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Fatal fulminant sepsis due to a cat bite in an immunocompromised patient

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Tödliche fulminante Sepsis nach einem Katzenbiss bei einem immunkompromittierten Patienten

Zusammenfassung. Durch *P. multocida* ausgelöste Infektionen können sich beim Menschen als lokalisierte Infektionen des die Läsion umgebenden Bindegewebes, als Infektionen im Respirationstrakt oder als systemische Infektionen mit langsamer oder fulminanter Entwicklung präsentieren. Über 90% der humanen Infektionen sind Wundinfektionen oder Abszesse, die sich in Folge von Bissen, Kratzern oder Ablecken von Hautläsionen durch Hunde oder Katzen entwickelt haben. Schwere systemische Erkrankungen wie Pneumonie, Lungenabszess, Peritonitis, Endokarditis, Meningitis und Sepsis sind vor allem auch bei Patienten mit vorbestehenden Erkrankungen wohl bekannt. In der vorliegenden Arbeit berichten wir über einen immunkompromittierten Patienten, der von einer ihm unbekanntem Katze gebissen worden war, und der in sehr kurzer Zeit eine fulminante Sepsis entwickelte. Der Patient verstarb schließlich 70 Stunden nach dem Katzenbiss, trotz Intensivbehandlung und Reanimationsversuchen. Leider hatte er zu spät medizinische Hilfe aufgesucht. Wir möchten an Hand dieses Falles darauf hinweisen, dass es schon für die Erstversorgung wichtig ist, infektionsgefährdete Patienten besser über die Infektionsgefahr durch den Kontakt mit Tieren zu informieren. Sie sollten vor möglichen Konsequenzen von Verletzungen, auch durch eigene Haustiere, gewarnt werden.

Summary. *Pasteurella multocida* infections in humans can present as localized infections of soft tissues surrounding the lesions, as respiratory tract infections or as systemic infections with slow or fulminant development. Over 90% of human infections are cases of wound

infections or abscesses related to a bite, scratch, or licking of skin lesions by a cat or dog. Severe systemic diseases such as pneumonia, lung abscess, peritonitis, endocarditis, meningitis and sepsis are also well known, especially in patients with underlying medical conditions. In this paper we report on an immunocompromised patient who was bitten by an unknown cat and very quickly developed fulminant sepsis, dying 70 hours after the cat bite, despite all the intensive care, therapy and reanimation he was given. Unfortunately, he asked for medical help too late. We emphasize the need for primary healthcare to provide more information to patients at risk of infections from contact with animals and to warn them about the possible consequences of injuries, even when the animals are pets.

Key words: *Pasteurella multocida*, septic shock, cat bite, liver cirrhosis, immunosuppression.

Introduction

Pasteurella spp. are rod-like or coccoid, nonmotile, facultatively anaerobic Gram-negative microorganisms that occur singly, in pairs or in short chains. Some species are very pleomorphic. Their habitats are the nasopharynx and gingiva of many healthy or diseased domestic and wild animals throughout the world. In humans, the most frequently encountered species is *P. multocida*, transmitted in the bite of a cat or dog [1, 2].

Over 90% of human infections are cases of wound infections or abscesses related to a bite, scratch, or licking of skin lesions, but infections via the upper respiratory tract can also occur, most often in patients with previous lung disease. Severe systemic diseases such as pneumonia, lung abscess, peritonitis, endocarditis, meningitis and sepsis are also well known [1–3].

Immunocompromised patients are at greater risk of disseminated infections [2]. For example, conditions such as liver cirrhosis, pregnancy, neonatal age, long-term corticosteroid therapy and HIV infections potenti-

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ate susceptibility to bacterial dissemination [2, 4, 5] and severity of disease.

In this paper we report on an immunocompromised patient who was bitten by an unknown cat and very quickly developed fulminant sepsis, dying 70 hours after the bite despite all the intensive care, therapy and reanimation he was given. Unfortunately, he asked for medical help too late. We emphasize the need for primary healthcare to provide more information to patients at risk of infections from contact with animals and to warn them about the possible consequences of injuries, even when the animals are pets.

Case report

A 64-year-old man was admitted to the Surgery Clinic with redness and edema of the left hand and forearm, high fever and general fatigue. An unknown cat had bitten him two days previously and the fever, edema and redness of the hand occurred the following day. He did not contact his physician immediately.

He was admitted some 48 hours after the bite with severely impaired general condition (febrile, pale, hypodynamic, tachypnoic, dehydrated) with heavy edema, redness and bullas on the skin of the left hand and forearm and a large hematoma on the upper arm.

For the past two years he had been taking prednisone 5–20 mg per day and non-steroid anti-inflammatory drugs because of psoriatic arthritis. Liver cirrhosis and esophageal varices were also documented. He also suffered from reflux esophagitis and erosive gastritis and was taking proton-pump inhibitors.

Laboratory analysis showed red blood cell (RBC) count 3.94×10^{12} cells/l, hemoglobin 94 g/l, hematocrit 0.320, prothrombin time 1.35 international normalized ratio (INR), lower antithrombin III 44%, and an elevated liver enzyme profile: aspartate aminotransferase (AST) 325 U/l, alanine aminotransferase (ALT) 124 U/l and gamma-glutamyl aminotransferase (GGT) 117 U/l. Blood glucose level was 3.9 mmol/l, urea 11.3 mmol/l, creatinine 284 μ mol/l, elevated C-reactive protein 83.6 mg/l and white blood cell (WBC) count 6.6×10^9 cells/l.

Surgical incision and drainage were made and empiric therapy was introduced with penicillin G 50,000 IU/kg per day (24 million IU/day divided into six doses), metronidazole 20 mg/kg per day (1500 mg/day divided into three doses) and gentamicin 3 mg/kg per day (240 mg/day divided into two doses) intravenously. The patient also received anti-tetanus and anti-rabies vaccines because of the contact with an unknown cat.

Anaerobic infection was doubtful, so hyperbaric oxygenation was indicated for one hour at a pressure of 2.2 atmospheres absolute (ATA).

During transport from the hyperbaric oxygen chamber the patient had a cardiac arrest therefore cardiopulmonary resuscitation was started, including intubation, external massage of the heart and epinephrine 1 mg intravenously. The heart restarted after 4–5 minutes, but not spontaneous breathing, the patient remaining unconscious and hypotensive. Mechanical ventilation was started and the inotropic agents dopamine up to 10 μ g/kg per min and epinephrine up to 0.5 μ g/kg per min were given to support the circulation. Hydrocortisone 300 mg/day was given.

On admission to the ICU, several hours after starting antibiotics, two sets of blood culture were taken: from a central vein immediately after positioning a central vein catheter and from a peripheral vein. The discharge from the wound was collected with a swab after removal of devitalized superficial debris and cleansing of the wound with normal saline.

In spite of intensive care treatment, the patient's condition progressively worsened and he died of multiorgan failure less than 20 hours after his admission to hospital.

Both blood cultures were sterile, but semiquantitative analysis of the wound swab [6] cultivated both aerobically and anaerobically revealed a heavy bacterial growth of a monoculture of *P. multocida* susceptible to penicillin, amoxicillin, amoxicillin-clavulanate, cefazolin, cefuroxime, cefotaxime, ceftriaxone, cefepime, imipenem, ciprofloxacin, trimethoprim-sulfamethoxazole, gentamicin and amikacin in disk-diffusion susceptibility tests performed in accordance with the recommendations of CLSI document M2-A9 [7]. *P. multocida* was identified using the biochemical test API 20 E (bioMerieux, Lyon, France).

After the autopsy, the pathology report revealed hypertrophy of the left ventricle, fibrosis and scar tissue of the myocardium, hydrothorax and hydropericardium, pulmonary edema, bronchopneumonia, pleural ecchymosis, macronodular cirrhosis, esophageal varices, multiple liver necrosis and acute tubular renal necrosis. The patient died of multiple organ failure as the result of fulminant sepsis caused by infection with *P. multocida*.

Discussion

The patient developed severe infection within 48 hours after the cat bite, which led to septic shock with lethal outcome some 70 hours after the bite. Blood cultures were sterile, possibly due to the timing of blood sampling after the administration of effective antibiotics. Isolation of *P. multocida* in the wound discharge together with clear clinical signs of circulatory shock confirmed severe systemic infection with concomitant multiorgan failure. Immunocompromised patients are particularly at risk [1, 2, 8, 9], like this patient whose immune system was impaired as the result of liver cirrhosis and long-term corticosteroid therapy. An immunocompetent patient would be expected to have an elevated WBC count in response to infection, but the count in this patient was normal, indicating that his immune system was disturbed. The patient was clearly not aware of his susceptibility to infection and did not contact his physician to begin prompt antibiotic prophylaxis. Unfortunately, antimicrobial treatment and surgical intervention were given too late, with a delay of 48 hours after the bite.

P. multocida infections in humans can present as localized infections of soft tissues surrounding the lesions, as respiratory tract infections (especially in patients with coexistence of respiratory tract disease), or as systemic infections with slow or fulminant development. Usually, more than 50% of cat bites are infected [1, 2, 8]. Hands and arms are the usual sites of the bites. Hand wounds are particularly susceptible to infection, because of the anatomic features, so every hand bite must be considered potentially dangerous [10, 11]. Infections after a cat bite occur within a few hours [12]. Patients prone to infection can develop bacteremia, usually within five days after the bite. Lethal outcome is recorded in 37% of patients who develop sepsis [13]. In the case of our patient, the acute physiological assessment and chronic health evaluation (APACHE II) score during those 20 hours was 39, and the sequential (sepsis)-related organ failure assessment (SOFA) score was 14 [14, 15], both of which indicate a mortality rate over 90%.

With all potentially infected wounds, adequate prophylactic antimicrobial treatment for 3–5 days

should be started immediately [1, 2, 10]; patients who are examined by a physician within eight hours after the event and receive appropriate treatment have the incidence of infection reduced from 15%–20% to 5% [2, 8]. Amoxicillin 875 mg with clavulanic acid 125 mg, twice daily by mouth, is a reasonable empiric therapy for all infected bites. Because of their susceptibility to Gram-negative infections, immunocompromised patients and those with underlying diseases such as diabetes mellitus should receive intravenous aminoglycoside antibiotic together with β -lactam [10].

The usual antibiotic treatment for *P. multocida* infections relies on β -lactam antibiotics. Penicillin or ampicillin or a third-generation cephalosporin should be given as the first choice, together with early identification of *P. multocida* [16].

An antibiogram should be performed routinely because of possible resistance to β -lactam antibiotics. Such resistance is rare, occurring as the result of a plasmid-mediated β -lactamase which is, however, susceptible to clavulanic acid [1, 17, 18]. The need for surgical intervention should also be considered [10].

Anti-tetanus prophylaxis should be given because of the possibility of wound contamination with *Clostridium tetani* spores. Anti-rabies prophylaxis should be considered if the contact was with an unknown cat [11]. In our patient, antimicrobial prophylaxis and earlier adequate antibiotic treatment might have moderated the progression of the infection and might have prevented the lethal outcome.

Conclusion

The most important factor responsible for the development of the severe infection following the cat bite in our patient was that he was immunocompromised.

Based on the heteroanamnesis, no-one had informed him of how to react in case of an animal bite, considering his immunoincompetence, and his ignorance led to the late contact with his physician, the delay of efficient treatment and the fatal outcome.

The circumstances of the death of this patient led us to conclude that it is necessary to increase the awareness of immunocompromised patients on the risks they are exposed to if bitten or scratched by animals. Patients with such risks factors should be instructed to visit their physician immediately so that adequate treatment can be started, thus reducing the chance for fatality to occur.

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