Warthin-Starrry test which showed small

pleomorphic bacillus. Biopsy findings depend on the time of disease presentation. At the beginning they may demonstrate lymphoid hyperplasia, arteriolar proliferation and reticular cells hyperplasia. Subsequently granulomas appear, usually with central necrosis and giant multinucleated cells. Lately star-like infiltrates become visible: these are not pathognomonic but very specific.¹

Treatment, especially for neuroretinitis, was initiated with doxicillin and rifampicin. The need for antibiotic therapy in immunocompetent individuals is not well established. However, in the immunosuppressed, antibiotics are formally indicated, improving the prognosis.

As CSD is not frequently described in immunosuppressed transplanted individuals-contrarily to what has been seen in immunocompetent people- this report would help physicians to become aware of this diagnosis, including it in the extensive list of opportunistic agents causing infection in the post-transplant phase. And finally the question: Cat Scratch Disease in kidney transplant receptors: is it a rare or still an under diagnosed pathology?

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