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Anna Materny¹, Ernest Kuchar²

Streptococcal sepsis and periorbital cellulitis as a complication of influenza in a 4-year-old girl

Sepsa paciorkowcowa i zapalenie tkanek miękkich oczodołu jako powikłanie grypy u 4-letniej dziewczynki

¹ Anna Gostyńska Wolski Hospital, Warsaw, Poland

² Department of Paediatrics with Clinical Assessment Unit, Medical University of Warsaw, Warsaw, Poland

Correspondence: Anna Materny, K. Jędrusik 1/17, 01-748 Warsaw, Poland, tel.: +48 509 606 799, e-mail: anna.materny@yahoo.com

Abstract

Influenza may pave the way for some specific bacterial infections. In this case study we present a rare complication of influenza A infection – periorbital cellulitis followed by streptococcal toxic shock syndrome and scarlet fever. A 4-year-old otherwise healthy girl presented with her mother to a general practitioner with fatigue, irritability and fever not responding to antipyretics. Due to the positive rapid influenza diagnostic test, treatment with oseltamivir was implemented. The Quick Strep Test was negative. During the following days, the patient's condition worsened, leading to an admission to a paediatric otolaryngology unit. Doctors observed an asymmetrical swelling of the lids with exophthalmos of the right eye, pharyngitis, petechiae in skin folds, a strawberry tongue and skin exfoliation on the lips. The patient was treated with intravenous broad-spectrum antibiotics (cefotaxime, vancomycin) and underwent drainage of sinuses, without any significant improvement. On the following day, the girl showed signs of systemic infection, confusion and further swelling of both eyes, and therefore was moved to an intensive care unit. Computed tomography of the head showed signs of periorbital cellulitis with destruction of the surrounding bones. After obtaining a positive blood culture for group A streptococcus, penicillin and clindamycin were immediately administered. The patient's condition improved within 24 hours. The described case emphasises the importance of yearly influenza vaccination, especially in the groups with risk factors like very young age. Early diagnosis of the streptococcal infection as a complication of influenza and a targeted treatment may prevent the potentially fatal outcome in the form of streptococcal toxic shock syndrome.

Keywords: streptococcal sepsis, scarlet fever, preseptal cellulitis

Streszczenie

Grypa może torować drogę zakażeniom bakteryjnym. W pracy przedstawiono przypadek rzadkiego powikłania grypy – zapalenia tkanek miękkich oczodołu, przebiegającego z zespołem paciorkowcowego wstrząsu toksycznego i wysypką szkarlatynową. Dotychczas zdrowa 4-letnia dziewczynka zgłosiła się z matką do lekarza z powodu ogólnego osłabienia, drażliwości i gorączki nieustępującej pomimo leczenia przeciwgorączkowego. Ze względu na dodatni wynik szybkiego testu grypowego przy ujemnym wyniku szybkiego testu paciorkowcowego zlecono oseltamivir. Mimo leczenia stan ogólny chorej się pogorszył i dziewczynka została przyjęta do szpitala klinicznego, gdzie stwierdzono obrzęk powiek z wytrzeszczem prawego oka, zapalenie gardła, wybroczyny w zgięciach skórnych, malinowy język i złuszczacą się skórę ust. Badania obrazowe uwidoczniły cechy naciekania tkanek miękkich oczodołu oraz destrukcji przylegających części kostnych, wobec czego zastosowano empiryczną antybiotykoterapię o szerokim spektrum działania (cefotaksym i wankomycyna dożylnie) i drenaż zatok przynosowych, co nie przyniosło poprawy. Kolejnego dnia wystąpiły objawy wstrząsu toksycznego, zaburzenia świadomości oraz asymetryczne narastanie obrzęku oczu. Pacjentka została przeniesiona na oddział intensywnej terapii. Z posiewu krwi wyhodowano paciorkowca ropnego. Leczenie celowane (penicylina z klindamycyną dożylnie) przyniosło spektakularną poprawę. Opisany przypadek dowodzi, jak istotne są coroczne szczepienia przeciwko wirusowi grypy w grupie ryzyka, do jakiej należą dzieci w pierwszych 5 latach życia. Należy pamiętać, że zapalenie tkanek miękkich o etiologii *Streptococcus pyogenes* może być powikłaniem grypy, które w szybkim tempie może doprowadzić do zagrożenia życia chorego.

Słowa kluczowe: sepsa paciorkowcowa, szkarlatyna, zapalenie przedprzegrodowe

INTRODUCTION

We present a case of a 4-year-old girl who developed generalised streptococcal infection with the symptoms of toxic shock syndrome, scarlet fever and rapidly progressing periorbital cellulitis secondary to influenza. We found no similar complication of influenza caused by group A beta-haemolytic streptococcus in the available literature.

CASE REPORT

An otherwise healthy 4-year-old girl with no chronic diseases reported with her mother to a general practitioner due to fatigue that had been increasing for 4 days, irritability, generalised pain, pharyngeal pain and fever of up to 37–38°C (measured under the armpit). It was found from medical interview that the girl developed correctly and was immunised in accordance with the Protective Vaccination Programme as well as received additional vaccinations against pneumococci, rotaviruses and varicella. Her present condition was managed symptomatically with oral ibuprofen administered at an appropriate dose. The patient's mother reported that she had been in contact with patients with influenza at her workplace.

The doctor confirmed fever of 38°C (measurement under the armpit), excluded tonsillitis, and recommended continuation of symptomatic treatment.

Due to the lack of improvement, persistent subfebrile temperature, thoracic rash and local petechiae in the groin and lower legs, the girl presented at the general practitioner the following day.

The doctor performed a rapid influenza test, which was positive for type A influenza, and excluded streptococcal pharyngitis (rapid test for bacterial tonsillitis and swab were negative). He also measured C-reactive protein (CRP) (34 mg/L; normal level up to 5 mg/L), diagnosed influenza and prescribed oseltamivir. On the same day in the evening, the girl developed a fever of 38.9°C. The parents reduced the fever by alternate administration of ibuprofen and paracetamol at doses appropriate for body weight; they additionally used cold compresses. On day 7 after the onset of symptoms, the high temperature persisted despite antipyretic treatment, the child was weak and presented with nasal discharge and cough as well as an aphthous ulcer about 1 cm in diameter appeared on the lower lip. The parents noticed that the girl's upper and lower eyelids were pink and slightly swollen. The oedema increased the following day, and was more pronounced on the right side. The child complained of an itchy right eye. Additionally, a strawberry tongue was present. The concerned parents reported to the hospital. In the hospital emergency department, the girl's condition was assessed as fairly good; the patient was circulatory and respiratory efficient, and was in full verbal and logical contact.

Small petechiae under the armpits, on both feet and the right thigh as well as minor limb oedema were observed. Bright red and parched lips; red, softened throat; fine aphthous ulcers on the oral mucosa; pain on opening the mouth. Bilaterally reddened and swollen eyelids, especially the right lid. No discharge was observed. Eye mobility and response to light maintained and symmetrical. Laboratory abnormalities included increased inflammatory markers [CRP 27 mg/L (normal <1 mg/L), PCT 4 µg/L (normal <0.1 µg/L), white blood cells, WBC 32 thousand/mL with 94% granulocyte fraction]. Arterial-blood gas analysis showed no signs of acidosis; there was increased fibrinogen (6.2 g/L; normal level up to 3.5 g/L); activated partial thromboplastin time (APTT) and international normalised ratio (INR) were in the upper limit of normal, serum albumin was reduced to 3.5 g/dL. Due to the suspicion of complicated paranasal sinusitis, the girl was admitted to a paediatric otolaryngology unit. IV cefotaxime and, after positive laboratory findings confirming the growth of Gram-positive coccal colonies, IV vancomycin were used. Oseltamivir was continued. Symptomatic treatment was additionally used to relieve itching and upper respiratory tract oedema (dimethindene, xylometazoline and ofloxacin in the form of eye drops). Fever and somnolence persisted the following day. Facial oedema, exophthalmia, and impaired mobility of the right eye were noticeable, indicating periorbital cellulitis and peripheral oedema. Drops in blood saturation to 86% were also observed. Inflammatory markers increased, while albumin levels decreased to 2.6 g/dL. For this reason, 20% albumin solution was administered. Head computed tomography showed a large purulent collection in the paranasal sinuses and infiltration of the soft tissues with the presence of air and right orbital bone destruction. Therefore, emergency endoscopic drainage of paranasal sinuses was performed; however, only a small amount of watery discharge with isolated purulent streaks was obtained. IV dexamethasone and nasal xylometazoline were administered to reduce nasal mucosa oedema. The girl's general condition significantly deteriorated the following day. She was unable to get out of bed, appeared to be in pain, and spoke only when instructed. Hyperaesthesia and photophobia appeared. It was necessary to transfer the patient to the intensive care unit. At the same time, blood culture was obtained (*Streptococcus pyogenes*), allowing for modification of antibiotic therapy (a switch to IV penicillin plus clindamycin). The girl's condition improved significantly the following day. Antibiotic therapy was continued for 14 days. The girl was discharged home in good overall condition with instructions to continue oral cefadroxil for 5 days. Three weeks after discharge, a follow-up contrast-enhanced magnetic resonance imaging of the head was performed, which showed the presence of post-inflammatory changes in the periorbital soft tissues and paranasal sinuses (Figs. 1, 2).

Fig. 1. Girl's face with asymmetrical eyelid oedema and raspberry tongue

Fig. 2. Septic patient, periorbital cellulitis, skin exfoliation on the lips

DISCUSSION

Although streptococcal pharyngitis and tonsillitis (*Streptococcus pyogenes*) is a common reason for reporting to primary care physicians, it poses no clinical challenge due to its self-limiting course and lack of resistance to the most commonly used beta-lactam antibiotics. In rare cases, however, it may give rise to serious complications, such as streptococcal toxic shock syndrome (STSS). When the described patient first presented at the doctor, her condition indicated a viral infection of the upper respiratory

tract – the most common cause of medical advice in this age group. However, the lack of improvement despite symptomatic and antiviral treatment raised doubts about the aetiology of the infection, even though a negative rapid test for bacterial tonsillitis was obtained. The specificity of this test is high (about 95%)^(1,2). The deteriorating clinical condition of the patient, persistent fever and increasing periorbital tissue oedema prompted an extension of diagnosis and the use of broad-spectrum antibiotic therapy. While preseptal cellulitis is a relatively mild complication of paranasal sinusitis caused by the same aetiological factors (*Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus* and *Moraxella catarrhalis*) that account for the vast majority of cases⁽³⁾, orbital (postseptal) cellulitis is a sight and even life threatening condition. Cases of streptococcal sepsis requiring eyeball enucleation have been described. The development of STSS is most often associated with wound and soft tissue infection. It cannot be excluded that in our patient the streptococci passed from the pharynx to periorbital structures via bloodstream, although streptococcal sepsis is a rare complication of upper respiratory tract infections (URTIs) and scarlet fever, accounting for only 0.3% of cases of febrile patients with scarlet fever⁽⁴⁾. However, up to 1/3 of generalised streptococcal infections are complicated by STSS, which may rapidly lead to a fatal outcome (mortality rates 2–8%)^(5,6). Regardless of systemic manifestations, the presence of streptococci in the blood is confirmed in 2–4 per 100,000 children; in two case series, the incidence of streptococcal bacteraemia was estimated at about 1–3 cases per 1,000 paediatric patients^(5–7). In recent years, the incidence of streptococcal sepsis has increased in Europe and worldwide, especially during the influenza season⁽⁸⁾, and so has the incidence of systemic complications of streptococcal URTIs^(5–7). The reasons for the described increase in morbidity in immunocompetent patients remain unknown. Common immunisation against pneumococci, which can be replaced by less common pathogens, is one of the possible reasons⁽⁷⁾. The use of nonsteroidal anti-inflammatory drugs may also be a risk factor for bacterial infections as well as it may mask the symptoms of infection⁽⁴⁾ and reduce the efficacy of some antimicrobials⁽⁹⁾. Previous viral infections, including influenza, as in the described patient, promote bacterial infections⁽¹⁰⁾. Studies in mice infected with group A streptococci have shown that vaccination against influenza significantly reduced sepsis-related mortality (from 78% to 15%)⁽¹¹⁾. Other conditions predisposing to bacteraemia in children include varicella, herpes zoster, reduced immunity, disrupted skin continuity and infancy^(4–6), all of which were absent in the described case. IV crystalline penicillin administered at doses of 200,000–400,000 units/kg/day at 4–6-hour intervals is the treatment of choice in streptococcal infections. In severe infections, clindamycin may be additionally included at a dose of 25–40 mg/kg/day given at 6–8-hour intervals, which inhibits streptococcal toxin production and reduces mortality. IV immunoglobulins have been reported to be beneficial in STSS.

Head imaging should be performed about 3 weeks after treatment completion to exclude active inflammation and complications of postseptal cellulitis.

CONCLUSIONS

Influenza may be complicated by severe bacterial infections, including streptococcal infections. Influenza prevention through vaccination and causative treatment with oseltamivir may therefore prevent life-threatening complications, such as periorbital cellulitis, streptococcal sepsis and STSS.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organisations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

References

1. Pritt BS, Patel R, Kirn TJ et al.: Point-counterpoint: a nucleic acid amplification test for *Streptococcus pyogenes* should replace antigen detection and culture for detection of bacterial pharyngitis. *J Clin Microbiol* 2016; 54: 2413–2419.
2. Cohen JF, Bertille N, Cohen R et al.: Rapid antigen detection test for group A streptococcus in children with pharyngitis. *Cochrane Database Syst Rev* 2016; 7: CD010502.
3. Fanella S, Singer A, Embree J: Presentation and management of pediatric orbital cellulitis. *Can J Infect Med Microbiol* 2011; 22: 97–100.
4. Stevens DL, Tanner MH, Winship J et al.: Severe group A streptococcal infections associated with a toxic shock-like syndrome and scarlet fever toxin A. *N Engl J Med* 1989; 321: 1–7.
5. Laupland KB, Davies HD, Low DE et al.: Invasive group A streptococcal disease in children and association with varicella-zoster virus infection. *Ontario Group A Streptococcal Study Group. Pediatrics* 2000; 105: E60.
6. Tapiainen T, Launonen S, Renko M et al.: Invasive group A streptococcal infections in children: a nationwide survey in Finland. *Pediatr Infect Dis J* 2016; 35: 123–128.
7. Dennison SH, Ask LS, Eriksson M et al.: Serious complications due to acute rhinosinusitis in children up to five years old in Stockholm, Sweden – still a challenge in the pneumococcal conjugate vaccine era. *Int J Pediatr Otorhinolaryngol* 2019; 121: 50–54.
8. Scaber J, Saeed S, Ihekweazu C et al.: Group A streptococcal infections during the seasonal influenza outbreak 2010/11 in South East England. *Euro Surveill* 2011; 16: 19780.
9. Hamilton SM, Bayer CR, Stevens DL et al.: Effects of selective and nonselective nonsteroidal anti-inflammatory drugs on antibiotic efficacy of experimental group A streptococcal myonecrosis. *J Infect Dis* 2014; 209: 1429–1435.
10. Herrera AL, Huber VC, Chaussee MS: The association between invasive group A streptococcal diseases and viral respiratory tract infections. *Front Microbiol* 2016; 7: 342.
11. Okamoto S, Kawabata S, Fujitaka H et al.: Vaccination with formalin-inactivated influenza vaccine protects mice against lethal influenza *Streptococcus pyogenes* superinfection. *Vaccine* 2004; 22: 2887–2893.