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Clinical case of spotted fever group rickettsiae

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ABSTRACT

We report a Astrakhan ricketsiosis fever in woman who came from Astrakhan. On admission she had fever, intoxication syndrome, exanthema. In complex examination of blood serum by ELISA were reveled IgM and IgG to *Rickettsia conorii* on the 15th day of the disease.

Introduction

In recent years, beliefs about the spread of spotted fever group (SFG) rickettsiae and the infections caused by them in Eurasia, including Russia, have changed significantly (Rudakov et al., 2012). In the Russian Federation, the incidence of rickettsioses during the years 2005 to 2018 varied from 1.25 to 1.63 per 100 000 population. In 2018, a total of 1952 patients with rickettsioses were registered (incidence of 1.33 per 100 000 population) (Anon, 2019).

Spotted fevers are most common in the Asian part of Russia. In the European part of the Russian Federation, in the regions of the Black and Caspian seas, up to four rickettsial genotypes of the SFG have been identified (Eremeeva and Balayeva, 1993). In the Astrakhan region, where the incidence of spotted fevers has reached 53.82 per 100 000 population (2013), with a mortality rate of five cases per year (2014 and 2015) (Anon, 2019), the etiological agent of Astrakhan spotted fever (ASF) has been identified and studied (Tarasevich et al., 1991a). The causative agent of ASF was *Rickettsia conorii* subsp. *caspia* subsp. nov., which was first described in the late 1980s (Tarasevich et al., 1991b; Fournier et al., 2003).

In Russia, ASF is the second most common officially registered rickettsiosis among the SFG rickettsiae after tick-borne rickettsiosis (Tarasevich, 2002). Clinical manifestations are similar to those of Mediterranean fever, except for concerningly rare eschar at the site of the tick bite (Eremeeva et al., 2014), which is the basic sign in clinical diagnosis, together with results of serological and PCR tests (Brouqui et al., 2004). The diagnosis of ASF is very difficult for general practitioners (Mediannikov et al., 2010) because of the rare occurrence of spotted fever in non-endemic regions.

Case report

A 58-year-old female physician presented to the infection hospital in Moscow on the sixth day of illness with a preliminary diagnosis of an acute respiratory viral infection and toxicoderma. Her symptoms were fever and a skin rash. Four days before disease onset, the patient had arrived from Astrakhan where she owned a house and had been walking in the forest before she had fallen ill. She denied tick bites. Her companions had remained healthy and also denied any tick bite.

The patient had fallen ill suddenly, with her temperature increasing to 38.5 °C on the day after the skin rash had appeared on the internal surface of her forearms. This rash spread over her whole body, except for her face and skull. Before admission, the patient had used the following medications: viride nitens (an antiseptic against rash), drotaverine, and non-steroidal anti-inflammatory drugs (NSAIDs). Pain in the small joints of the upper and lower limbs appeared on the fifth day of the disease.

On admission, her condition was of moderate severity. She had clear consciousness, answered adequately to questions, and was well-orientated. Meningeal and focal neurological symptoms were not observed. Her skin had the normal color. The patient had a small spotted rash comprising single papules on the chest, abdomen, back, buttock, and dorsal surface of the feet (Figure 1). In addition, the examination showed the following symptoms: injection of sclera vessels and hyperemia of the posterior pharyngeal wall. Her tonsils were not enlarged. The submandibular and anterior cervical lymph nodes were palpated. Heart tones were normal. Breathing was vesicular, and wheezing could not be heard. Her tongue was moist and furred. The abdomen was soft and painless on palpation. Her liver protruded by 2 cm

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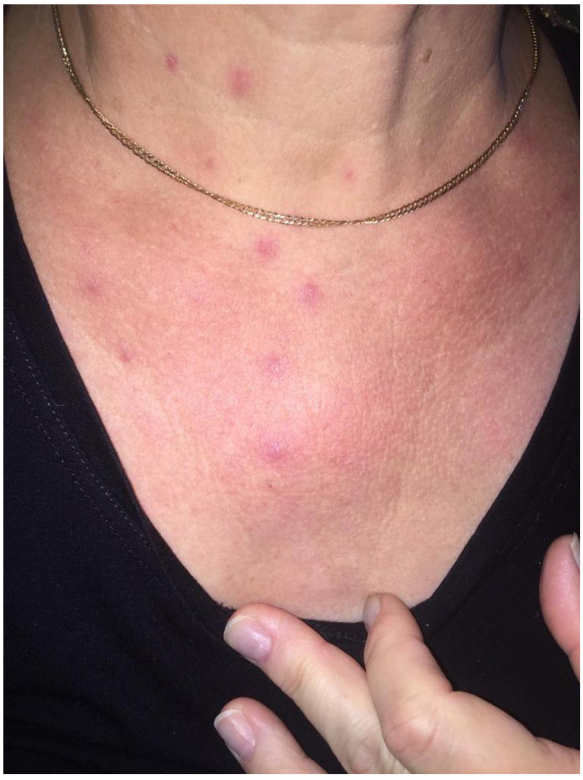

Figure 1. Rash in a patient with Spotted fever.

from under the rib arc; her spleen was not palpated. Kidney effleurage symptom was negative on both sides.

Laboratory tests revealed a white blood cell count within the reference range (9.3×10^9 cells/l; reference range $4.0–9.0 \times 10^9$ cells/l), with increased band neutrophils to 12% (reference range 1–6%) and with thrombocytopenia (111×10^9 cells/l; reference range $180–320 \times 10^9$ cells/l). The level of total protein was low at 50.3 g/l (reference range 64.0–83.0 g/l) and C-reactive protein was increased at 68.2 mg/l (reference range 0.0–5.0 mg/l). Both alanine aminotransferase and aspartate aminotransferase levels were slightly higher than the reference range (43 U/l and 42 U/l, respectively; reference range 10–40 U/l). Creatinine and serum urea were within the reference range (108 μkmol/l and 5.8 mmol/l, respectively; reference range creatinine 53–115 μkmol/l, serum urea 2.5–8.5 mmol/l).

The general analysis of urine revealed proteinuria (0.55 g/l; reference range 0–0.033 g/l), leukocyturia (5–9 in the field of view; reference range 0–5 in the field of view), mild hematuria (1–3 in the field of view; reference range 0–2 in the field of view), and bacteriuria (8.4×10^5 cells/ml; no reference range).

An ultrasound examination of the abdominal cavity showed increasing and diffuse changes in the parenchyma of the liver, diffuse changes in the parenchyma of the pancreas, and increasing and diffuse changes in the parenchyma of the spleen.

On day 12 of the disease, the symptoms included a subfebrile temperature up to 37.7 °C, enlarged and painful ankle joints, and elements of the rash becoming pale; C-reactive protein was still increased at 28.1 mg/l.

A comprehensive examination by PCR was performed for Enterovirus RNA in blood and feces, as well as DNA of parvovirus B19, Epstein–Barr virus, cytomegalovirus, human herpesvirus 6, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae* in blood plasma and a swab of the oropharynx; none of these was detected (AmpliSens kits; Central Research Institute of Epidemiology, Russia). Direct hemagglutination tests with *Yersinia* for pseudotuberculosis diagnosis (Berlise, St. Petersburg, Russia), and Salmonella and Shigella diagnostics (BioDiagnosis, Moscow, Russia) were negative.

After antibiotic therapy for 7 days (ceftriaxone 4 g per day), the patient was discharged from the hospital in a satisfactory state; this was on day 12 of hospitalization and day 18 of the disease.

The presence of specific IgM and IgG antibodies against *R. conorii* was detected using a commercial indirect ELISA (*Rickettsia conorii* ELISA IgM/IgG; Vircell, Spain) on day 15 of the disease (day 9 of hospitalization). Results for anti-rickettsial antibodies were positive for IgM (antibody index = 17.1; interpretation: <9 is negative, 9–11 is equivocal; >11 is positive) and IgG (antibody index = 10.1; equivocal) in the patient's serum on day 15 of the disease.

The acute onset of the disease, prolonged fever, moderately marked intoxication syndrome, multiple polymorphic rash, and ELISA results (revealing IgM and IgG to *R. conorii*) allowed a clinical diagnosis of spotted fever of moderate severity to be established. Given that the patient lives in the natural and anthropurgic focus of Astrakhan hemorrhagic fever, it can be assumed that the clinical picture was caused by this rickettsiosis.

The patient was discharged in satisfactory condition on day 12 of hospitalization. During the 6 months following discharge from the hospital, the patient continued to show slowly regressing residual effects, including weakness and enlarged cervical, submandibular, and axillary lymph nodes. A lymph node biopsy was performed and reactive inflammation was detected. The patient has depigmentation of the skin in the locations of the rash up to the present time.

Discussion

Moscow and the Moscow region are not part of the area endemic for spotted fever group rickettsiae; therefore, examination for rickettsioses is not included in the algorithm of the initial examination of fever patients. Information on the patient's stay in the SFG endemic region was not taken into consideration during examinations on the first days of hospitalization, and broad-spectrum antibiotic therapy was used until the diagnosis of spotted fever was established. This, unfortunately, led to a prolonged convalescence.

This clinical case indicates that spotted fevers should be considered as a possible cause of fever of unclear etiology in areas endemic for this disease in people with rashes, especially during the season with increased numbers and activity of the tick *Rhipicephalus pumilio*, which is a source of spread of *Rickettsia conorii* subsp. *caspia*.

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Ethical approval

Not applicable.

Conflict of interest

The authors declare no conflicts of interest.

References

https://rospotrebnadzor.ru/activities/statistical-materials/statistic_detail.php.
Brouqui P, Bacellar F, Baranton G, Birtles RJ, Bjoërsdorff A, Blanco JR, et al. Guidelines for the diagnosis of tick-borne bacterial diseases in Europe. Clin Microbiol Infect 2004;12:1108–32.

Eremeeva ME, Balayeva NM. Proteinic and Genomic Identification of Spotted Fever Group Rickettsiae Isolated in the Former USSR. J Clinic Microbiol (October) 1993;2625–33.
Eremeeva ME, Shpynov SN, Tokarevich NK. Modern approaches to laboratory diagnosis of rickettsial diseases. Infect Immun 2014;4(2):113–34.
Fournier Pierre-Edouard, Xeridat Bernard, Raoult Didier. Isolation of a Rickettsia Related to Astrakhan Fever Rickettsia from a Patient in Chad. Ann NY Acad Sci 2003;990:152–7.
Mediannikov O, Diatta G, Fenollar F, Sokhna C, Trape J-F, Raoult D. Tick-borne rickettsioses, neglected emerging diseases 92. in rural Senegal. PLoS Negl Trop Dis 2010;4(9):e821.
Rudakov NV, Shpynov SN, Samojlenko IE, Jastrebov VK, Obert AS, Kurepina NU. Rickettsiae and rickettsial diseases of spotted fever group in Siberia. Omsk 2012;288.
Tarasevich IV. Astrakhan spotted fever.– M. Medicine 2002;171.
Tarasevich IV, Makarova VA, Fetisova NF, Stepanov AV, Miskarova ED, Raoult D. Studies of a "new" rickettsiosis "Astrakhan" spotted fever. Eur J Epidemiol 1991a;7(3):294–8.
Tarasevich IV, Makarova VA, Fetisova NF, Stepanov AV, Miskarova ED, Balayeva N, Raoult D. Astrakhan fever: new spotted fever group rickettsiosis. Lancet 1991b;337:172–3.

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