REVISTA DO INSTITUTO DE MEDICINA TROPICAL DE SÃO PAULO

JOURNAL OF THE SÃO PAULO INSTITUTE OF TROPICAL MEDICINE

CASE REPORT

http://doi.org/10.1590/S1678-9946202163068

Atypical presentation of secondary syphilis: annular lesions in an elderly patient

Danielle Machado Pagani[1], **Fernanda Brandão Pacheco**[2,3], **Natália Andressa Buss Venier**[2,3], **Isadora da Luz Silva**[2,3], **Giselda Kipper Richter**[4], **Laura Luzzatto**[2,3], **Maria Lúcia Scroferneker**[5,6]

ABSTRACT

Syphilis is a chronic bacterial sexually transmitted infectious disease caused by *Treponema pallidum*. Different age groups are affected by heterogeneous clinical forms of the disease. We report a case of atypical secondary syphilis in an elderly patient with diffuse annular erythematous lesions on the chest, back, upper and lower limbs diagnosed by histopathological, immunohistochemical and serological tests.

KEYWORDS: Syphilis. Cutaneous syphilis. Rash. *Treponema pallidum*. Infection.

INTRODUCTION

Syphilis is a sexually transmitted infection caused by *Treponema pallidum*, a spiral-shaped bacterium that belongs to the Class Spirochaetes. During the 2000s, cases of syphilis were mostly reported in homosexual and HIV-infected patients. The Center for Diseases Control and Prevention (CDC) in the United States reported an increase of 80% in the number of cases between 2014 and 2018[1].

The diagnosis of syphilis can be a challenge even for the most experienced dermatologist due to several clinical forms and a number of differential diagnoses that must be excluded. The disease's natural history evolved with alternating periods of activity and different clinical, immunological characteristics (primary, secondary and tertiary) and latency periods. Primary syphilis is characterized by a solitary, ulcerated, painless lesion with a hardened edge and an inside portion of the lesion clean. Lesions appear on average three weeks after the infection and disappear in 3-8 weeks, regardless of treatment[2,3].

Secondary syphilis occurs between 6 to 8 weeks after the primary lesion. Syphilitic roseola is the first manifestation, characterized by erythematous, lenticular, oval or circular, isolated or confluent lesions. These lesions are highly variable and may vary from fine, slightly scaly papules to exophytic verrucous forms, mainly affecting the trunk and thighs. Erythematous lesions with a flat surface and striking collar scales can affect the palms and feet soles[2]. Nodular variants of secondary syphilis can present as erythematous, violaceous plaques, or nodules[3].

The morphology of secondary annular syphilis varies from fine, slightly scaly papules to exophytic verrucous forms that can affect the scalp, trunk, perioral, perianal and genital regions. They may be accompanied by non-specific symptoms (fever, malaise, headache, odynophagia) in 12% of patients. Iritis, anterior uveitis, osteitis, periostitis, glomerulonephritis, hepatitis and nephrotic syndrome are secondary syphilis manifestations[3]. Painless generalized adenopathies are present in

[1]Universidade Federal do Rio Grande do Sul, Programa de Pós-Graduação em Microbiologia Agrícola e do Ambiente, Porto Alegre, Rio Grande do Sul, Brazil

[2]Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, Rio Grande do Sul, Brazil

[3]Santa Casa de Misericórdia de Porto Alegre, Porto Alegre, Rio Grande do Sul, Brazil

[4]Clínica Richter Dermatologia, Santa Cruz do Sul, Rio Grande do Sul, Brazil

[5]Universidade Federal do Rio Grande do Sul, Programa de Pós-Graduação em Medicina: Ciências Médicas, Porto Alegre, Rio Grande do Sul, Brazil

[6]Universidade Federal do Rio Grande do Sul, Departamento de Microbiologia, Imunologia e Parasitologia, Porto Alegre, Rio Grande do Sul, Brazil

Correspondence to: Maria Lúcia Scroferneker
Universidade Federal do Rio Grande do Sul, Departamento de Microbiologia, Imunologia e Parasitologia, Rua Sarmento Leite, 500, CEP 90050170, Porto Alegre, RS, Brazil

E-mail: scrofern@ufrgs.br

Received: 25 January 2021

Accepted: 3 August 2021

up to 70 to 85% of patients. Due to the variety of secondary presentation forms, it is essential to pay attention to the different diagnoses, such as pharmacodermia, viral rash, pityriasis rosea, figured erythema and leprosy[2,4].

Tertiary syphilis occurs in approximately 15% to 25% of untreated infections. It can appear between 1-40 years after the onset of the infection[1]. It is characterized by the involvement of the nervous system, cardiovascular system, and the formation of the syphilitic gumma, a proliferative granulomatous process that can affect any tissue in the body. In the reported case, the patient had diffuse erythematous annular lesions characterizing an atypical secondary syphilis.

CASE REPORT

The patient was a male, caucasian, 86 years old patient. He reported to be a retired military, heterosexual, widowed, with a previous history of hypertension and a of sexual intercourses with a prostitute. On admission, he presented diffuse spots on his body that appeared three weeks before his first evaluation at a dermatology clinic in Santa Cruz do Sul, Rio Grande do Sul State, Brazil. Later, he was admitted to the Hospital Santa Casa de Misericordia in Porto Alegre, Rio Grande do Sul State, Brazil , two months after the onset of the first lesion (day 0). When he arrived, he did not present the typical primary syphilis lesions, and denied other skin lesions preceding the current condition. However, he had mild symptoms of fatigue and joint pain. He also reported a weight loss of 10 kg in the last two months without a calorie-restricted diet. During the physical examination, we found diffuse annular erythematous plaques on the chest, back, upper and lower limbs (Figure 1). No palpable lymph node enlargement or other changes were identified in the physical examination.

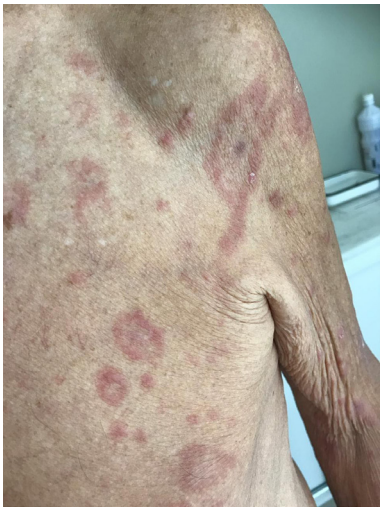

Figure 1 - Annular erythematous plaques with spared centers on the chest and upper limb.

When he arrived at the hospital, he no longer had the typical primary syphilis lesions. Serology and a biopsy of an anterior chest lesion were requested. The VDRL test found a ½ titer, and the anti-*Treponema pallidum* IgM antibody was positive. The serological assessment for HIV, hepatitis B, and hepatitis C was negative (day 5). The histopathological examination showed a dense mononuclear infiltrate in the epidermis and hypodermis, with perivascular and perianexial involvement (day 14) (Figure 2). The immunohistochemistry showed the presence of anti-treponemal antibodies and numerous spirochetes (Figure 3). The clinical protocol and therapeutic guidelines for sexually transmitted infections[5] recommend the use of benzathine benzylpenicillin 2.4 million international units (IU), intramuscularly (IM), in a single-dose (1.2 million in each gluteus). However, most treated cases report a better outcome with the administration of three doses[6,7]. The dermatologist, in this case, chose to treat the suggestive secondary syphilis with benzathine penicillin and a total

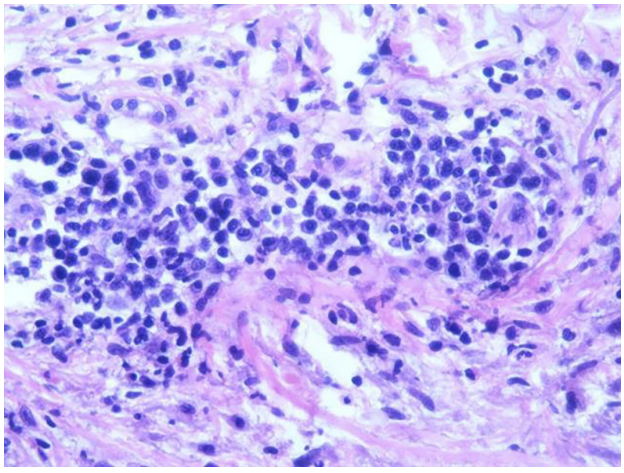

Figure 2 - A histopathological exam showing a perivascular lymphoplasmacytic infiltrate (HE, 40X).

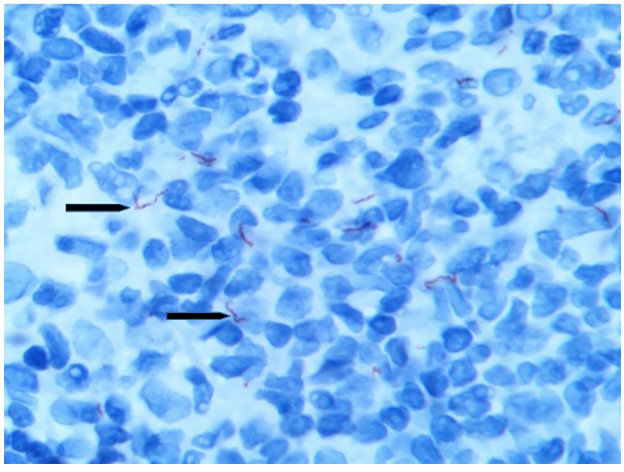

Figure 3 - Anti-treponemal antibodies and spirochetes in an immunohistochemistry test (40X, indicated by the arrows).

dose of 4,800,000 IU as a precaution. The first dose on the first day of treatment was 2,400,000 IU; on day seven, the patient received a second dose of 1,200,000 IU; and on day 14, the third dose of 1,200,000 IU. The lesions disappeared in 30 days.

DISCUSSION

Currently, the treatment of syphilis can be troublesome. The disease can have different forms of lesions and difficult-to interpret laboratory results[8]. Patients with secondary syphilis usually have one or more systemic symptoms associated with a positive serology. Tertiary syphilis, on the other hand, usually occurs decades after the primary infection and includes aortitis, gum lesions, dementia and tabes dorsalis in people with positive serology[8,9].

Non-treponemal tests include the rapid plasma reagin (RPR) and the Venereal Disease Research Laboratory (VDRL). The results of these tests are expressed in titles, indicating the last dilution of the sample that still shows reactivity or visible flocculation. These two tests are not equivalent and can vary according to the laboratory. Treponemal tests measure specific IgM and IgG antibodies against *T. pallidum* proteins, including the *T. pallidum* particle agglutination (TPPA), the Fluorescent Treponemal Antibody Absortion Test (FTA-ABS), and the treponemal pallidum hemagglutination assay by [TPHA], and more recently, the enzyme immunoassay (EIA) and the chemiluminescent immunoassay [CLIA][10]. Furthermore, different factors can interfere with the evolution of serological markers, such as age, sex, stage of syphilis at the time of diagnosis[11]. False-positive results of VDRL generally show titers below ⅛. However, values like ½ can be found in patients with true syphilis. False-positive VDRL can occur due to several different health conditions, particularly in older people. The elderly patients can present with rheumatoid factor, antinuclear antibodies and hypergammaglobulinemia. These findings corroborate the importance of combining different diagnostic tests[9,12]. Although serological methods are the main tools to confirm the diagnosis of secondary syphilis, skin biopsies are often performed to control possible false positive and negative results[13]. In the case reported here the anti-*T. Pallidum* IgM can be considered low, however, the detection of IgM antibodies is important in the differentiation between late (tertiary) and recent infection (primary and secondary)[14]. It is known that after treatment of primary and secondary syphilis, IgM antibodies against *T. pallidum* become undetectable within 6-12 months[15]. Our patient did not report antibiotic therapy in the months before the hospital admission, so we could not confirm that the low IgM title was due to previous medication. However, his clinical conditions were not compatible with late/tertiary syphilis. Based on the clinical findings, the time elapsed since the appearance of the skin lesions until he sought medical attention, and the results of the exams, a case of secondary syphilis was suggested even if the presentation was uncommon for a secondary syphilis. Usually, in secondary syphilis the cutaneous rash is diffuse, symmetric, erythematous and annulopapular[16].

The increase in life expectancy, in the quality of life, and the availability of medication that allows a prolonged sexual life have caused changes in the sexual behavior of the elderly, making this age group more vulnerable to sexually transmitted infections, such as syphilis[17].

CONCLUSION

An important factor change in the characteristics of patients with syphilis is the growth of this infection among the elderly. The diagnosis of patients with manifestations of disseminated annular erythematous lesions can be difficult due to the variety of differential diagnoses and the criteria to define risk groups. Syphilis in the elderly population has increased in recent years, requiring a more careful observation by dermatologists.

AUTHORS' CONTRIBUTIONS

DMP, MLS: article writing and revision; FBP, NABS, GKR: the patient's diagnosis; ILS, LL: the pathological exams. All authors approved the article submission.

CONFLICT OF INTERESTS

None to declare.

FUNDING

None to declare.

REFERENCES

1. Ghanem KG, Ram S, Rice PA. The modern epidemic of syphilis. N Engl J Med. 2020;382:845-54.
2. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. Protocolo clínico e diretrizes terapêuticas para atenção integral às pessoas com infecções sexualmente transmissíveis (IST). Brasília: Ministério da Saúde; 2020.

3. Ivars Lleó M, Clavo Escribano P, Menéndez Prieto B. Atypical cutaneous manifestations in syphilis. Actas Dermosifiliogr. 2016;107:275-83.
4. Bonamigo RR, Dornelles SI, editors. Dermatology in public health environments: a comprehensive textbook. Switzerland: Springer; 2018.
5. Freitas FL, Benzaken AS, Passos MR, Coelho IC, Miranda AE. Brazilian Protocol for Sexually Transmitted Infections 2020: acquired syphilis. Rev Soc Bras Med Trop. 2021;54 Suppl 1:e2020616.
6. Correia C, Mendes R, Sanches M, Fernandes S, Soares-Almeida L, Borges-Costa J, et al. A unique presentation of papulonodular secondary syphilis in an elderly patient. Int J Dermatol, 2021;60:e304-6.
7. Guillén BF, von der Weth MM, Oñate CV, Tapial JM, Bel PH. Secondary syphilis as a single annular plaque on the penis mimicking granuloma annulare. Indian J Dermatol Venereol Leprol. 2021;87:438.
8. O'Byrne P, Orser L, MacPherson P. Discussing current syphilis case definitions: a proposal for a "probable infectious" case. Public Health Nurs. 2021;38:390-5.
9. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. Atlanta: CDC; 2015.
10. Forrestel AK, Kovarik CL, Katz KA. Sexually acquired syphilis: laboratory diagnosis, management, and prevention. J Am Acad Dermatol. 2019;82:17-28.
11. Arando M, Mota-Foix M, Armegol P, Barberá MJ, Esperalba J, Vall-Mayans M. La evolución serológica en sífilis precoz. Enferm Infecc Microbiol Clin. 2019;37:183-6.
12. Geusau A, Kittler H, Hein U, Dangl-Erlach E, Stingl G, Tschachler E. Biological false-positive tests comprise a high proportion of venereal disease research laboratory reactions in an analysis of 300,000 sera. Int J STD AIDS. 2005;16:722-6.
13. Putri I, Mercer SE, Phelps RG, Levitt JO. False-negative anti-treponemal immunohistochemistry in secondary syphilis. Int J Dermatol. 2013;52:172-6.
14. Castro R, Prieto ES, Santo I, Azevedo J, Exposto FL. Evaluation of an enzyme immunoassay technique for detection of antibodies against Treponema pallidum. J Clin Microbiol. 2003;41:250-3.
15. Seña AC, White BL, Sparling PF. Novel Treponema pallidum serologic tests: a paradigm shift in syphilis screening for the 21st century. Clin Infect Dis. 2010;51:700-8.
16. Trayes KP, Savage K, Studdiford JS. Annular lesions: diagnosis and treatment. Am Fam Physician. 2018;98:283-91.
17. Bastos LM, Tolentino JM, Frota MA, Tomaz WC, Fialho ML, Batista AC, et al. Avaliação do nível de conhecimento em relação à Aids e sífilis por idosos do interior cearense, Brasil. Cien Saude Colet. 2018;23:2495-502.