**Atypical form of cat scratch disease in immunocompetent patient**

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**Abstract**

**Introduction.** Cat scratch disease (CSD) is an acute infectious disease with benign course caused by the bacteria *Bartonella henselae*. Clinically, it is usually manifested as regional lymphadenopathy and mild infective syndrome. Rare forms of the disease which usually occur in immunocompromised persons are: encephalitis, transverse myelitis, neuroretinitis, granulomatous conjunctivitis, arthritis, hepatitis etc. **Case report.** We presented an atypical form of cat scratch disease in a young immunocompetent female person. The disease was manifested with prolonged fever, rash, purulent lymphadenitis and hepatitis. The diagnosis was based on characteristic pathohistological finding and exclusion of the other causes of lymphadenopathy. The patient was treated by antibiotics for a few weeks, with surgical incision and drainage of the purulent lymphadenitis. **Conclusion.** Atypical forms of CSD could be an important differential-diagnostic problem, especially if there is no opportunity for serological confirmation of the disease.

**Key words:** cat-scratch disease; lymphadenitis; diagnosis; drug therapy; antibacterial agents; treatment outcome.

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**Conclusion.** Atypical forms of CSD could be an important differential-diagnostic problem, especially if there is no opportunity for serological confirmation of the disease.
Incubation period is 1–2 weeks in 90% of patients (3–12 days). It is followed by papulopustular lesion on the bitten or scratched place (primary lesion), which lasts about 1–3 weeks. After that, in 90% of patients, characteristic regional lymphadenopathy is developed and is followed by mild fever, anorexia, nausea, fatigue or headache. Truncal maculopapular rash appears rarely. Lymph nodes are painful and suppurate in 25%–30% of cases. CSD is a self-limited disease with excellent prognosis even in a severe form of the disease. Recovery is spontaneous in 2–5 months, but immunocompromised persons can develop severe and potentially life-threatening forms of the disease. Atypical forms of the disease, without papula at the site of inoculation and visible regional lymphadenopathy are present in 10% of cases with CSD. They include: encephalitis with seizures, transverse myelitis, arthritis, neuroretinitis, granulomatous conjunctivitis, aseptic meningitis, hepatitis, osteomyelitis, endocarditis, myocarditis, pneumonia, splenic abscess, hemolytic anemia, trombocytopenic purpura etc.

The aim of this study was to show rare form of CSD with prolonged fever, purulent regional lymphadenitis, maculopapular rash and hepatitis in a young immunocompetent female person.

Case report

A 29-year-old female person was bitten by a kitten the third finger of her left hand on 12 June 2010. Three weeks later papulopustular lesion appeared on the bitten place. After about 6 weeks, her axillary lymph nodes became swollen and painful on palpation and a tumor formation appeared in the region of the left elbow on 24 July 2010. By the end of July, the patient became febrile, about 39°C, followed by extensive night sweets. In that period her lymph nodes were grouped into packages, followed by skin redness behind them and extreme palpatory tenderness. Laboratory analyses from that period are shown in Table 1. As causative agents were excluded hepatitis A, B and C viruses, Epstein-Barr virus and Cytomegalovirus. The therapy with ciprofloxacin 1,000 mg per day was initiated in the regional hospital with suspicion on CSD, but maculopapular rash on truncus, limbs and face appeared after 10 days. Ciprofloxacin was changed with doxycycline in a daily dose of 200 mg and antialergic therapy was initiated by a dermatologist. Since the treatment did not lead to a significant improvement, the patient was admitted to the Clinic for Infectious and Tropical Disease, Military Medical Academy, Belgrade, on 18 August 2010.

At admission, the patient was subfebrile, pale, in good general condition, with the present crust on the bitten place and with rash in regression at the medial side of both forearms, which absolutely dissapeared after 7 days. In the region of the left axilla, a lymph node package was registrered (Figure 1). It was painful on palpation and without signs of supuration. In the region of the medial side of the left elbow, a tumor formation of firmer consistency about 2 cm in diameter was noticed. Physical examinations of pharynx, lung and heart were normal; there was no hepatosplenomegaly.

Pathological laboratory analyses at admission are shown in Table 1. Using serological analyses, as causative agents were excluded Human Immunodeficiency Virus (HIV), Toxoplasma gondii, Francisella tularensis, Echinococcus granulosus and Toxocara canis.

Table 1

<table>
<thead>
<tr>
<th>Laboratory analyses</th>
<th>Before admission</th>
<th>On admission</th>
<th>After three months</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR (mm/1h)</td>
<td>106</td>
<td>139</td>
<td>16</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>47.3</td>
<td>30.4</td>
<td>3.4</td>
</tr>
<tr>
<td>Fibrinogen (g/L)</td>
<td>/</td>
<td>6.4</td>
<td>/</td>
</tr>
<tr>
<td>Procalcitonin (ng/L)</td>
<td>/</td>
<td>0.05</td>
<td>/</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>162</td>
<td>101</td>
<td>104</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>507</td>
<td>178</td>
<td>304</td>
</tr>
<tr>
<td>Gamma GT (U/L)</td>
<td>/</td>
<td>159</td>
<td>/</td>
</tr>
</tbody>
</table>

ESR – Erythrocyte Sedimentation Rate; CRP – C reactive protein; AST – aspartate aminotransferase; ALT – alanine aminotransferase; gamma GT – gamma glutamyl transpeptidase

Fig. 1 – Regional lymphadenitis in the patient with cat scratch disease
sule of the tumor was opened, pus drained, which culture was sterile. Histopathological analyses of the tumor showed star-shaped granulomas with caseous necrosis and palisade deployed histiocytes which correspond to CSD. No microorganisms were isolated in the tissue specimen using special paintings, including silver painting by the Warthin Starry method. The antimicrobial therapy was reintroduced on September 3 with doxycycline in a daily dose of 200 mg, for 20 days and was continued with ciprofloxacin 500 mg per day, for 3 weeks.

In repeated ultrasound examination, 5 weeks after the first one, a lobular heterogeneous liquid collection was registered, 4 cm in diameter, without capsule. Beside it a reactive lymph node was noticed 12 mm large (Figure 2). There were no pathologic findings in the subcutaneous tissue and muscle of the left axilla. A spontaneous drainage of abscess collection happened at that time and the patient became afebrile, with elevated erythrocyte sedimentation rate (ESR), C reactive protein (CRP), fibrinogen and serum transaminases (Figure 3). On October 4 2010, surgical procedure, incision and drainage of abscess collection, was done and a necrotic lymph node in the left axilla was eliminated. Purulent content was obtained, with no growth on pathogenic bacteria or Mycobacterium tuberculosis.

The antimicrobial therapy was definitely stopped on October 18 2010 when the patient was without symptoms and with absolutely normal physical examination. Laboratory findings performed at the end of October are shown in Table 1. Elevated serum transaminases and other normal biochemical findings were noticed in the middle of December, while total laboratory findings were normal only at the end of January 2011.

Discussion

CSD is an illness of children and youths under the age of 20 and is manifested as benign and self-limited lymphadenopathy caused by bacteria B. henselae. According to Erik the disease appears in patients younger than 21 in 80% of cases. The reason for this could be in the fact that children are in contact with cats and kittens more frequently, so it is more probable to be scratched or bitten. The incidence of disease is not known in our country and only sporadic cases are reported.

After the incubation period of 3–12 days, on the bitten or scratched place, papulopustular lesions appear in about 90% of patients which lasts about 1–3 weeks. In the presented patient the lesions were present but they appeared a little bit later, 3 weeks after the bite. The most impressive clinical sign of infection is regional lymphadenopathy and it is present in 80% of patients. In about 10% of inflamed lymph nodes, the skin behind them becomes red. After that they fluctuate, what is the sign of suppuration and it is followed by spontaneous drainage. Erik cites in his research that lymphadenopathy is manifested primary in axillary lymph nodes and that they suppurate in about 25%–30% of cases. According to the same author, in 50% of cases only one lymph node is changed, in 30% more lymph nodes from different part of the body are infected and in 20% of cases a few lymph nodes from the same region are infected. In the presented patient one cubital and a few axillary lymph nodes were changed.

Mild fever is present in 30%–60% of patients and usually lasts about 1–2 weeks. The presented patient was febrile about 20 days with some episodes of high fever. In the literature are described cases of systemic illness in immunocompetent persons which arise hematogenously. These forms are characterized with long-lasting fever, hepatosplenomegaly, granulomatous hepatitis, abdominal pain, weight loss, headache, weakness and malaise. The presented patient had prolonged fever and signs of hepatitis with values of serum transaminases which were multiple as high, but granulomatous lesions in liver were not detected by ultrasound, and other diagnostic procedures (MSCT and liver biopsy) were not performed.

Dermal manifestations of CSD are quite infrequent and appear in about 5% of patients. Eryhema nodosum, erythema multiforme, erythema marginatum and non-specific maculopapular, morbilliform or petechial rash have been described till now. Dzelalija et al. described a similar case to the case we presented, with maculopapular rash, purulent lymphadenitis, slightly elevated serum transaminases and parameters of inflammation. The presented patient had macu-
llopapular rash considered allergic manifestation, but the same was excluded later, with the reintroduction of ciprofloxacin in the therapy, in hospital settings.

Diagnostic criteria for CSD are characteristic clinical picture, positive epidemiological data, exclusion of other causes of lymphadenitis, morphological and histopathological examination of the biopsied lymph nodes, serological confirmation by detecting specific serum antibodies using immunofluorescence methods and detection of *B. henselae* genome using PCR method.

Morphological examinations (US, CT, NMR) are of great importance for diagnosing CSD. Lymph nodes are visualised as round or ovoid masses in diameter of about 1–5 cm by ultrasound examination. In about ½ of patients it is affected only one or more lymph nodes from the same region (hand, neck or axilla). Affecting more different regions is a sign of multiple inoculations or dissemination of the disease. Disseminated form of the disease can be registered by finding granulomas in the liver and the spleen by ultrasound. The presented patient showed some signs for disseminated form of the disease, but on ultrasound no granuloma was detected.

The causative agent is difficult to be isolated from the human tissue, but isolation and identification of the agent is important in the detection of the disease in animals. Cultivation of the microorganism from tissue specimens requires special circumstances and is possible in well-equipped laboratories. In modest labs, using special paintings (Gram, special circumstances and is possible in well-equipped laboratories). Characteristic histopathological findings can indicate CSD by the characteristic shape of granuloma what was used for the diagnosis in the presented patient. According to data from the literature, the presence of *B. henselae* in lymph node specimens is more frequent in patients with suppurative lymphadenitis (67%) comparing to patients with non-suppurative lymphadenitis (22%) in our patient, although it was suppurative lymphadenitis a causative agent is not proven using silver painting by the Warthin Starry method, probably because the patient had already started antimicrobial therapy. The most applied serological method for detection of serum antibodies against *B. henselae* is indirect immunofluorescence (IIF). Sensitivity of the method is 88% and specificity 97%, although they vary between labs, so sensitivity of the method ranges from less than 30% to 100% in our country, unfortunately, no reference laboratory performs serological diagnosis of CSD.

The course of the disease in immunocompetent persons is favourable, yet complications appear in 5%–13% of patients as purulent lymphadenitis, maculopapular rash, bilateral recurrent iridocyclitis, endocarditis, pericarditis, and/or myocarditis. The presented patient had a prolonged-course fever that lasted about a month, with reverse damage of the liver which lasted almost 6 months. *B. henselae* is sensitive on macrolids, fluoroquinolones, tetracyclines, rifampicin and sulfametoxazol-trimetoprim. However, antimicrobial therapy very often has no effect on the course of the disease. There is no consensus about antimicrobial therapy of CSD in immunocompetent person, nor on duration of therapy, and the need for therapy. The presented patient was treated with ciprofloxacin and tetracyclines for 9 weeks, but according to the clinical and laboratory monitoring we could not conclude that antimicrobial therapy had good effect on the course of the disease.

Conclusion

Atypical forms of CSD could be an important differential-diagnostic problem, especially if there is no opportunity for serological confirmation of disease.

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