



***Streptococcus pyogenes* sepsis in 32-year-old man as rare complication of bacterial pharyngitis**

Sepsa o etiologii *Streptococcus pyogenes* u 32-letniego mężczyzny
jako rzadkie powikłanie bakteryjnego zapalenia gardła

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ABSTRACT

Group A beta-hemolytic streptococci (*Streptococcus pyogenes* – *S. pyogenes*) are the etiological factor of a wide range of infections, primarily pharyngitis, inflammation of the skin and subcutaneous tissue, as well as invasive infections. They can also lead to immunological complications, such as acute glomerulonephritis, rheumatic fever, and rheumatic heart disease. Although *S. pyogenes* may be the etiological factor for sepsis, sepsis of this etiology is rarely observed as a complication of upper respiratory tract infections in clinical practice. The aim of this paper is to present a case report of a 32-year-old man, previously untreated for chronic diseases, who was hospitalized for sepsis caused by *S. pyogenes*, which was a complication of an upper respiratory tract infection. As a result of targeted treatment with benzyl penicillin, significant improvement in the clinical condition of the patient and normalization of the inflammatory parameters were achieved. Due to a significant increase in the cardiac troponin serum concentration during hospitalization, the diagnostics were extended to include evaluation of the cardiovascular system.

KEYWORDS

sepsis, *Streptococcus pyogenes*, bacterial pharyngitis, troponin

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STRESZCZENIE

Paciorkowce beta-hemolizujące grupy A (*Streptococcus pyogenes* – *S. pyogenes*) są czynnikiem etiologicznym szerokiego spektrum zakażeń, przede wszystkim zapalenia gardła, zapalenia skóry i tkanki podskórnej, a także zakażeń inwazyjnych. Mogą również prowadzić do powikłań o charakterze immunologicznym, takich jak ostre kłębuszkowe zapalenia nerek, gorączka reumatyczna i reumatyczna choroba serca. Chociaż *S. pyogenes* może być czynnikiem etiologicznym sepsy, to w praktyce klinicznej rzadko obserwuje się posocznicę o takiej etiologii jako powikłanie infekcji górnych dróg oddechowych. Celem niniejszej publikacji jest przedstawienie opisu przypadku 32-letniego mężczyzny, nieleczonego wcześniej z powodu chorób przewlekłych, hospitalizowanego z powodu posocznicy wywołanej przez *S. pyogenes*, będącej powikłaniem infekcji górnych dróg oddechowych. W wyniku zastosowanego leczenia celowanego za pomocą penicyliny benzylowej uzyskano znaczącą poprawę stanu klinicznego chorego oraz normalizację parametrów zapalnych. Z uwagi na znamienny wzrost stężenia troponiny sercowej w surowicy w trakcie hospitalizacji diagnostykę poszerzono o ocenę układu sercowo-naczyniowego.

SŁOWA KLUCZOWE

sepsa, *Streptococcus pyogenes*, bakteryjne zapalenie gardła, troponina

INTRODUCTION

Sepsis is a medical condition that includes features of generalized infection, understood primarily as the presence of pathogenic microorganisms in the blood, and systemic inflammatory response syndrome [1]. Sepsis is not a homogeneous disease entity, but depending on the primary cause and source of infection in addition to the etiological factor, it may have a diverse course and clinical picture [2,3]. Due to the spreading resistance of bacteria to available antibiotics, the treatment of sepsis and other bacterial infections is becoming more problematic [4]. Sepsis and its treatment also pose a significant financial burden on the healthcare system. The quick and accurate diagnosis of sepsis is very important because it is crucial to start treatment early as untreated sepsis can quickly lead to the development of multi-organ failure and death [5].

In the case of patients hospitalized in internal medicine departments, sepsis often develops in the course of organ infections, such as pneumonia, urinary tract infections or gastrointestinal tract infections, especially in the case of people with numerous risk factors for the development of infection, i.e. elderly people with multi-morbidities, disabilities, and severe frailty syndrome [6]. In clinical practice, sepsis cases are less frequently observed in young people with no chronic diseases or disabilities. Moreover, sepsis as a complication of upper respiratory tract infections is rare.

The purpose of this paper is to present a case report of a 32-year-old man, previously untreated for chronic diseases, who was hospitalized because of sepsis caused by *Streptococcus pyogenes* (*S. pyogenes*), which was a complication of an upper respiratory tract infection.

CASE REPORT

Anamnesis and physical examination

A 32-year-old male patient was brought to the emergency room by the Emergency Medical Team. In the anamnesis, he complained of fever up to approximately 40.0 degrees Celsius, cough with sputum, pain in the paranasal sinuses area, and muscle pain. He also complained of discomfort when urinating. According to the patient, the symptoms had been present for approximately three days. Moreover, during the two weeks preceding admission to the hospital, the patient was treated for symptoms of upper respiratory tract infection with amoxicillin and clavulanic acid. However, the patient did not follow the doctor's recommendations, in particular the recommendation to rest and stay in bed for several days, and he took the prescribed medications irregularly. To that time, the patient had not had any chronic diseases and did not use any medications on a regular basis. He denied allergies, including to medications. He denied having undergone any surgical treatment. He denied smoking, but admitted that he drank beer every day.

At the time of admission to the Clinic, the patient was conscious and did not present any disturbances of consciousness. During auscultation of the lung fields, no obvious pathological changes were detected. The heart rate was regular with a frequency of approximately 120 beats per minute. The abdomen was soft and painless, without pathological resistance or peritoneal symptoms. There was no swelling in the lower limbs. No significant pathological changes were found in the skin. During the physical examination, an excessive accumulation of fat tissue, typical of obesity, was noted. Physical examination of the throat



revealed no mucosal redness or other abnormalities. There were, however, signs of caries.

The 12-lead electrocardiography (ECG) on admission revealed sinus tachycardia at the rate of 120 per minute, and the blood pressure was approximately 135/80 mmHg.

In the initial days of hospitalization, the patient also periodically reported abdominal pain, which responded well to treatment, but a repeated physical examination did not reveal any changes.

Laboratory tests

The laboratory tests revealed significantly increased values of inflammatory parameters. The concentration of C-reactive protein (CRP) in the blood was 179.66 mg/L, and the next day (i.e. after several hours) it was 439.11 mg/L, even though the patient received an antibiotic immediately after admission to the Clinic. In subsequent tests, the concentration of CRP systematically decreased. The concentration of procalcitonin was also significantly elevated upon admission to the hospital (12.46 ng/mL) with a systematic decrease during the course of treatment. Leucocytosis at admission was relatively low ($11.8 \times 10^3/\mu\text{L}$) but with a clear shift in the percentage towards neutrophils (90.3%). The fibrinogen level was also significantly elevated ($> 9.0 \text{ g/L}$; the fibrinogen measurement was not repeated during hospitalization). The sedimentation rate of red blood cells was significantly accelerated (73 mm/h; the measurement was not repeated during hospitalization).

Immediately after admission of the patient to the Clinic, biological material was collected for microbiological tests (blood, sputum, and urine). The blood culture revealed group A beta-hemolytic *Streptococcus* (*Streptococcus pyogenes*) with good sensitivity to penicillin. Pathogenic microorganism growth was not detected in the sputum or urine cultures.

At admission, slightly elevated aspartate aminotransferase activity was found (52.6 U/L) with normal alanine aminotransferase activity (32.4 U/L). During hospitalization, a transient, non-significant increase in transaminase activity values was observed. Increased gamma-glutamyl transferase activity was also demonstrated (up to 206.0 U/L), with a tendency to normalize during hospitalization. The alkaline phosphatase activity was normal. The concentrations of bilirubin and total protein, as well as the values of prothrombin time and kaolin-cephalin time, were normal. Renal function evaluated by the serum creatinine concentration and estimated glomerular filtration rate (eGFR) was normal throughout the hospitalization period. During the initial period of

hospitalization, slight hyponatremia (132 mmol/L) was observed, with subsequent normalization. Moreover, no significant disturbances in water-electrolyte and acid-base balance were observed.

In terms of the plasma lipid profile, there was a significantly reduced concentration of high-density lipoprotein cholesterol (16.9 mg/dL) and an increased concentration of triglycerides (221.0 mg/dL), with normal concentrations of the total cholesterol (111.0 mg/dL) and low-density lipoprotein (49.0 mg/dL). The fasting venous plasma glucose concentration was normal. The thyroid function parameters were normal.

During hospitalization, the HbS antigen in the blood and antibodies typical of human immunodeficiency virus infection were also determined (negative results). Serum protein electrophoresis was performed (without significant abnormalities).

During hospitalization, a significant increase in the cardiac troponin concentration in the blood was observed, followed by normalization (Figure 1).

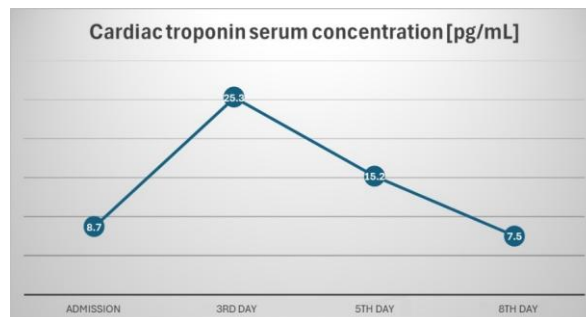


Fig. 1. Change in cardiac troponin serum concentration during hospitalization.

Anthropometric measurements

The basic anthropometric measurements showed features of central obesity (body mass index 33.1 kg/m^2 , waist circumference 107 cm). Body composition analysis was performed using the bioelectrical impedance method and a TANITA MC-780 apparatus to supplement the basic anthropometric measurements. The percentage of fat was estimated at 27.9%.

Diagnostic imaging

A classic chest radiograph was performed, which described inflammatory-looking pericardial densities in the middle-lower field of the right lung (Figure 2). Due to the abdominal pain reported during the initial period of hospitalization, an abdominal radiograph was performed, which revealed no signs of intestinal obstruction or perforation of the gastrointestinal tract.

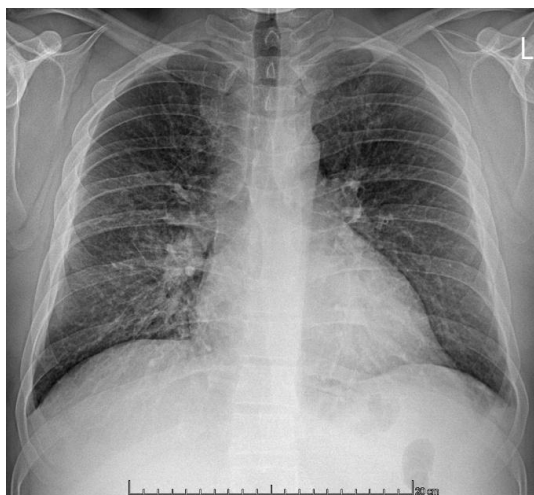


Fig. 2. Chest radiograph. Pericardial inflammatory masses were found in middle-lower field of right lung.

Owing to the reported pain in the area of the paranasal sinuses, the diagnostics were extended to include computed tomography, which showed post-inflammatory thickening of the mucosa (Figure 3A and 3B).

An abdominal ultrasound was performed, which revealed an enlarged liver with signs of steatosis and

foci of hyposteatosis, without focal lesions. Apart from that, no abnormalities were found, but it should be emphasized that the imaging conditions were suboptimal (the abdominal aorta and pancreas could not be assessed).

Treatment

Immediately after the patient's admission to the Clinic, empirical antibiotic therapy with a third-generation cephalosporin (ceftriaxone) was initiated. Before antibiotic administration, blood and urine were collected for culture. After receiving the blood culture results (about 24 hours after admission to the Department), ceftriaxone was replaced with crystalline penicillin. During hospitalization, intravenous hydration with potassium supplementation, steroid therapy, mucolytic treatment, antithrombotic prophylaxis with low molecular weight heparin, as well as painkillers and antipyretics (metamizole and paracetamol) were also used.

During the therapy, significant improvement in the patient's clinical condition and a systematic decrease in the values of inflammatory parameters were observed. The full distribution of inflammatory parameter values is presented in Table I.

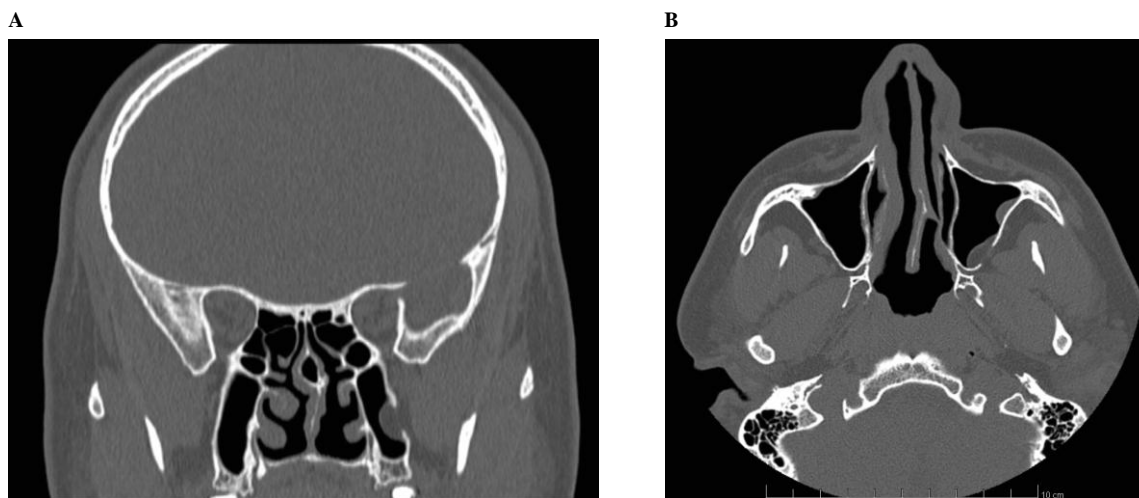


Fig. 3. Computed tomography image of paranasal sinuses (post-inflammatory changes).

Table I. Change in values of inflammatory parameters during hospitalization

Day number	Leucocytosis [$\times 10^3/\mu\text{L}$]	Neutrophil percentage [%]	C-reactive protein [mg/L]	Procalcitonin [ng/mL]
Admission	11.8	90.3	179.66	12.46
1	12.0	90.5	439.11	not measured
3	8.3	71.6	150.76	4.31
5	8.8	60.1	45.47	1.27
8	7.4	48.3	11.13	not measured
14	6.6	48.8	2.98	0.06



During hospitalization, elevated blood pressure values were also observed, therefore arterial hypertension was diagnosed and treatment with perindopril and indapamide was initiated.

Due to the observed increase in liver enzyme activity, treatment with ursodeoxycholic acid was used.

Assessment of the cardiovascular system and metabolic status

After the patient's clinical condition stabilized during hospitalization, the cardiovascular system was also assessed owing to the diagnosed arterial hypertension and the above-described increase in serum cardiac troponin concentration. Moreover, because of obesity, diagnosed metabolic syndrome and metabolic fatty liver disease, body composition analysis was performed.

Transthoracic echocardiography showed only a trace of pathological fluid in the pericardium, as well as a borderline thickness of the left ventricular myocardium (11 mm in the interventricular septum and 10 mm in the inferolateral wall). No valve defects were detected. The size of the heart chambers and great arteries was assessed as normal, as was the systolic and diastolic function of the left ventricle and the systolic function of the right ventricle. During Holter ECG monitoring, only single supraventricular extra beats were detected. 24-hour monitoring of blood pressure showed elevated blood pressure values. Ultrasound of the carotid and vertebral arteries did not show atherosclerotic lesions, and the blood flow velocity and spectrum were normal. The value of the ankle-brachial index was normal both on the right and left side (1.1 and 1.05, respectively). The value of the carotid-femoral pulse wave velocity (Sphygmocor XCEL, AtCor Medical, Australia) was within the normal range, although it was quite high in relation to the age (7.7 m/s). The measurement of the central arterial pressure and pulse wave analysis parameters did not reveal any abnormalities.

DISCUSSION

Group A beta-hemolytic streptococci (*S. pyogenes*) remain a relatively rare etiological factor of sepsis among patients hospitalized in the internal medicine department. The patient described in this publication was a young, previously chronically untreated, obese man who abused alcohol and was diagnosed during hospitalization with metabolic syndrome, hypertension, dyslipidaemia, and metabolic fatty liver disease. In the two weeks preceding hospitalization, he was treated for a respiratory infection, but he did not fully comply with the medical recommendations. Upon admission to the hospital, he presented fever, cough, and muscle pain. As a result of the treatment,

the patient's condition improved and he was discharged home on the sixteenth day of hospitalization.

Streptococcus pyogenes remains an important etiological factor of different diseases, among which the following should be emphasised: purulent tonsillitis, erysipelas, pharyngitis, and cellulitis; invasive infections (necrotizing fasciitis, bacteremia, and meningitis); toxin-mediated diseases such as scarlet fever and streptococcal toxic shock syndrome (STSS); as well as immune-mediated diseases such as acute glomerulonephritis, acute rheumatic fever, and rheumatic heart disease [7]. Among the virulence factors of *S. pyogenes*, the following seem to be significant: M protein [8], streptococcal cysteine protease (SpeB) [9], streptococcus C5a peptidase (SCPA) [10], streptolysin O [11], and *S. pyogenes* cell-envelope protease (SpyCEP) [12]. Bacterial protein R28 was shown to target the human CEACAM1 receptor, which is considered to play a role in the pathogenesis of puerperal sepsis caused by *S. pyogenes* [13].

In 2018, a case of an elderly woman with *S. pyogenes*-caused sepsis was described, presenting symptoms of septic shock and septic arthritis, whose illness ended in death despite penicillin treatment in combination with clindamycin [14]. In 2022, a team from the United States described the case of an 18-year-old girl who developed *S. pyogenes* sepsis during treatment for genital infection with herpes simplex virus type 2 (HSV-2) [15].

The basis for typing *S. pyogenes* is the presence of a specific isoform of the M protein. Currently, the gold standard remains typing based not on the serological method, but molecular typing based on the DNA sequence within the *emm* gene [16]. Individual serotypes differ in their tendency to cause specific diseases brought about by *S. pyogenes*. For example, *emm* types 1, 4, 12, 49, 55, 57, and 60 tend to cause acute glomerulonephritis, and *emm* type 28 tends to cause puerperal sepsis [17]. Unfortunately, in the case we described, no typing of the *S. pyogenes* strain was performed, which would undoubtedly have been a valuable addition to the collected information. Interestingly, according to recent research, the diversity of *S. pyogenes* strains varies in different countries around the world, showing a negative correlation with the degree of socioeconomic development of a given region of the world [18].

In the course of infections caused by *S. pyogenes*, heart damage may develop in the course of rheumatic fever. This is the result of the similarity of some structures within human tissues to the M protein, which is related to the possibility of antibodies generated during infection that react with the body's own tissues [17]. Resulting from the fact that in our case a significant increase in cardiac troponin concentration was found during hospitalisation, the diagnostics were extended to



include non-invasive assessment of the cardiovascular system, which revealed no significant abnormalities. Hence, it was concluded that the increase in the cardiac troponin concentration was the result of acute myocardial damage in the course of generalized infection [19].

It should be noted that infections caused by *S. pyogenes* remain a major public health problem. It is estimated that there are over 600 million cases of pharyngitis and over 100 million infections of the skin and subcutaneous tissue of this type in the world each year. It is also estimated that over half a million deaths worldwide each year are caused by the complications of infections caused by *S. pyogenes* [20]. Therefore, the development of effective methods of immunoprophylaxis against infections caused by *S. pyogenes* remains a very important challenge. Despite research conducted in this direction for many years, no vaccine is yet available, although many preparations with various mechanisms of action are in the research stage, primarily preclinical [7].

A significant limitation of the paper we have prepared is the lack of long-term follow-up of the patient after discharge from the Clinic. On the other hand, however, the strength of this paper is the careful clinical assessment of the patient, taking into account various aspects, including a detailed assessment of the cardiometabolic health using numerous additional tests.

It is especially important because diabetes and its complications was discussed as significant for the clinical course of infection and the antimicrobial treatment [21].

CONCLUSIONS

Streptococcus pyogenes remains a significant etiologic factor for severe infections, also in young people. In the presented case report, the patient was diagnosed with several chronic diseases which are associated with an increased risk of infection. It is difficult to predict how important the impact of chronic diseases diagnosed in the clinical course of infection was, finally, complicated by sepsis.

Upper respiratory tract infection with features of bacterial aetiology should always be carefully assessed in each case with regard to the necessity of antibiotic treatment, but on the other hand, the unnecessary use of antibiotics should obviously be avoided.

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Authors' contribution

Study design – G.K. Jakubiak

Data collection – G.K. Jakubiak, P. Oleś

Manuscript preparation – G.K. Jakubiak, G. Cieślak, A. Stanek

Literature research – G.K. Jakubiak

Final approval of the version to be published – G.K. Jakubiak, P. Oleś, G. Cieślak, A. Stanek

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