

Sepsis caused by *Chromobacterium violaceum* – probably the first case in Europe, or *Macbeth* read anew

Anna Jędruszczak^{1,A-D}, Marta Węgrzyn- Bąk^{1,C-F}, Renata Budzyńska-Nosal^{1,B-C,E},
Marek Maciejewski^{1,B,E}, Krzysztof Marczewski^{1,2,A-F}

¹ Department of Nephrology, Endocrinology, Hypertension and Internal Medicine, Pope John Paul II Regional Hospital in Zamosc, Poland

² Faculty of Health Sciences University of Economics and Innovation, Lublin, Poland

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of article

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Abstract

Rare diseases, almost by definition, present us with diagnostic as well as therapeutic difficulties as. They also include infectious diseases outside endemic areas. Without expecting them, we are not preparing to fight them. Like *Macbeth*, we feel safe, convinced that tropical diseases do not reach us, like Birnam forest towards his castle. Nevertheless, the forest moved according to the prophecy of the three witches, and in a similar way tropical flora is moving towards us according to the predictions of environmentalists. This is illustrated by the history of the presented patient, who was admitted to hospital because of sepsis caused by *Chromobacterium violaceum* (CV), a Gram-negative facultatively anaerobic, oxidase-positive bacterium producing a dark violet antioxidant pigment called violacein. This is probably the first documented case report of sepsis in this part of the world. To the best of the authors' knowledge, the patient is the first to require dialysis after *Chromobacterium violaceum* infection.

Key words

infection, sepsis, bacteria, medicine, climate change, *Chromobacterium violaceum*

INTRODUCTION

Rare diseases, almost by definition, give us difficulties with diagnostics and therapeutics. They also include infectious diseases, especially those occurring outside endemic areas. However, it is in this environment that they are particularly dangerous. Without expecting them, we are not preparing to fight them. Like *Macbeth*, we feel safe, convinced that tropical diseases do not reach us, like Birnam forest reaching his castle. Nevertheless, the forest moved according to the prophecy of the three witches, and in a similar way tropical flora is moving towards us according to the predictions of environmentalists. This is illustrated by the history of the presented patient, who was admitted to hospital because of sepsis caused by *Chromobacterium violaceum* (CV), a Gram-negative facultatively anaerobic, oxidase-positive bacterium producing a dark violet antioxidant pigment called violacein [1]. In the available literature, less than 100 descriptions were found of sepsis caused by CV in the vast majority from the African and Asian countries. Unfortunately, the majority of patients died [2, 3]. In Europe, this is a definite rarity and this study is probably the first documented case report of sepsis in this part of the world. Fortunately, the patient survived. However, he required chronic dialysis, and to the best of the authors' knowledge he is also the first patient to require dialysis after *Chromobacterium violaceum* infection.

CASE STUDY

The 55-year old male was admitted to our department with a one week history of nausea, vomiting and decreased oral intake. His medical history included paranoid schizophrenia, hypertension and previous alcohol intake with chronic pancreatitis. On admission, he was dehydrated, drowsy and confused. On physical examination, the patient had jaundice, a temperature of 37°C, heart rate – 120 bpm, blood pressure – 110/60 mmHg, oxygen saturation – 89%. Laboratory data showed acute kidney injury, profound metabolic acidosis and elevated liver enzymes. No skin lesions or any irregularities, nor enlarged lymph nodes were found. ECG, chest X-ray showed no significant abnormalities. Abdominal ultrasound showed slightly enlarged, hyperechogenic liver without any focal changes, and a small amount of fluid in the peritoneal cavity. Laboratory investigations revealed the following changes:

Tests for Hepatitis B and C, mononucleosis and CMV were negative. Urine analysis showed no abnormalities. He was treated with intravenous antibiotic ciprofloxacin and daily haemodialysis. Blood culture was positive for *Chromobacterium violaceum* which was susceptible to carbapenems and fluoroquinolones (Tab. 2). Treatment was continued according to antibiogram (Levofloxacin 1+ Meropenem i.v.).

A general improvement in the patient's condition was observed after three days of treatment. He was discharged from the hospital after 30 days, and assigned to the haemodialysis programme due to kidney insufficiency.

Address for correspondence: Krzysztof Marczewski, University of Economics and Innovation, Lublin, Poland
e-mail: kmarczewski@me.com

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Table 1. Patients selected laboratory results on days of admission and discharge from hospital

Laboratory test	Admission tests	Discharge tests	Reference range
AST [U/L]	1536	31	<40
ALT [U/L]	4512	11	<40
LDH [U/L]	1536		<480
Bilirubin, total [mg/dl]	6.16	1.45	0.3–1.2
Bilirubin conjugated [mg/dl]	5.74		0.1–0.4
PT [s]	22.80		12–16
INR	1.98	1.03	0.9–1.2
Procalcitonin [ng/ml]	16.73	0.63	<0.1
CRP [mg/l]	27.5	7.6	0.08–3.1
Creatinine [mg/dl]	6.23	6.29	0.6–1.3
Urea [mg/dl]	150	61	15–40
Platelets [tys./uL]	88	122	150–400
CK [U/L]	1249		55–370

Table 2. Antibiogram results

Antibiotic	Antibiogram results	MIC*
Cefotaxime	Resistant	64
Ceftazidime	Resistant	>256
Levofloxacin	Sensitive	0.19
Imipenem	Sensitive	0.5
Meropenem	Sensitive	1

*MIC – minimal inhibitory concentration [mg/L].

Chromobacterium violaceum, described for the first time in 1872 by Schroeter, is a tropical pathogen potentially harmful to people and animals, but rarely isolated at our latitude [4]. Gram-negative, facultative anaerobic motile bacillus took its name from the purple pigment – violacein. Some reports state that it may have various properties, including antibacterial, anti-mycobacterial, preventing stomach ulcers or even antineoplastic. Bacterium grows easily on simple culture media, including MacConcey agar, at a temperature between 35 – 37°C. It is a natural constituent of water and soil in tropical and subtropical regions [5]. The presence of *Chromobacterium violaceum* in the ticks was discovered in the proximity of our hospital in 2004 [6].

Human infection is rare and usually occurs after exposure of damaged skin or mucous membrane to contaminated soil or water. Infection can present with fulminant sepsis, multiple abscesses and rapidly spreading soft tissue infection [7]. Approximately 50% of cases infections of the skin and soft tissue, mostly concerning limbs. A slightly more frequent occurrence of infection is observed among men (55.6%), usually between 16 – 66 years of age. Mortality rate is 7.1% [8]. Most cases of *Chromobacterium violaceum* infection resulting in death come from Argentina, Australia, Brazil, Nigeria, Singapore, Taiwan and Vietnam. Reports also include manifestations such as chronic granulomatosis, osteomyelitis, lymphadenitis, cellulitis and periorbicular infection with eye involvement. Various publications also include information about the possibilities of bacteria

transfer through infected ticks, contaminated seafood or being bitten by an infected fish.

To-date, probably only one confirmed case of the illness has been described in Europe. It concerned a 14-year-old boy, born in Guinea and who had lived in Italy for 7 years [9]. This case concerned inflammation of the lymph nodes with an increased inflammatory marker in the blood. However, the patient did not have sepsis. Reports of blood infection come mainly from countries such as Indonesia, Nepal, Japan, India, Bahrain, Congo, Cambodia, Vietnam and Brazil. There is no description of sepsis caused by *Chromobacterium violaceum* in Europe.

The presented patient had never been to tropical countries and had no contact with anyone who had travelled there. The most likely scenario seems to be that the bacterium came within his vicinity with the warming of the climate [10]. The earth's temperature has increased by 0.7 – 0.8°C during last 100 years. Scientists' prognosis state a constant and rather fast warming of the surface of the planet and an increase in mean Earth's temperature of 2°C by the year 2100. Researh by the National Oceanic and Atmospheric Administration (NOAA) has displayed a widening of the tropical climate region by 200–400 km from the equator towards the poles over last 25 years [11]. One may suspect that with the gradual warming of the climate, the geographic distribution of *Chromobacterium violaceum* infections will also change. The authors of the presented study conclude that in the search for causes of infections, especially severe sepsis, one should also consider pathogens that do not occur commonly in our climate zone.

On a more optimistic note, it is worth mentioning the attempts to use violacein to treat gastroenterological diseases, including malignancies, and well as other cancers, e.g. melanoma [12, 13, 14].

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