ERIZIPEL NAKON UJEDA MAČKE IZAZVAN BAKTERIJOM *PASTEURELLA MULTOCIDA* – PRIKAZ SLUČAJA

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CASE REPORT

ERYSIPELAS IN A CAT-BITE VICTIM CAUSED BY *PASTEURELLA MULTOCIDA* - CASE REPORT

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SAŽETAK

Uvod: Erizipel je karakterističan oblik površinskog akutnog streptokoknog celulitisa, koji se često leči ambulantno, prvenstveno penicilinom, a eritromicinom u slučaju da je oboleli alergičan na penicilin. Iznosimo slučaj pacijentkinje kojoj je, nakon ujeda mačke, preventivno dat eritromicin, da bi u toku terapije razvila erizipel, za koji se, nakon bakteriološkog pregleda brisa rane, ustanovilo da je izazvan bakterijom *Pasteurella multocida*, rezistentnom na eritromicin.

Prikaz slučaja: Ženska osoba, stara 53 godine, javila se na pregled zbog tegoba koje su odgovarale kliničkoj dijagnozi erizipela potkolenice. Nedelju dana ranije, ujela ju je sopstvena mačka. Rana je hirurški zbrinuta i ordiniran je profilaktički eritromicin, u dozi od 4 x 500 mg. Rana je bila mirna. Petog dana od povrede, pacijentkinja je postala visoko febrilna (39,2°C), bez drugih tegoba, što je shvaćeno kao gripozno stanje. Šestog dana nakon povrede, javio se eritem i edem oko mesta povrede, sa lokalnim limfangitisom i regionalnim limfadenitisom, a iz rane se cedio sangvilentan sekret. Dijagnostikovan je erizipel. U perifernoj krvnoj slici je postojala leukocitoza sa predominacijom neutrofilnih leukocita (LE = 13.9 x 10^9/l; NE = 82%), CRP je bio četvorostruko povišen (CRP = 43 IU). Uzet je bris i ordiniran penicilin. Sedmog dana terapije, lokalni nalaz je bio uredan, nalaz leukocita u perifernoj krvi bio je normalan (LE = 5.1 x 10^9/l; NE = 52%), a CRP dvostruko povišen (CRP = 24 IU). Izolovana je *Pasteurella multocida*, rezistentna na eritromicin, a osetljiva na penicilin.

Zaključak: Erizipel, iako jasno prepoznatljiv klinički entitet, može biti izazvan i drugim mikroorganizmima osim streptokoka, što je neophodno da se ima u vidu, u cilju, kako pravilne etiološke dijagnoze, tako i adekvatne i pravovremene terapije.

Ključne reči: Erizipel, *Pasteurella multocida,* Eritromicin

ABSTRACT

Introduction: Erysipelas is a characteristic form of acute superficial streptococcal cellulitis, usually treated in outpatient service, primarily with penicillin, or erythromycin, in cases where the patient is allergic to penicillin. We are reporting the case of a patient who was preventively treated with erythromycin, after a cat bite, but during treatment developed erysipelas, which, after a swab sample from the wound was analyzed, proved to be caused by *Pasteurella multocida*, resistant to erythromycin.

Case report: A 53-year-old woman came to the outpatient clinic with clinical signs of *erysipelas cruris*. Seven days before, she had been bitten by her own cat. The wound was surgically treated, and erythromycin, 500 mg qid, was prescribed as prophylaxis of wound infection. There were no signs of infection. On the 5th day following the bite, the patient was running a very high fever (39.2°C), but she was without other symptoms, thus the fever was considered to be a symptom of the flu. On the following day, prominent erythematous swelling appeared around the site of the wound, with localized lymphangitis and regional lymphadenitis, and discharge from the wound. The diagnosis of erysipelas was made. The peripheral blood test results were as follows: WBC = 13.9 x 10^9/l; NE = 82%, CRP = 43 IU. A swab sample was collected from the wound and the patient was started on penicillin. On the 7th day of penicillin administration, there were no signs of inflammation, while the blood test results were as follows: WBC = 5.1 x 10^9/l; NE = 52%; CRP = 24 IU. *Pasteurella multocida*, resistant to erythromycin but sensitive to penicillin was isolated from the swab sample.

Conclusion: Erysipelas, although an easily recognized clinical entity, can be caused by other microorganisms, besides streptococcus. It is very important to consider this in order to make an accurate diagnosis and prescribe the appropriate therapy.

Key words: Erysipelas, *Pasteurella multocida,* erythromycin

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Primljeno • *Received*: February 22, 2021; **Revidirano • *Revised*:** May 18, 2021; **Prihvaćeno • *Accepted*:** February 15, 2022; ***Online first*:** Mach 25, 2022.

DOI: 10.5937/3-30991

UVOD

Erizipel

Erizipel (lat. *erysipelas*) je vrsta površinskog celulitisa sa sistemskim manifestacijama, koji izaziva b-hemolitični streptokok, grupe A, ređe grupe C i G, a grupe B samo kod novorođenčadi. Bolest je sporadičnog karaktera. Infekcija se prenosi direktnim kontaktom. Izvor infekcije je najčešće gornji respiratorni trakt samog obolelog, ređe osobe koja ga je negovala, u smislu asimptomatskog nosilaštva.

Erizipel počinje naglo, visokom temperaturom, jezom, drhtavicom, uz malaksalost, mučninu, nekad i povraćanje, bolom na mestu gde će se pojaviti karakteristične promene u vidu jasno bedemasto ograničenog crvenog otoka, najčešće sa regionalnim limfadenitisom i limfangitisom. Sistemske manifestacije traju kratko, dok lokalne promene imaju različitu evoluciju, koja zavisi od intenziteta zapaljenja [1–5].

Dijagnoza erizipela je klinička dijagnoza, postavlja se na osnovu anamneze i pregleda obolelog. Laboratorijski nalazi ukazuju na bakterijsko oboljenje.

Od erizipela obolevaju osobe oba pola, uglavnom starijeg doba, tokom cele godine [3,5–8]. Nakon preležane bolesti, ostaju diskretne promene na sabirnim limfnim sudovima, što otežava mikrocirkulaciju, što je podloga za ponovno javljanje istog oboljenja na istom mestu, odnosno, nakon preležanog erizipela ostaje predispozicija za ponovno obolevanje [2,9,10].

Pre pojave antibiotika, erizipel je imao samoograničavajući (laka do umereno teška bolest) ili letalni karakter (teška bolest). U retkim slučajevima javljala se migrirajuća forma bolesti, u toku koje su se eritematozne ploče nadovezivale jedna na drugu. Dok su prethodne bledele, nove bi se stvarale. Ova forma bolesti imala je izrazito maligni karakter [5]. U preantiseptičkom periodu, maligni karakter je takođe imao i erizipel koji se javljao posle hirurških intervencija i u porodilištu; javljao se u obliku epidemija, odnoseći mnoge živote, jer su ulazna vrata bila velika, a izvor infekcije je bio stalno prisutan, u vidu zaposlenog osoblja.

Sredinom XX veka, erizipel je počeo da biva lakša bolest. Ima se utisak da je tome doprinelo to što se sam streptokok promenio, a s druge strane, i pojava antibiotika, na koje nije pokazivao otpornost. Od tog vremena, vidimo erizipel kao oboljenje koje se najčešće leči ambulantno. U lečenju se najčešće koriste penicilin i penicilinski preparati, ili eritromicin, kod osoba koje su alergične na penicilin [6].

Postupak sa ranom koju je nanela životinja

Svaka rana zahteva adekvatnu obradu, a rane koje su nanele životinje zahtevaju dodatno i prijavu, na prvom

INTRODUCTION

Erysipelas

Erysipelas is a type of superficial cellulitis with systemic manifestations, caused by group A β-hemolytic streptococcus, less frequently by group C and G β-hemolytic streptococci, and by group B β-hemolytic streptococcus, only in newborns. The disease is sporadic in character. Infection is transmitted through direct contact. The source of infection is most commonly the upper respiratory tract of the infected person, i.e., patient themselves, less frequently the upper respiratory tract of a person providing care for the patient (asymptomatic carrier).

The onset of erysipelas is sudden, with high fever, chills, shivering, weakness, nausea, sometimes vomiting, and pain at the site where it will apear, where characteristic changes occur, in the form of a clearly delineated red swelling with raised edges, most commonly with regional lymphadenitis and lymphangitis. Systemic manifestations are of short duration, while localized changes have a different evolution, depending on the intensity of the inflammation [1–5].

The diagnosis of erysipelas is a clinical one, it is established on the basis of the anamnesis and examination of the patient. Laboratory findings indicate bacterial infection.

Erysipelas can be contracted year-round by persons of both sexes. It usually affects persons of older age [3,5–8]. After the patient recovers from the disease, discreet changes on collecting lymph vessels remain, obstructing microcirculation, thus providing the substrate for the return of the same disease in the same location, i.e., after a person has had erysipelas, a predisposition towards the disease remains [2,9,10].

Before the advent of antibiotics, erysipelas had a self-limiting (mild to moderately severe form of the disease) or lethal character (severe disease). In rare cases, the migrating from of the disease appeared, wherein erythematous plaques extended one upon the other. While the previous plaques faded, new ones formed. This form of the disease had a distinctly malignant character [5]. In the pre-antiseptic era, the form of erysipelas developing after surgical procedures and in maternity hospitals or wards was also a malignant variant of the disease; it broke out in the form of epidemics, taking many lives, since the gate for the entry of the infections was wide open, and the source of the infection was ever-present, in the form of the hospital staff.

In the mid 1900s, erysipelas started to become a less serious disease. The belief is that this was partially the result of a change in the streptococcus itself, but also the result of the advent of antibiotics, towards which the streptococcus did not show resistance. Since that time,

mestu u cilju borbe protiv besnila. S obzirom na rad Luja Pastera na prevenciji besnila, formirana je mreža ambulanti na čelu sa Pasterovim institutom u Parizu, kao centralnom ustanovom za borbu protiv besnila. U Beogradu se Pasterova ambulanta nalazi u okviru Klinike za infektivne i tropske bolesti Univerzitetskog kliničkog centra Srbije (UKCS). Ozleđene treba prvo da pregleda hirurg, koji daje opis povrede i terapiju. Zatim se u Pasterovoj ambulanti pravi zapisnik o tome kako je povreda nastala, proceni vakcinalni status životinje koja je nanela povredu i povređenog, ordinira postekspoziciona profilaksa i, po potrebi, izda nalog Gradskoj veterinarskoj službi za pregled životinje koja je nanela povredu [11].

Pasteurella multocida

Pasteurella multocida je mikroorganizam iz roda *Mannheimia*. Ove bakterije se pod svetlosnim mikroskopom vide kao koko-štapići. Po Gramu se boje negativno. Aerobne su i fakultativno anaerobne, imaju kapsulu, nepokretne su i asporogene. *Pasteurella multocida* je prvi put opisana 1878. godine, kod kolere živine [12]. Živi kao saprofit u ustima mnogih životinja; od domaćih životinja na prvom mestu su mačka i pas [13].

Ova bakterija je osetljiva na dejstvo penicilina. Njena invazivnost zavisi od različitih faktora virulencije, kao što su sastav kapsule, lipopolisaharida, površinskih adhezina i mnogih drugih elemenata koji još uvek nisu identifikovani [14]. Iako saprofit, može da izazove različita oboljenja životinja, prvenstveno respiratornog trakta. Ima veliku ulogu u morbiditetu goveda i svinja u kolektivnom uzgoju [15–19].

Ljudi prvenstveno obolevaju od pasteriloze u neposrednom kontaktu sa životinjama, u smislu infekcije ujedne rane, mada i lizanje životinje može da bude opasno. Ishod bolesti je najčešće povoljan, mada može biti i letalan, prvenstveno kod imunokompromitovanih pacijenata i kada ne postoji podatak o ugrizu životinje [20,21].

Pored infekcije ujedne rane, kod ljudi može da izazove sepsu, empijem, meningitis, endokarditis i infekcije drugih organa. U lečenju treba imati na umu da je ova bakterija otporna na dejstvo određenih antibiotika i da u terapiju treba da budu uključeni prvenstveno antibiotici na koje se zna da ne pokazuje rezistenciju, a terapiju treba korigovati prema antibiogramu [22–29]. Na prvom mestu je i dalje penicilin G, zatim slede amoksicilin, piperacilin, cefalosporini i antibiotici novih generacija [30–32].

Iznosimo slučaj erizipela (površinskog celulitisa) rezistentnog na eritromicin, nastalog nakon ujeda kućne mačke, kod kojeg je iz brisa rane izolovana *pasteurella multocida*.

erysipelas has most commonly been encountered as a disease treated in outpatient care. Penicillin and penicillin-based medication is most commonly used for its treatment, or erythromycin, in patients allergic to penicillin [6].

Procedure with an animal-inflicted wound

Any wound requires proper treatment, and for wounds inflicted by animals it is additionally required that they are reported, primarily for the purpose of rabies control. Due to the dedicated work of Louis Pasteur on rabies prevention, a network of outpatient clinics was formed, led by the Pasteur Institute in Paris, as the central institution for rabies control. In Belgrade, the Pasteur Unit operates within the Clinic for Infectious and Tropical Diseases of the University Clinical Center of Serbia (UCCS). Injured persons should first be examined by a surgeon, who needs to provide the description of the wound and prescribe therapy. After this, at the Pasteur Unit, a record is made of the circumstances of the injury, of the assessment of the vaccination status of the animal who had inflicted the wound, as well as of the injured individual, upon which post-exposure prophylaxis is prescribed, and, if needed, a directive is issued to the City Veterinary Service to examine the animal who had inflicted the wound [11].

Pasteurella multocida

Pasteurella multocida is a microorganism of the *Mannheimia* genus. These bacteria can be seen under the microscope as coccobacilli. They give a negative result on the Gram stain test. They are aerobes and facultative anaerobes. They have a capsule and are nonmotile and asporogenic. *Pasteurella multocida* was first described in 1878, in fowl cholera [12]. It lives as a saprophyte in the oral cavities of many animals; in domesticated animals and pets. Cats and dogs are the primary carriers [13].

This bacterium is sensitive to penicillin. Its invasiveness depends on different virulence factors, such as the structure of the capsule, lipopolysaccharides, surface adhesins, and many other elements which have as yet not been identified [14]. Although a saprophyte, this bacterium can cause different animal diseases, primarily of the respiratory tract. It plays a significant role in bovine and swine mortality, in collective breeding [15–19].

People primarily contract pasteurellosis as the result of direct contact with animals, in the sense of the infection of a bite wound, although being licked by an animal may also be dangerous. The outcome of the disease is most commonly favorable, although it may be lethal, primarily in immunocompromised patients and when data on the animal bite is lacking [20,21]. In addition to the infection of the bite wound, in people, this disease can also cause sepsis, empyema, meningitis, endocarditis, and infection of other organs. When

Prikaz slučaja

Ženska osoba, stara 53 godine, javila se na pregled zbog tegoba koje su odgovarale kliničkoj dijagnozi erizipela potkolenice. Nedelju dana ranije, bila je pregledana u Pasterovoj ambulanti Klinike za infektivne i tropske bolesti, zbog ujeda sopstvene mačke. Povreda je bila minorna, ordinirana je antitetanusna postekspoziciona profilaksa i antibiotska profilaksa infekcije rane eritromicinom. Prvih dana, okolina rane je bila mirna. AT zaštita je uredno sprovedena i pila je predloženi antibiotik. Petog dana od povrede došlo je do skoka temperature na 39,2°C, bez drugih tegoba. U tom momentu, na mestu povrede videla se krasta oko koje je bila minorna zapaljenska reakcija, ali iz koje se secernirao serosangvinolentni sadržaj. Temperatura je shvaćena kao gripozno stanje, a laka hiperemija oko kraste je zanemarena. Narednog dana temperatura se održavala, a oko kraste se videlo izraženo zapaljenje; javio se limfangitis i ingvinalni limfadenitis. Tada je postavljena dijagnoza erizipela, uzet je bris rane i ordiniran penicilin (1.600.000 IU). Od laboratorijskih analiza, nađeno je: Le = 13,9 x10^9/l; NE = 82%; fibrinogen = 6,2 g/l; CRP = 43 IU; SE = 30. Posle tri dana terapije, povukao se limfangitis i limfadenitis, nije bilo secernacije ispod kraste, okolni eritem se smanjio, ali se održavao edem okolnog tkiva. Iz brisa rane je izolovana *Pasteurella multocida*, rezistentna na eritromicin a osetljiva na penicilin. Sedmog dana terapije, krasta je bila oivičena lakim infiltratom, nije bilo znakova zapaljenja, a u laboratorijskim analizama se jasno videlo smanjenje zapaljenskog sindroma (Le = 5,1 x10^9/l; NE = 52%; CRP = 24 IU; fibrinogen = 5,2 g/l; SE = 32).

ZAKLJUČAK

Erizipel je dobro poznato oboljenje. Dobro je poznata njegova etiologija i patogeneza, kao i način lečenja, a penicilin je lek izbora. Visoka temperatura sa sistemskim manifestacijama traje kratko i ne zabrinjava terapeuta. Uglavnom zabrinjavaju izrazito povišene vrednosti pokazatelja zapaljenskog sindroma, koje treba pratiti, ali se u praćenju i lečenju obolelog treba orijentisati prema kliničkoj slici.

Sa ranama koje su nanele životinje neophodno je postupati sa posebnom pažnjom i saznanjem da se ugrizom mogu preneti bakterije koje mogu da izazovu invazivne infekcije, što zavisi od faktora virulencije same bakterije.

U svojoj praksi, retko viđamo infekcije nakon povreda koje su nanele životinje, kada se uradi adekvatna primarna obrada rane. Smatrajući da su mesta povrede nakon stručne obrade bila čista, infekcije ovih rana posmatramo kao infekcije izazvane streptokokama ili stafilokokama, ređe drugim bakterijama, kao sekundarnu

treating this infection, one must bear in mind that this bacterium is resistant to certain antibiotics, and that treatment should primarily be based on those antibiotics which this bacterium is known not be resistant to, while the treatment needs to be adjusted according to the antibiogram [22–29]. The drug of first choice is still penicillin G, followed by amoxicillin, piperacillin, cephalosporines, and new-generation antibiotics [30–32].

We present an erysipelas (surface cellulitis) case, resistant to erythromycin, which developed following the bite of a house cat, wherein *pasteurella multocida* was isolated from the swab sample of the wound.

Case report

A 53-year-old woman came in for an examination due to complaints which matched the clinical diagnosis of *erysipelas cruris*. Seven days before, she had been examined at the Pasteur Unit of the Clinic for Infectious and Tropical Diseases, following a bite inflicted by her own cat. The bite was minor, anti-tetanus post-exposure prophylaxis was prescribed, as well as antibiotic prophylaxis of wound infection with erythromycin. In the first few days, the surrounding area of the wound was without signs of inflammation. Anti-tetanus protection was carried out, as prescribed, and the patient took the prescribed antibiotic therapy. On the fifth day following the cat bite, the patient developed a fever of 39.2°C, with no other symptoms. At that point, the wound was covered with a scab, with minor inflammation surrounding the wound, but which exuded serosanguinous content. The fever was attributed to the flu, while the slight hyperemia surrounding the wound was disregarded. On the following day, the fever persisted, while the area surrounding the scab showed signs of marked inflammation; lymphangitis and inguinal lymphadenitis also developed. The diagnosis of erysipelas was established at this point, a swab sample was collected from the wound, and penicillin (1,600,000 IU) was prescribed. Laboratory tests were performed, with the following results: WBC = 13.9 x 10/9/l; NE = 82%, fibrinogen = 6.2 g/l; CRP = 43 IU; SE = 30. After three days of treatment, lymphangitis and lymphadenitis subsided, there was no more exudation from underneath the scab, the erythema of the surrounding area decreased, however the edema of the surrounding tissue persisted. *Pasteurella multocida*, resistant to erythromycin but sensitive to penicillin, was isolated from the swab sample of the wound.

On the seventh day of treatment, the scab was delineated with mild infiltrate, there were no remaining signs of inflammation, and the laboratory test results clearly showed a drop in the inflammatory syndrome markers (WBC = 5.1 x 10^9/l; NE = 52%; CRP = 24 IU; fibrinogen = 5.2 g/l; SE = 32).

infekciju rane, praktično isključujući mogućnost da je rana bila primarno inficirana.

U Srbiji se o bakteriji *Pasteurella multocida* govori jedino u veterinarskoj literaturi. Retki su izveštaji o izolaciji ovog patogena u humanoj medicini, mada se mogu naći izveštaji da, pored infekcije ujedne rane, izaziva teška oboljenja različitih organa i sepsu. Ove činjenice moraju da nas nateraju da, bez obzira na prepoznatljivu kliničku sliku, tražimo i etiološku potvrdu. U navedenom slučaju, klinička slika je odgovarala erizipelu, ali je nedostajala inicijalna mučnina i povraćanje, što se i ne javlja kod svih obolelih.

Kao i mnogi drugi mikroorganizmi, *Pasteurella multocida* je karakteristična za veterinarsku medicinu, podložna je promeni osetljivosti na antibiotike, tako da je potrebno stalno praćenje rezistencije. U ovom slučaju, da je preventivno dat penicilin ili cefalosporin, ne bi ni došlo do razvoja infekcije. Stoga sugerišemo da se, u cilju prevencije infekcije rana nanesenih životinjskim ujedom ili ogrebom, ordiniraju penicilinski ili cefalosporinski preparati, u uobičajenim terapijskim dozama.

Sukob interesa: Nije prijavljen.

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CONCLUSION

Erysipelas is a well-known disease. Its etiology and pathogenesis are well understood, as is the method of treatment, with penicillin being the medication of choice. High fever with systemic manifestations does not last long and is not a cause for concern. Primarily, the cause for concern are cases with markedly elevated levels of inflammatory syndrome markers, which must be monitored. However, both in monitoring and in treatment of the patient, one must be led by the clinical presentation.

It is necessary to treat animal-inflicted wounds with special care and with the notion that an animal bite may transfer bacteria that can cause invasive infections, depending on the virulence of the bacterium itself.

In our everyday clinical practice, when the appropriate treatment of the wound is carried out, we rarely see infection of wounds inflicted by animals. Considering the sites of the wounds clean, after professional treatment, we regard infections of these wounds as secondary infections caused by streptococci or staphylococci, less frequently by other bacteria, in this way practically excluding the possibility that the wound had been primarily infected.

In Serbia, *Pasteurella multocida* is discussed only in publications pertaining to veterinary medicine. Reports of this pathogen being isolated in the domain of human medicine are rare, although reports can be found. In addition to bite wound infection, this bacterium can cause severe disease of different organs, as well as sepsis. These facts must motivate us to seek etiological confirmation, regardless of the recognizable clinical presentation. In the above-described case, the clinical presentation matched erysipelas, but the initial nausea and vomiting were absent, which, indeed, do not necessarily occur in all patients.

Just like many other microorganisms, *Pasteurella multocida* is characteristic of veterinary medicine. It is prone to change with respect to its sensitivity to antibiotics, which is why its resistance needs to be constantly monitored. In this case, had penicillin or a cephalosporin been prescribed as preventive treatment, the infection would not have developed. This is why we suggest that, for the purpose of preventing the infection of animal-inflicted wounds (bite or scratch), penicillin or cephalosporin medication should be prescribed in the usual therapeutic doses.

Conflict of interest: None declared.

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