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Generalised infection evoked by Aeromonas hydrophilia in a patient with unclassified arthritis

ABSTRACT

Generalised infection evoked by the bacterium of Aeromonas hydrophilia in a 69-year-old patient with unclassified arthritis, hospitalised due to an exacerbation of rheumatic disease at the Rheumatology Ward, in September 2019. From the very beginning of the disease, the patient was chronically treated with steroids, for the next few years with chloroquine and a brief moment with methotrexate (MTX) which had to be discontinued due to the patient's gastrointestinal intolerance. The bacterium of Aeromonas hydrophilia is commonly known as an etiological factor of fish diseases (e.g. salmonid ulcers or carp erythrodermatitis). Hitherto only Aeromonas hydrophilia, Aeromonas Caviae and Aeromonas Sobria have been the Aeromonas strains known to threaten human health. Aeromonas hydrophilia causes opportunistic infection in individuals with a disturbed immune system. In the literature, one can find described and analysed the cases of skin and soft tissue infections, in tropical and subtropical countries in particular.

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KEY WORDS: Aeromonas hydrophilia; unclassified arthritis; steroids

INTRODUCTION

Generalised infection evoked by the bacterium of Aeromonas hydrophilia in a 69-year-old patient with unclassified arthritis, hospitalised due to an exacerbation of rheumatic disease at the Rheumatology Ward, in September 2019. From the very beginning of the disease, the patient was chronically treated with steroids, for the next few years with chloroquine and a brief moment with methotrexate (MTX) which had to be discontinued due to the patient's gastrointestinal intolerance. The bacterium of Aeromonas hydrophilia is commonly known as an aetiological factor of fish diseases (e.g. salmonid ulcers or carp erythrodermatitis) [1]. Hitherto only Aeromonas hydrophilia, Aeromonas Caviae and Aeromonas Sobria have been the Aeromonas strains known to threaten human health. Aeromonas hydrophilia causes opportunistic infection in individuals with a disturbed immune system. In the literature, one can find described and analysed the cases of skin and soft tissue infections, in tropical and subtropical countries in particular [2].

CASE REPORT

A 69-year-old patient with unclassified arthritis was admitted to the Rheumatology Ward in September 2019 for a further diagnosis and treatment of the exacerbation of arthritis. She had been treated for arthritis since 2011. In the course of the disease, the patient experienced pain and oedema of hand, foot and knee joints as well as shoulder and knee joint pain. Temporarily, she also experienced the limitation of peripheral joint mobility. The patient suffered from persistent night pain in the joints and morning stiffness for several hours. From the very beginning of the disease, there was visible livedo reticularis on the patient's limbs and torso. Based on the further laboratory investigation the following was stated: no rheumatoid factor, no anti-cyclic

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citrullinated peptide autoantibodies (aCCP antibodies), indirect fluorescent antibodies (IFA) periodically present in low titters 1:160, 1:320 with a speckled and homogenous pattern, the presence of anticytoplasmic antibodies in the years 2015/2016/2017.

The patient was treated (from the beginning of the disease in 2011) with a small dosage of steroids (owing to her intolerance to nonsteroidal anti-inflammatory drugs and elevated kidney indicators). From 2014 to 2016 she was also treated with chloroquine (250 mg per day). In 2014 there was an attempted treatment of arthritis with methotrexate (MTX) at a dose of 15 mg per week. The drug was in treatment for a few weeks, however, due to the patient's gastrointestinal intolerance (biliousness and emesis), it had to be discontinued. Furthermore, the patient was treated for depression, hypertension, NYHA II chronic heart failure, additionally, according to the medical reconnaissance — multifocal cerebral stroke with tetraparesis.

At the time of admission to the Rheumatology Ward in September 2019, the patient reported shoulder joint pain, wrist pain, metacarpal joint pain, knee pain, ankle pain, pain in the cervical and lumbosacral episode of the spine, lower leg pain, the left one, in particular, increased exercise intolerance as well as exertional dyspnoea. The patient complained about frequent episodes of forgetfulness and memory problems. Based on the further laboratory investigation the following was stated: negative tumour indicators, the normal concentration of C-reactive protein (CRP), normal morphology results, normal erythrocyte sedimentation reaction (ESR), elevated kidney indicators suggesting IIIa stadium of chronic renal failure (eGFR 50 mL/min/1,73 m^2 with the norm > 60, creatinine 1,12 mg/dL), the antinuclear antibodies, IgG and IgM anticardiolipin antibodies or antibodies against IgG or IgM beta 2 glycoprotein were not found, whereas the result of lupus anticoagulant was equivocal. The patient was found to have a high level of D-dimmers — 2552 ng/mL (with the norm being 0–500). On having performed angio-CT (computed tomography of arteries), peripheral pulmonary thromboembolism was diagnosed. The patient was consulted by the vascular surgeon. In the performed 2D Doppler ultrasound scan (USG) of the patient's lower extremities, the vascular surgeon diagnosed left shin vein thrombosis and indirect features of iliac patency; whereas femoral veins and popliteal veins were found to be normal; one of the posterior tibial veins and one of the fibula veins were found to be filled with clots, while the great and small saphenous veins were found to be unobstructed. The patient was consulted by the cardiologist. The anticoagulant treatment was started — initially, with rivaroxaban 30mg per day, subsequently, due to the GFR decrease — the dosage was reduced to 15mg per day. On the 10th day of the hospitalisation, the patient reported severe pain in the right lower limb, particularly on the inside of the thigh; she also suffered from lower abdominal pain. On the physical examination the skin of the right thigh turned out to be with no redness, with no sign of any injury, the abdomen was soft with no peritoneal symptoms, the body temperature was normal. Given chronic steroid therapy, in the differential diagnosis, pelvic fractures, fractures of the right hip joint and diverticulitis were taken into consideration. Due to the permanent abdominal pain, the patient was consulted by the surgeon. In the performed CT of the abdomen and the pelvis minor and in the performed RTG of the pelvic bones and the tight hip joint no abnormality was detected. In the control laboratory examinations the increase of inflammation indicators was found: CRP 460 mg/L, 482 mg/L (with the norm being below 5mg/L), procalcitonin 78,35 ng/mL (with the norm being 0,5 ng/mL), in the complete blood count (CBC) there was a decrease of PLT level to 78 10^3/uL (with the norm for thrombocytes being between 150 and 400 10^3/uL), WBC 5,00 10^3/uL (leukocyte norm 4,00–11,00 10^3/uL), RBC 4,19 10^3/uL (erythrocyte norm 4,00–5,50 10^3/uL), HgB 13,2 g/dL (haemoglobin 12,0–16,0 g/dL). In the subsequent laboratory examinations, the following was observed: the decrease of haemoglobin to 11,2 g/dL and the decrease of thrombocytes to 70 10^3/uL, while the level of leukocytes remained within the norm margins. Additionally, an increase in OB from 17 to 46 mm/h was observed. On the 11th day, on the medial surface of the right thigh, both in the skin and in the subcutaneous tissue an expanding inflammatory infiltration was found which was deeply penetrating the tissues (Fig. 1, 2). Simultaneously, massive pasty oedema of the tissues of the back of the right hand was found. The above-mentioned changes were accompanied by the redness of the skin and great soreness; however, the body temperature remained normal. The blood was taken for bacteriological tests; the empirical antibiotic therapy was started: cephalosporin with a carbapenem (ceftriaxone

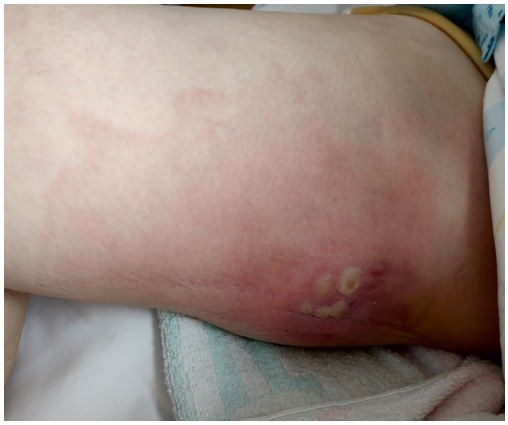

Figure 1. On the medial surface of the right thigh in the skin and subcutaneous tissue, an inflammatory infiltrate, deeply penetrating the tissues

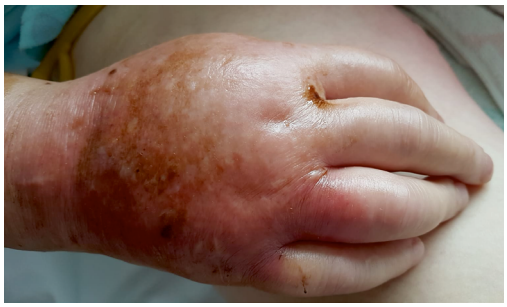

Figure 2. Massive swelling of the right-hand tissues

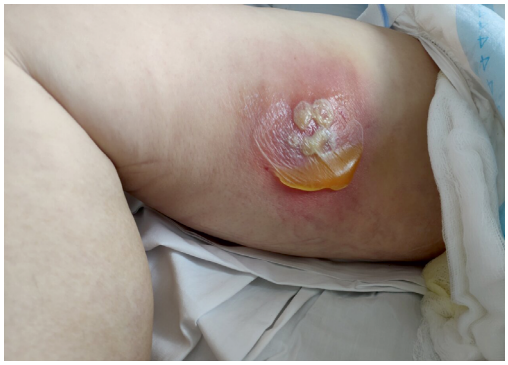

Figure 3. Evolution of infiltrative changes into a blister with transparent content

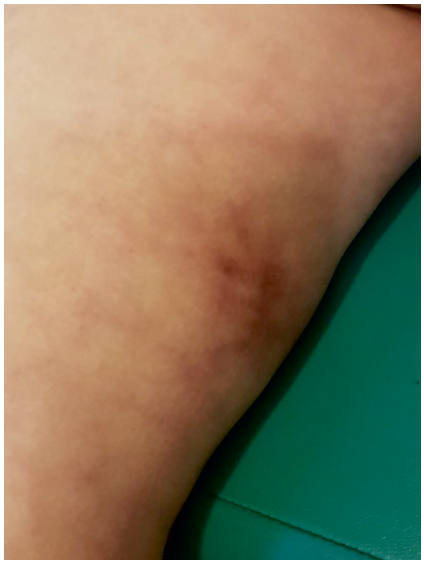

Figure 4. Patient after curing a soft tissue infection caused by Aeromonas hydrophila

1 × 2 g i.v., meropenem 3 × 1g i.v.). In the obtained results of the blood culture, the bacterium of Aeromonas hydrophilia was cultured, and therefore the treatment was changed for the one consistent with antibiogram: ciprofloxacin in combination with ceftriaxone i.v. In the following days, the patient reported severe soreness of the soft tissue changes in the thigh and the right hand. With time, the evolution of infiltrative lesion into the bullous lesion with transparent content was observed; the changes were spreading peripherally (Fig. 3), and the symptoms were accompanied by severe pain poorly responsive to the analgesic treatment (tramadol, buprenofin). In the following days, the blisters burst and the changes were slowly absorbed. The condition of the patient was gradually improving, laboratory parameters were slowly being normalised. On the 26th day of hospitalisation, CRP was 6mh/L, procalcitonin 0,09 mmol/L, creatinine 0,91 mg/dL, GFR > 60, PLT 364 10^3/uL, WBC 6,20 10^3/uL, RBC 3,55 10^3/uL, control aerobic and anaerobic blood cultures were negative.

After three months, in January 2020 — the patient was again hospitalised in the Rheumatology Ward (Fig. 4) to broaden diagnostics toward antiphospholipid syndrome. At admission, the patient reported pain in the shanks, the cervical spine and the left upper extremity. She also reported exertional dyspnoea as well as increased fatigue. In the physical examination, the following was found: livedo reticularis of the torso skin, the limitation of shoulder mobility and tenderness of the knuckle joints of both hands. In the laboratory examinations: low inflammation markers. The lupus anticoagulant (LAC) was not found. The patient did not meet the criteria that would have qualified her for antiphospholipid syndrome. The patient was consulted by the vascular surgeon. In the performed 2D Doppler ultrasound scan (USG) of the patient's peripheral vessels, the vascular surgeon did not find any fresh thrombosis. The steroid treatment was sustained (prednisone 10 mg per day). VAK (warfarin) was added to the treatment. In December 2019 due to epistaxis, the patient stopped the treatment with NOAC.

AEROMONAS HYDROPHYLIA CHARACTERISTICS

Aeromonas hydrophilia is a heterotrophic, gram-negative, rod-shaped active bacterium usually from 1 to 3,5 μ [1] in length. It belongs to the family of Aeromonadaceae [3]. The bacteria reside in the aquatic environment (fresh waters, salt waters, sewage, non-chlorinated waters, tap water). Not only are the bacteria able to survive in such an environment, but also, they can proliferate in water at low temperatures from –2 to –10°C [4,5]. They exhibit strong adhesive properties, positive for oxidase and haemolysis [4]. Amongst the Aeromonas bacteria, 14 types of DNA are distinguished, whereas the species of Aeromonas were divided into two main groups: the first one contains mesophilic bacteria equipped with a polar flagellum thus motile, e.g. A. hydrophila, A. caviae, A. sorbia, A. eucrenophilia, A. media, A. veronii, A. schuberti; the second one comprises of psychrophilic bacteria not equipped with a flagellum, thus immotile. The Aeromonas bacteria are considered to be an etiological factor of many fish diseases, e.g. salmonid ulcers or carp erythrodermatitis, but also diseases of some amphibians and mammals [1].

For humans, the bacteria types of Aeromonas hydrophila, A. caviae and A. veronii are clinically significant. These bacterium strains can compromise the digestive system in individuals with a properly functioning immune system and cause diseases, whereas in individuals with a disturbed immune system not only can they cause opportunistic infections, cellulitis, osteitis and nonclostridial gangrene, but also necrotising fasciitis [5, 6]. An individual can get infected with Aeromonas while eating unprocessed produce (vegetables, meat or milk) [7] or by getting bitten by a snake. The infection may also happen following the injury in which the wound gets contaminated by polluted water [3]. In the course of Aeromonas-hydrophilia-caused infection treatment, antibiotic therapy is employed. The recommended groups of antibiotics to which Aeromonas hydrophilia is said to be sensitive are fluoroquinolones (ciprofloxacin), trimethoprim with sulfamethoxazole, tetracycline, ceftriaxone [6]. With widespread dermatitis and muscle penetration, it is often necessary to employ a surgical wound treatment, in some cases also a limb amputation.

In the literature, one can find described and analysed the cases of Aeromonas hydrophilia infection, in tropical and subtropical countries in particular [2].

In the Journal of Microbiology, Immunology and Infection in 2012 one could find a described and analysed case of sepsis caused by Aeromonas hydrophilia in a child patient with acute lymphoblastic leukaemia who had shown non-specific signs of infection, with non-injurious skin damage of the lower extremity (redness), neutropenic fever which quickly transformed into bacteraemia and widespread thigh suppuration, fasciitis, osteitis and osteomyelitis. Apart from the antibiotic therapy, immediately a surgical cleansing of the wound was carried out, thanks to which the child's life was saved [8]. Another case of Aeromonas hydrophilia infection was described in the publication in 2011 of Infect Chemother — namely, that was the case of a soft tissue infection in a 53-year-old Korean woman without any underlying disease who was successfully treated with antibiotics [9]. Aeromonas hydrophilia infection of soft tissue can prove to develop into fulminant sepsis with multisystem organ failure which is proved by the fatal case of a 28-year-old person living in India that was described in the Journal of Clinical and Diagnostic Research [3]. In the American Society of Tropical Medicine and Hygiene in 2010 one could find research titled 'Aeromonas hydrophilia Complex Caused Bacteraemia in the Caribbean's — the islands of Martinique and Guadeloupe' which was carried out amongst 37 patients over 14 years. The average patient's age was 55, in 89% of cases the patients suffered from underlying diseases, i.e. diseases of the digestive system, skin wounds and immunosuppression in the course of neoplastic diseases. Five of the most frequent symptoms were distinguished: fever, fatigue, chills, loss of appetite and abdominal pain. The examination results suggest that the patients with diagnosed bacteraemia caused by Aeromonas hydrophilia Complex can be treated with beta-lactam preparations with the extended-spectrum, extended action cephalosporins, piperacillin-tazobactam, imipenem or fluoroquinolone. The authors of the research draw attention to the possible risk of the appearance of atypical strains resistant to cephalosporins [2].

DISCUSSION

The presented case of the 69-year-old woman with a malfunctioning immune system is an example of the opportunistic Aeromonas-hydrophilia-caused infection with accompanying sepsis and soft tissue inflammation.

Thanks to the immediate institution of combined broad-spectrum antibiotic therapy both the irreversible damages described in the literature and the amputation of the infected limbs were avoided.

Patients with inflammatory rheumatic diseases, with immune deficiency, during immunosuppressive treatment, exhibit predispositions to an atypical, frequently apyrexial, infection course. Therefore, those patients should be closely monitored for infections since they are often a cause of the exacerbation of the underlying diseases, e.g. systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA).

The pathway of bacteria entering the organism of the presented patient remains unknown since the quality of hospital water was assessed. Because the first infection symptoms appeared after 72 hours after the hospitalisation — at this moment the hospital infection could be assumed. Given the lack of gastrointestinal symptoms (such as looseness of the bowels, diarrhoea and nausea) the stool culture was not performed.

SUMMARY

The presented case is a good example of a severe course of infectious complications in individuals with immunodeficiency due to the course of connective tissue diseases, the course of chronic steroid therapy, with multiple morbidities. It is visible proof of how great diagnostic vigilance must be maintained in the case of such patients since at the beginning the infectious complications in these patients can have a feverless, even asymptomatic, course or they can take the form of intensified chronic pains reported repeatedly.

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