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OPIS PRZYPADKU
CASE REPORT

Adult cutaneous diphtheria in Poland – a case report and literature overview

Błonica skóry u dorosłego pacjenta w Polsce – opis przypadku i przegląd literatury

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ABSTRACT

Corynebacterium diphtheriae (*C. diphtheriae*) is the primary pathogen causing diphtheria, which basically exists in two forms: nasopharyngeal and cutaneous. According to a commonly introduced vaccination programme against diphtheria, pertussis and tetanus (DPT), the incidence of diphtheria has significantly dropped around the world, in some areas disappearing almost completely. However nowadays, we observe the reappearance of diphtheria, especially the cutaneous form, even in countries with very high vaccination rates due to the increasing migration from countries with a lower level of vaccinated citizens.

We present a case study of a Ukrainian immigrant diagnosed with cutaneous diphtheria to raise the awareness of the medical community about this returning disease, its cutaneous form and new medical challenges connected to it. It has been the first reported case of *C. diphtheriae* infection in Poland since 2005. We analysed the most recent articles available in PubMed and Google Scholar databases using criterion keywords such as: "diphtheria case", "diphtheria case report", "cutaneous diphtheria". We selected the most suitable out of approximately 1,700 articles.

The presented case report and analysis of scientific publications on cutaneous diphtheria show the importance of this form of the disease in the modern, post-vaccination era. We claim that the importance of vaccination, self-protection during contact with patients, and awareness of the risks of the medical environment are becoming even more important.

KEYWORDS

review, case report, cutaneous diphtheria, diphtheria

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STRESZCZENIE

Corynebacterium diphtheriae (*C. diphtheriae*) jest pierwotnym patogenem wywołującym błonicę, która zasadniczo występuje w dwóch postaciach: nosowo-gardłowej i skórnej. W związku z powszechnymi szczepieniami przeciwko błonicy, krztuścowi i tężcowi (*diphtheria, pertussis and tetanus* – DPT) częstość występowania błonicy na świecie znacząco zmalała, na niektórych obszarach zanikając niemal całkowicie. W dzisiejszych czasach ponownie obserwujemy przypadki błonicy, zwłaszcza postaci skórnej, nawet w krajach z wysokim wskaźnikiem wyszczepienia, w związku z nasilającą się migracją z krajów o niższym odsetku zaszczepionych obywateli.
Prezentujemy studium przypadku ukraińskiego imigranta ze zdiagnozowaną błonicą skóry, by zwiększyć świadomość środowiska medycznego o tej powracającej chorobie, jej postaci skórnej oraz związanych z tym nowych wyzwaniach. To pierwszy zaraportowany przypadek zakażenia *C. diphtheriae* w Polsce od 2005 r. Przeanalizowano najnowsze artykuły dostępne w bazach PubMed i Google Scholar, używając jako kryterium następujących słów kluczowych: „błonica przypadek", „błonica opis przypadku", „błonica skóry". Wybrano artykuły o najwyższej korelacji z ponad 1700 wyników wyszukiwania.
Opis przypadku i analiza publikacji naukowych na temat błonicy skóry pokazują znaczenie tej postaci choroby w nowej, poszczepiennej erze. Twierdzimy, że szczepienia, stosowanie ochrony osobistej podczas kontaktu z pacjentem oraz świadomość środowiska medycznego dotycząca możliwych zagrożeń stają się jeszcze bardziej istotne.

SŁOWA KLUCZOWE

przegląd, opis przypadku, błonica skóry, błonica

INTRODUCTION

Corynebacterium diphtheriae (*C. diphtheriae*) is a Gram-positive, club-shaped pathogenic bacterium causing diphtheria [1], a respiratory tract disease potentially complicated by systemic effects of exotoxin. However, it is also capable of causing cutaneous and wound infections [2].
We observe toxic strains of *C. diphtheriae*, whose diphtheria toxin (DT) is a determinant of the classic course of the disease and non-toxic strains, considered potential emerging pathogens as they are also capable of causing severe diseases, which are not vaccine--preventable [1]. Diphtheria is an airborne disease in its classic form, observed mainly in the population of children in countries with lower vaccination coverage, or adults living in poor social and hygiene conditions. The most common symptoms of the disease connected to the DT are fever, white/brown pseudomembranes in the nasopharyngeal area, sore throat, enlargement of the lymph nodes and soft tissues of the neck, a characteristic smell of breath, salivation, dysphagia, myocarditis, and paralysis of the soft palate. The incubation period of the disease lasts approx. 2–4 days. Cutaneous diphtheria may be transmitted by direct contact with infected wounds, and the classically described symptoms may not occur.
According to our analysis, the last reported case of diphtheria in Poland was published in 2005. Until then, no cases had been observed since 1996 [2]. Furthermore, the latest reports published by the National Institute of Hygiene in Warsaw do not show any presence of diphtheria in Poland between the years 2010–2017 [3]. The only way to reduce the incidence of the disease is through universal vaccination. Nonetheless, in countries with optimal vaccine coverage, the carrier status of diphtheria is much lower, except among individuals with low immunisation conditions and people who abuse alcohol [1,4]. The aim of our study was to present a case report and analysis of scientific publications of cutaneous diphtheria as the importance of this form of the disease in the modern, post-vaccination era.

CASE REPORT

In April 2021, a 41-year-old, neglected Ukrainian immigrant male was admitted to hospital with moderated pain – 6 in Numerical Rating Scale (NRS) and swelling on his left limb. There were also other typical signs of soft tissue inflammation in the left leg area, such as redness, increased warmth and leakage of a serous-purulent content from ulcers (Figure 1). It was the first medical intervention for this reason. The SARS-CoV-2 antigen test was carried out, but the result was negative.

Fig. 1. Wounds on left limb.
Ryc. 1. Rany w obrębie lewego podudzia.

The patient was aggressive and uncooperative and lived in a poor social environment as a homeless man. The

patient was an active smoker, alcoholic, epileptic and had anaemia. The history of chronic diseases, medications were taken, and family burdens were irrelevant. There was no information about the patient's vaccination history. Physical examination revealed tachycardia (140 bpm), normal blood pressure, and increased body temperature (37.6°C). During palpation, there was a tender, painful, fixed lymphatic node of dimensions about 8 × 10 mm in the left lower limb region. The patient had no symptoms of respiratory tract infection. Some diagnostic tests were taken, such as an X-ray of the left limb, which showed increased irregular shading in the projection of the gastrocnemius muscle. Many small periaortic lymphatic nodes and numerous (approx. 13 mm in short axis long) lymph nodes lying along the left iliac arteries were found in computer tomography (CT), and bigger nodes (up to 17 mm on the short axis) were present in the inguinal region, mostly on the left side.

Blood samples and swabs from the inflammatory changes were taken. The results of the blood test are presented in Table I. Empiric antibiotic therapy of ciprofloxacin (400 mg twice daily, intravenous) was initiated. Also, typical analgesic therapy was started with good results.

Table I. Results of blood test on day of admission
Tabela I. Wyniki badań krwi w dniu przyjęcia

Test	Result	Range of standards
RBCs	3.37 MM/µl	4.63–6.08
Leukocytes	46.04 K/µl	4.23–9.07
Hb	11.5 g/dl	13.7–17.5
Hematocrit	35.7%	40.1–51.0
MCV	105.9 fl	79–92.2
MCH	34.1 pg	25.7–32.2
MCHC	32.2 g/dl	32.3–36.5
Platelets	568 K/µl	150–400
PDW	7.9 fl	9.8–16.1
MPV	8.3 fl	9.4–12.6
P-LCR	11.3%	19.2–47
Neutrophils	43.06 K/µl	2–7
Lymphocytes	0.49 K/µl	1–3
Eosinophils	0.00 K/µl	0.02–0.5
Neutrophils	93%	40–80
Lymphocytes	1.1%	20–40
Eosinophils	0.0%	1–6
Monocytes	1.3%	2–10

RBCs – red blood cells; Hb – hemoglobin; MCV – mean corpuscular volume; MCH – mean corpuscular hemoglobin; MCHC – mean corpuscular hemoglobin concentration; PDW – platelet distribution width; MPV – mean platelet volume; P-LCR – platelet large cell ratio.

During the bacteriological examination, *C. diphtheriae* of the nontoxigenic biotype *gravis* and *Streptococcus* spp. were isolated from the samples taken from the inflammatory changes. The microbiological examination was carried out using a breeding method (under aerobic and anaerobic conditions) and mass spectroscopy for identification. The outcome was compared with the mass spectra library (MDB IVD Library – March 2019).

The patient was admitted in isolation, and all epidemiological procedures were implemented. Due to the lack of information about the patient's vaccinations, he had to be treated as unvaccinated. Because *C. diphtheriae* found in the wounds was resistant to penicillin, imipenem and cilastatin (Tienam 500 mg x 4/day i.v.) were introduced to the treatment, instead of the previous antibiotic, owing to the received antibiogram and hospital antibiotics policy.

The outcome of the treatment was good. The wounds on the left limb were healing very well thanks to applied dressing treatment (Figure 1). Reduced inflammatory indicators were also received. On the 13th day of hospitalisation, an additional pharyngeal swab was taken for microbiological tests, which did not show any presence of *C. diphtheriae*.

The patient was handed over to the Infectious Diseases Department, where he was treated for several days by a continuation of the previous curation. He was discharged in overall good condition, with a healed wound and did not report to the clinic for check-up.

DISCUSSION

Diphtheria is a disease caused by *C. diphtheriae* infection. We observe two main types of this disease: the respiratory (nasopharyngeal) form and cutaneous form [5,6]. Most of the time, the area of infection is limited, but some cases report the occurrence of bacteremia [2,7]. Prior to the era of childhood vaccination, there were many cases of mainly respiratory diphtheria, especially in the children's age group < 15 years of age [1,8,9]. Two main strains of *C. diphtheriae* were described: toxigenic and nontoxigenic. Both of them can cause cutaneous versions of diphtheria, but the course of the disease and clinical picture differ depending on the bacterial strain. The characteristics for the toxigenic strain are pseudomembranes present on non-healing ulcers. Pseudomembranes are very similar to those found in the parts of the upper respiratory tract, in the classic – nasopharyngeal course of the disease [5]. Such findings were not described in the cases of colonisation by non-toxigenic strains, which seemed to be compatible with the observations from our patient's

case, who presented shallow, rolled-edge ulcers without a blue-grey pseudomembrane in the most common location for such infections [8].

The swabs from our patient's wounds showed the presence of not only *C. diphtheriae* but also *Streptococcus* spp. The dualistic nature of the infection is frequently observed, particularly with the participation of the mentioned pathogens, but frequent coinfection of *C. diphtheriae* and *Staphylococcus aureus* were also described [5,6].

Antibiotic therapy was conducted in accordance with the hospital antibiotics management policy and guidelines. Typically, the first-choice antibiotic is procaine penicillin [10], which could not be used in our case as a consequence of the antibiogram. Bacterial resistance to erythromycin was not tested. Antibiotic therapy against *C. diphtheriae* should be carried out for 14 days [10]. In the present case, there was no need to use diphtheria antitoxin (DAT) because our patient was infected with a non-toxigenic strain and did not present any typical symptoms that DT could cause.

The infection of *C. diphtheriae* may cause a number of complications such as bacteremia, septicemia, myocarditis and endocarditis [1,2,6,7,11]. The diagnostics executed on our patient did not reveal any of those complications, possibly due to the unknown duration of the infection. Nevertheless, additional vaccination during convalescence is recommended in every diphtheria case [10].

The most repeatedly appearing risk factors in case reports of cutaneous diphtheria are: a poor social and economic environment, drug addiction, alcoholism, decreased immunity, low hygiene standards and a lack of vaccination [1,2,6,12,13]. Some authors note that because of increased migration and travel, we can observe the reappearance of diphtheria, even in countries with high vaccination coverage [1,9]. Citizens of developing countries (Indonesia, Bangladesh, Yemen and Venezuela) are especially exposed to diphtheria. However, single outbreaks were described in developed countries in populations with a lower socioeconomic status, whose living conditions were similar to those observed in countries with a higher occurrence of diphtheria [14]. Our patient represented a higher risk group as a homeless alcoholic with poor personal hygiene. Last but not least, he was a Ukrainian immigrant. Recent reports showed that Ukraine has a significantly lower vaccination level than Poland and most European countries [1]. They also observed 56 cases in 2010––2018 [15], which suggests the continuous presence of *C. diphtheriae* in the population inhabituating this geographical region.

This is a new challenge for not only Polish healthcare but in the whole of Europe. We should consider diseases like diphtheria when examining our patients, especially if they were born, lived or recently travelled to regions with a lower vaccination coverage. It should again emphasise the value of self-protection and disinfection during every contact with a patient. One's own vaccination should be a priority for every medical worker exposed to potential contact with *C. diphtheriae*.

CONCLUSIONS

The presented case report and analysis of scientific publications of cutaneous diphtheria show the importance of this form of the disease in the modern, post-vaccination era. Medical workers should not underestimate rare diseases like diphtheria, remembering the possible different forms such as cutaneous and nasopharyngeal. Observing the reappearance of diphtheria and its spread from previously endemic places, we claim that the importance of vaccination, self-protection during contact with patients, and awareness of the medical community is becoming increasingly more important at the moment. It is vital in countries with high vaccination coverage, which experience high levels and intensity of immigration and travel, especially from places with lower vaccination standards.

Ethics statement

All the followed procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from the patient for being included in the study.

Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Author's contribution

Study design – M. Rudzki, D. Waniczek
Manuscript preparation – J. Fick, B. Bichalski, M. Bichalska-Lach
Photography documentation – B. Bichalski
Literature research – J. Fick
Final approval of the version to be published – M. Bichalska-Lach

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