CASE REPORT

Fever, bone pain and erectile dysfunction. Where is the cat?

Quentin Trefois,¹ Jean-Christophe Marot,¹ Halil Yildiz,² Gregoire Wieers¹¹Department of internal medicine, Clinique Saint-Pierre Ottignies, Ottignies, Belgium²Department of internal medicine, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium**Correspondence to**
Dr Halil Yildiz,
halil.yildiz@uclouvain.be

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SUMMARY

Cat-scratch disease is due to *Bartonella henselae* and commonly presents as a localised papular lesion with regional lymphadenopathy. We report the case of a young man suffering general symptoms and dysautonomy characterised by an erectile dysfunction due to an invasive cat-scratch disease. He was successfully treated by tetracyclines during 3 weeks.

BACKGROUND

Cat-scratch disease is an infectious disease due to Gram-negative aerobic bacteria *Bartonella henselae* which occurs after a cat bite or scratch. It most frequently presents as a localised papular lesion with regional lymphadenopathy. However, it may be the cause of many various clinical presentations. Here, we describe a patient with cat-scratch disease manifesting as general symptoms and erectile dysfunction.

CASE PRESENTATION

A 23-year-old man presented to the emergency department with a 5-day history of fever, chills and intense sweating occurring especially at night. He complained of diffuse pain predominating in the low back and in the pelvis. He also suffered from pain in the testicles and in the penis glands accompanied by dysuria and erectile dysfunction. He noticed a weight loss of 10 kg in 6 months without any change in diet or physical activity. He spent a 2 week vacation in Croatia 6 months ago. He has no medical history and has had no unprotected sexual intercourse.

Physical examination was normal except swollen lymph nodes in the left axillary region. There were no other lymphadenopathies. Blood test revealed an elevated C-reactive protein (41.4 mg/L; normal value <5) and serum transaminases (aspartate aminotransferase 109 U/L; normal value <34, alanine aminotransferase 121 U/L; normal value <44). Urinalysis was normal. Blood and urinary cultures remained sterile. Abdominal ultrasound showed a splenomegaly containing infracentimetric hypoechoic nodular lesions. 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET)-CT scan revealed hypermetabolic axillary and abdominal lymphadenopathy as well as an intense uptake in the backbone and pelvic bones suggesting a lymphoma stage IV (figure 1A). Bone marrow aspiration and biopsy were normal and culture remained sterile. Serologies for HIV,

hepatitis B virus, hepatitis C virus and syphilis were negative. IgG anti-Bartonella were positive.

Histological analysis of an axillary lymph node obtained after a surgical resection showed granulomatous and abscessed adenitis (figure 1B, C). PCR realised in both bone marrow and lymph node biopsy was positive for *B. henselae*.

Diagnosis of invasive cat-scratch disease, with lymph node and bone infiltration, was therefore made. On further questioning, it was confirmed that the patient was recently scratched by a young cat at home.

OUTCOME AND FOLLOW-UP

The patient was treated with tetracycline (doxycycline) 100 mg twice a day for 3 weeks. Symptoms quickly vanished and he fully regained his erectile function.

DISCUSSION

Cat-scratch disease is a well-known infectious disease due to Gram-negative aerobic bacteria *B. henselae*. The bacteria is transmitted by scratches and bites of infected animals but is also thought to be transmitted to human by fleas, ticks, body lice and sand fly. Cats and dogs are considered as the principal reservoir of *B. henselae* but wild animals as rabbits and hedgehog can also host the bacteria. The genus *Bartonella* contains 16 species of which *B. henselae*, *B. bacilliformis* and *B. quintana* are the pathogens, respectively, associated with cat-scratch disease, Oroya fever (Carrion's disease) and trench fever (quintan fever). Other *Bartonella* species could also be pathogenic in human as *B. talpae*, *grahamii*, *clarridgeiae*, *koehlerae*, *berkoffii*, *vinsonii*, *elizabethae*, *tribocorum*, *alsatica* were detected by genetic analysis in human tissues and were associated with fever, ophthalmic infection, endocarditis or remained asymptomatic.¹

Bartonella species primarily invades vascular endothelial cells and thereafter erythrocytes with the help of type IV pili. Bacteraemia with *Bartonella* could remain asymptomatic, what is an exception for pathogenic microorganisms probably conferred by a low endotoxicity conferred by its lipopolysaccharide and the intraerythrocytic bacteraemia. Metastatic colonies will induce angiogenesis once in the tissues by the local production of hypoxia-inducible factor-1 and secondary production of vascular endothelial growth factor.²

Clinically, Bartonellosis commonly presents as localised erythematous and papular lesion with

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Figure 1 (A) 18F-fluorodeoxyglucose (FDG)-positron emission tomography-CT in Maximal Intensity Projection mode show multiple uptakes of FDG in lymphadenopathies distributed asymmetrically in the upper and lower body evoking a lymphoma stage IV. Arrow shows spleen granuloma showing uptake of FDG. The box highlights lymph nodes that were biopsied. (B) At low magnification, histological examination of the axillary lymph node shows hyperplastic follicles but also several large well-defined granulomas with necrotic centres (original magnification $\times 25$). Granulomas are characterised by a suppurative central area surrounded by palisading epithelioid cells. (C) High magnification of the suppurative centre demonstrates a mixture of necrotic cells, histiocytes and a predominance of neutrophils (original magnification $\times 400$).

regional lymphadenopathy but could also cause endocarditis. Visceral involvement is rare and corresponds to multiple septic metastases. If bacteraemia seems to be part of the natural cycle of *Bartonella* infection, it is questionable why immunocompetent young adult develops visceral disease.³ It is generally assumed that the bacterial load transmitted during contamination could determine the severity of the clinical presentation. This also results in the activation of several inflammatory mediators as interferon-gamma and interleukin-10 and cellular response mediated by Th-1 lymphocytes which appears to be associated with the severity of the clinical damage in mice.⁴ It is therefore questionable if the severity of the clinical damage may be influenced by the greater virulence of a specific strain of *B. henselae*. The role of the inflammatory cascade in the host may also be questioned, as well as the possible consequences of some defects in inflammatory mediators. Severity of the symptoms could also be related to autoimmunity as a case of autoimmune thyroiditis associated with *B. henselae* was described in a young patient. Notably, an amino acid stretch corresponding to potential antigen of *B. henselae* is similar with a major immunoreactive epitope of the ribosome leading to the production of autoantibodies found in lupus erythematosus and associated with central nervous system symptoms.^{5,6}

The patient also reported testicular pain with erectile dysfunction. Pain could disrupt erection as well as an altered general condition, but in this case the patient was unable to provoke erection despite his will even during periods of calm symptoms.

B. henselae causes (is known to be the cause of) central neurological disorders, especially acute encephalopathy. Nevertheless,

some cases with peripheral neuropathy, for example, facial paralysis, have also been described.⁷ Physiopathology of *Bartonella*-associated neuropathy is not fully understood but could involve molecular mimicry that induces to autoimmune reaction resulting in vasa nervorum vasculitis and axonal neuropathy remitting after an antibiotic treatment but not after corticotherapy. Pudendal neuropathy could therefore have fostered erectile disorders and caused testicular pain as both resolved after an antibiotic treatment.⁸

FDG-PET-scanner demonstrated highly metabolic nodular lesion in the spleen that could correspond to angioma, which are typical of *B. bacilliformis* infection but could also occurs during *B. henselae* infection.⁹

This case reports atypical presentation of *Bartonella* infection. Differential diagnosis is broad in the presence of fever, intense sweating and chills associated with persistent lymphadenopathy. First illness to rule out is of course lymphoma, especially in a young adult with unusual symptoms like in our case. Systemic diseases, such as systemic lupus erythematosus, Still's disease or sarcoidosis, should also be considered. Tuberculosis could be responsible for the clinical picture, as well as some rare infections like leishmaniasis or brucellosis.

Unfortunately, there is no randomised controlled trials exploring therapeutic management of visceral cat-scratch disease.¹⁰ First of all, it is still unknown whether every case of cat-scratch disease should be treated with antibiotherapy. Decision to treat or not must be taken on the basis of patient's immunological status and clinical presentation of the disease. Despite the lack of guidelines in literature, it seems clear that

disseminated or hepatosplenic diseases are indications to treat, as well as cat-scratch disease occurring in immunocompromised patient. On the contrary, typical lymphadenitis in immunocompetent may not be treated because no antibiotic is proven to be effective in curing the disease or reducing the time to recover. When it is decided to treat, macrolides and especially azithromycin are the gold standard because it is the only molecule studied in a randomised controlled study.¹¹ Other molecules such as rifampin, trimethoprim-sulfamethoxazole or gentamicin have been compared in only one non-randomised observational study, but could also be used.¹² In the particular case of neuroretinitis and neurological disease, doxycycline (tetracycline) might have shown its efficacy in one study and could therefore be considered as a first choice in these situations.¹³

B. henselae is a facultative intracellular pathogen leading to intraphagocytic infection. In order to achieve the adequate bactericidal intracellular concentration, antibiotic must consequently be able to cross another barrier than that of *B. henselae*. Cellular membrane penetration is therefore a key determinant for effective antibiotherapy. Macrolides and tetracyclines have well shown their ability to penetrate phagocytic cell membrane unlike other molecules such as penicillins.¹⁴

In this case, given the symptoms of the patient, the possible underlying peripheral neuropathy, and despite the lack of proven immune incompetence, we opted to give to the patient a regimen of tetracycline 100mg two times a day for 3 weeks, leading to quick and complete clinical and biological healing.

In conclusion, cat-scratch disease seems to affect the skin and lymph nodes but is frequently associated with bacteraemia. The clinical expression of visceral involvement is very variable, putting cat-scratch disease among numerous differential diagnosis, including neoplastic diseases such as lymphoma. Therapeutic guidelines are lacking but in patients with severe

symptoms or immunodepression oral antibiotherapy with tetracyclines seems to be sufficient and efficient.

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Learning points

- Cat-scratch disease is responsible for many various clinical presentations. In a patient with general weakness and erectile dysfunction, cat-scratch disease must be excluded. Tetracyclines and macrolides are the preferred antibiotics when faced with systemic forms of the disease.

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