

Late latent syphilis as a challenging issue in the twenty-first century

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Abstract

Introduction: Syphilis is one of the oldest sexually transmitted diseases caused by the bacterium *Treponema pallidum*. It is characterized by multiple clinical presentations and a long duration. Acquired syphilis is divided into early (≤ 1 year after infection) and late (> 1 year after infection) stages. Venereal diseases, more often defined as sexually transmitted diseases (STDs), result from behaviours influenced by socio-economic, psychological, and cultural factors. Although the spectrum of sexually transmitted diseases, apart from classic syphilis and gonorrhoea, encompasses a wide range of aerobic and anaerobic bacteria, viruses, protozoans, fungi, and even insects, the frequency of late syphilis has been on the rise in recent years. It is a significant clinical problem in our country. Irrespective of the COVID SARS-19 pandemic, this is an important issue of contemporary epidemiology.

Objectives: The objective of this study was to present two cases of women diagnosed with acquired late syphilis of unknown duration, treated at the Department and Clinic of Dermatology at the Poznań University of Medical Sciences.

Material and methods: CASE 1 — A 72-year-old female patient was admitted to the Clinic of Dermatology with late latent syphilis of unknown duration. The results of laboratory tests showed: a positive syphilis reaction: FTA-ABS 1:100, TPHA — 1:160. One dose of 2.4 million units of intramuscular benzathine penicillin was administered. It was recommended to administer the second dose of 2.4 million units of benzathine penicillin within 7 days of the first dose.

CASE 2 — A 29-year-old female patient was admitted to the Department and Clinic of Dermatology at the Poznań University of Medical Sciences with late latent syphilis of unknown duration. A primary lesion on the right labium major, regional lymphadenopathy, and a rash on the right side of the chest were observed. The results of laboratory tests showed: qualitative TPHA test — positive, quantitative TPHA test — positive (titre 1:180), RPR — positive (RPR – titre 1:1).

Conclusions: In recent years, the incidence of late syphilis has been on the rise globally. This disease has again become a significant clinical issue requiring particular attention in dermatological and venereological practice. When syphilis is diagnosed, adequate treatment is necessary in accordance with the updated EADV guidelines.

Keywords: late syphilis, treatment

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Introduction

Syphilis is a sexually transmitted infection caused by *Treponema pallidum* subs. *pallidum*. *Treponema pallidum* gets into broken skin, mucosa or directly

into the bloodstream. The most common way syphilis is spread is through sexual, oral or rectal contact with an infected person. Late syphilis includes late latent syphilis and tertiary syphilis. Late syphilis is defined by European guideline on the management of syphilis (ECDC) as syphilis acquired ≥ 1 year earlier or of unknown duration, and WHO defines late syphilis as syphilis acquired ≥ 2 years earlier. Latent syphilis is the period during which nontreponemal and tre-

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ponemal tests are reactive, but there are no clinical manifestations [1–4].

In the case of primary syphilis, the risk of infecting a sexual partner is 25–30%, while in the case of secondary syphilis, this risk increases to ca. 50–60% [1–3].

The World Health Organization (WHO) estimates that there are about 6 million new cases of syphilis every year [4]. Between 2001 and 2015, the average incidence rate of syphilis in Poland was 2.0 cases per 100,000 inhabitants. In 2005 it was 1.6, in 2013 — 2.6, and in 2021 — 2.95 (lower than in neighbouring countries) [5, 6].

Contrary to popular opinion, syphilis remains an important problem in everyday medical practice in the twenty-first century. The number of diagnoses of late syphilis has been increasing, which results from unusual locations and morphology of lesions [1–4]. Delayed diagnosis and implementation of appropriate treatment lead to the spread of this disease. It is essential to increase the awareness of clinicians, namely primary healthcare physicians, of diverse symptomatology of syphilis and the importance of serological tests, particularly in patients with uncommon clinical manifestations [1, 5, 6].

The objective of this study was to present the clinical descriptions of two women diagnosed with acquired late syphilis of unknown duration, treated at the Department and Clinic of Dermatology at the Poznań University of Medical Sciences.

Material and methods

Case 1

A 72-year-old female patient was admitted to the Clinic of Dermatology with late latent syphilis. Medical history from 2010 — infection through heterosexual contact. Initially her symptoms were malaise, headaches, weight loss and recurring pus-filled lesions in the throat. The patient had previously been administered Doxycycline for 28 days. On admission, she reported malaise and headaches.

The results of serological tests (on admission) showed: FTA-ABS 1:100, TPHA 1:160. She also had a history of hypertension, mild mitral valve insufficiency, paroxysmal atrial fibrillation, hypercholesterolaemia and degenerative cervical spine changes.

During hospitalisation, laboratory tests revealed an elevated fasting glucose level (116 mg/dL). Cardiovascular, neurological and laryngological consultations did not show any significant deviations. The ophthalmological consultation revealed hyperopia, hyperopic astigmatism in the two eyes and grade 1/2 hypertensive angiopathy. Chest X-ray examination description: lung fields with no focal lesions, normal cardiac silhouette,

sclerotic aorta, aortic arch calcifications. Abdominal ultrasound description: echogenic liver, not enlarged, a cyst of 1 cm in diameter in the left hepatic lobe, no detectable focal lesions. Bile ducts not enlarged. Pancreas not enlarged, normal echogenicity observed in the parenchyma, no pancreatic duct dilatation. Kidneys of normal structure and shape, without retention or deposits. Homogenous spleen, not enlarged. Retroperitoneal space and large vessels in the abdomen sonographically unremarkable. Unfilled bladder.

One dose of 2.4 million units of intramuscular benzathine penicillin was administered. It was recommended to administer a second dose in hospital within 7 days of the first dose. The patient was discharged in overall good condition.

Case 2

A 29-year-old female patient was admitted with late latent syphilis of unknown duration. Positive serological tests: VDRL — 1/16, FTA-ABS, FTA 1/450 and TPHA 1/10240.

At the University Dermatological Outpatient Clinic, the patient and her partner were given Doxycycline (2 × 100 mg) for 28 days, and then Azithromycin (2 g).

During hospitalization, serological tests were repeated (TPHA — POSITIVE 1:2560, FTA-ABS titre was added 1:800). After performing penicillin testing (negative result), 2.4 million units of intramuscular procaine penicillin were administered. Laboratory tests did not show any significant deviations. ECG was performed — normal impression. The ophthalmological consultation revealed high myopia, no other deviations were observed. Neurological examination — normal. After angio-CT of the head, a lumbar puncture was performed — negative TPHA serological reaction. During her stay at the Clinic, the patient was treated with procaine penicillin (2.4 million units), which she tolerated well. She was discharged in overall good condition with the following instructions: to administer 2.4 million units of procaine penicillin for the next 14 days on an outpatient basis, periodically check the levels of serological reactions and undergo further treatment depending on the results.

Discussion

As one of the most common sexually transmitted infections, syphilis is considered as “embarrassing” disease in Poland, which is why patients do not contact their doctors when the first symptoms occur. The above presented cases confirm this phenomenon.

According to the National Institute of Public Health, between 2013 and 2022, the incidence rates of diseases

caused by *Treponema pallidum* were definitely on the rise in Poland. This concerned mainly men aged 29–39 years living in cities [5, 6]. In 2019, there were 1631 new cases of syphilis, i.e. 4.25 cases per 100,000 inhabitants in Poland. Moreover, it is essential to highlight the marked increase in diagnoses of late syphilis among the Polish population in recent years. In 2020 diagnosis rate of late syphilis was 0.09 per 100,000. However, in 2022 the rate increased to 0.25 [5, 6].

Women, compared to men, are biologically more susceptible to contract sexually transmitted diseases (STDs) [7–10]. Moreover, the course of STD infections in women, also syphilis, is far more likely to be asymptomatic or with nonspecific symptoms. In addition, often painless sores of primary syphilis that develop about three weeks after contact locate mainly in challenging to visualize areas (vagina, cervix, rectum). These facts undoubtedly cause a diagnostic delay at an early stage of syphilis in women and lead to various complications, including the transmission of the infection from mother to fetus [7–10].

Nowadays, people aged 50 and older are at greater risk for sexually transmitted infections, such as syphilis, due to increased quality of life and the availability of medications to prolong sexual life [6, 11, 12]. In 2021, people from this age group accounted for 12% of syphilis infection cases in Poland [6]. Studies report that elderly people are more likely to present syphilis at a late or unknown stage [6, 11, 12]. Clinicians, unfortunately, often forget about this and overlook the symptoms of the disease caused by *Treponema palladium* so that proper diagnosis is delayed, as happened with the first 72-year-old female patient mentioned in our manuscript [6, 11, 12].

A retrospective analysis of syphilis cases among 69 patients treated at the Department of Dermatology, Venereology, and Allergology in Wrocław between 2009 and 2016 showed that late latent syphilis accounted for 81.2% of cases. The largest percentage of patients (46.4%) were between the ages of 21 and 30. According to the Polish National Institute of Public Health, in 2021, syphilis was diagnosed in 36% of women between the ages of 20 and 29 [6, 13]. The second described case shows that preventive measures among young adults, such as promoting safer sexual behaviour, should be implemented. It is important to educate adolescents about the symptoms of syphilis infection. People need to start realizing the consequences and complications of STD infection [14].

The number of tests for *Treponema pallidum* infection in venereology centres has been decreasing markedly for years. Before health care reform, about 8 million tests for syphilis infection were performed in Poland, while in 2011, less than 100,000 blood samples were tested, which is only 2% of the tests from a decade ago. This directly impacts the diagnosis of early and

late latent syphilis, which is diagnosed based on blood tests [15, 16]. In addition, many countries in the WHO European region (a total of 98 centres) reported that STDs prevention, detection, and treatment methods due to the global COVID-19 pandemic were less accessible to patients. The number of laboratory tests for syphilis was shown to have decreased in 95% of cases compared to the previous year. Many centres where diagnostic material was collected were closed, a significant number of medical personnel were delegated to centres associated with the fight against COVID-19, and patients with STDs and dermatological diseases were not admitted. Difficult access to medical advice and diagnosis contributed to the prolonged infectiousness of STDs, including syphilis. This led to an increase in syphilis cases in subsequent years. Undoubtedly, it also led to increased rates of late latent syphilis [14, 17, 18].

Also, due to shifts in morality and a lack of knowledge of prophylaxis, the risk of spreading sexually transmitted infections (STIs) is growing [6, 19]. In Poland, screening tests for infections caused by *Treponema pallidum* are obligatory among women in the first (week 7–8) and third (week 33–37) trimester of pregnancy, which impacts relative indices of epidemiological data regarding congenital syphilis. Nevertheless, this issue has not been eliminated entirely [19]. Despite prophylaxis, 14 cases of congenital syphilis were recorded in 2019 [6]. It should be borne in mind that according to the preventive guidelines, serological tests for syphilis should also be suggested to any woman after week 20 of pregnancy [20].

It is also recommended that serological tests for syphilis be performed among patients with accompanying neurological symptoms, e.g. a sudden loss of vision or visual dysfunction of unknown origin, meningitis of unknown aetiology, sudden disorders of unknown origin in cranial nerves, ischaemic stroke (including transient ischaemic attack, TIA), particularly in people below 40 years of age, and rapidly progressive dementia, namely in people over 60 years of age [21–24]. What is more, serological tests for infections caused by *Treponema pallidum* should be considered among patients undergoing psychiatric treatment, where clinical symptoms appear suddenly, and the clinical picture and course of the disease do not give any grounds for a final diagnosis [22].

It also needs to be emphasized that according to EU principles, specialized dermatological and venereological centres should be responsible for diagnosing and treating STDs, which seems to be totally obvious, yet not always observed in everyday clinical practice in our country.

In accordance with the 2020 edition of EADV, the recommended treatment for syphilis is a penicillin class antibiotic and maintaining an appropriate level in the blood [3]. When *Treponema pallidum* also infects

the nervous system, the therapeutic concentration of penicillin needs to be maintained in the cerebrospinal fluid. First-line treatment for syphilis is **2.4 million units of intramuscular benzathine penicillin; if long-acting penicillin is not available, it is recommended to administer 600,000 units of procaine penicillin daily for 17–21 days**. In the event of an allergy or intolerance to penicillin antibodies, or refusal of treatment with penicillin according the presented regimen, it is recommended to take 200 mg of oral doxycycline daily for 21–28 days [3].

Due to the fact that the main route of transmission of *Treponema pallidum* is sexual intercourse, patients with syphilis should undergo a full package of examinations for potential accompanying sexually transmitted diseases/infections. Especially HIV co-infection [25, 26].

Conclusions

In recent years, the incidence rate of syphilis has been increasing in our country, which is a significant clinical issue. Despite various preventive and educational activities, awareness of society is insufficient in this respect. **Syphilis, considered by many as a “forgotten disease”, is taking its toll and becoming a serious health problem**, as late detection of infections caused by *Treponema pallidum* leads to multiple complications, e.g. in the nervous system.

Conflict of interest

Authors declare that there is no conflict of interest.

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