



SYPHILITIC STOMATITIS: RAISING AWARENESS ON AN OFTEN-OVERLOOKED PRESENTATION OF SECONDARY SYPHILIS

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Received: 22/02/2024 Accepted: 03/04/2024 Published: 22/04/2024

Conflicts of Interests: The Authors declare that there are no competing interests.

Patient Consent: The authors confirm the acquisition of the signed patient consent.

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How to cite this article: Atalaia-Barbacena H, Lopes CI, Lopes IM, Howell Monteiro P. Syphilitic stomatitis: raising awareness on an often-overlooked presentation of secondary syphilis. EJCRIM 2024;11:doi:10.12890/2024_004416

ABSTRACT

Syphilis, a disease caused by the bacteria *Treponema pallidum*, has a multitude of clinical manifestations and is classified into primary syphilis, secondary syphilis and tertiary syphilis, based on clinical presentations and the time elapsed since the primary infection. The secondary stage of the disease can affect multiple organs and systems, and some of these involvements may be general and non-specific, justifying its name as 'the great imitator'. We present a case of a 30-year-old woman with a history of painful neck lymph nodes with progressive enlargement, persistent headache, weight loss, myalgia and alopecia. During investigations, stomatitis on the dorsal face of the tongue developed. A secondary study showed serum positive for rapid plasma reagin (RPR) and *T. pallidum* haemagglutination (TPHA), negative RPR in cerebrospinal fluid and normal MRI, thus the diagnosis of secondary syphilis was made. The patient was treated with a single dose of penicillin with complete resolution of symptoms. The case highlights the need for an exhaustive clinical examination, especially in cases presenting with non-specific and general symptoms, and raises awareness for this disease which has increased its prevalence in the last decades.

KEYWORDS

| Syphilis, tongue, stomatitis, secondary syphilis

LEARNING POINTS

- Syphilis is a resurgent infection with increasing prevalence, and its manifestations in the secondary stage of the disease are general and non-specific, being able to affect every organ system.
- The oral mucosa may be involved at any stage of the disease and the tongue, often a neglected organ, can be particularly affected and should be routinely observed.
- The internist, integrating a cornerstone speciality able to manage and diagnose systemic diseases, must be aware of the individual aspects of the physical examination, notably the appreciation and interpretation of each clue and sign found.

INTRODUCTION

Syphilis is an infectious disease caused by the bacteria *Treponema pallidum*, with a predominant, but not exclusive, sexual transmission^[1,2]. Epidemiologically, syphilis was considered an infection of the past; however, according to the European Centre for Disease Control, its prevalence is rising, being particularly high in countries such as Portugal, Spain, Ireland and Iceland^[3]. Syphilis can be classified based on its symptoms and time of evolution from initial infection into three types. First, primary syphilis, which is recognised by the non-painful, hard ulcer (chancre) that resolves spontaneously in 3–6 weeks without medical care. Secondary syphilis, which is able to affect every organ, is mainly recognised by its cutaneous lesions and non-tender adenopathies. The third category is tertiary syphilis, arising years after the initial infection, affecting mainly eyes, vessels and the central nervous system (CNS) (tabes dorsalis and general paresis)^[1,2,4]. Specifically in secondary syphilis, cutaneous manifestations are cornerstone signs, particularly the maculopapular exanthema involving the palm of the hands and soles of the feet^[1,2,4]. It must be recognised that the oral mucosa may also be involved at any stage of the disease, and therefore must be subject to examination^[1,2,5,6]. Its importance cannot be understated. Oral syphilitic manifestations depend upon the stage of the disease and can be multiple and with diverse characteristics, increasing the diagnostic complexity. In primary syphilis, the chancre lesion can be recognised anywhere on the oral mucosa if inoculation happens in such an area^[1,2,4–6]. In secondary syphilis, the tongue, an often-forgotten organ, is particularly affected, with some reports describing a prevalence of up to 30%, mainly by mucous patches in a white-pinkish colour which may exhibit a serpentine or snail-like trail^[5,6], leading to an extensive differential diagnosis. The lesions may mimic numerous other diseases: traumatic granulomas or ulcerations, atypical aphthous ulcerations, geographic tongue, deep fungal infections, tuberculosis, squamous cell carcinoma, Crohn's disease, pyostomatitis vegetans, erosive lichen planus, drug-related ulcerations or granulomatosis with polyangiitis^[5]. Thus, a high degree of suspicion is needed for the correct diagnosis.

Regarding the CNS involvement in syphilis, it is important to note that spirochetes can invade the CNS in every stage of the disease course. In an early stage, CNS involvement can be asymptomatic or present as early neurosyphilis with

meningitis or meningo-vascular disease. In asymptomatic cases of CNS involvement, spirochetes can become dormant and cause late neurosyphilis, often in the tertiary stage of the disease. CNS involvement has therapeutic implications, since the duration of the penicillin schemes is different^[1,2,4]. To diagnose syphilis, non-treponemal and treponemal serologic tests are used. The first two - RPR test and venereal disease research laboratory (VDRL) test - are cheap, quick and unspecific, based upon the reactivity of infected patients' serum to a cardiolipin-cholesterol-lecithin antigen, being a useful way to rule out the absence of the disease^[5]. Once positive, these tests must be confirmed by a treponemal test, such as the TPHA, a more complex and laborious test, but highly specific. It must be noted that non-treponemal tests can become permanently positive after an initial infection, and therefore are not useful to rule out reinfections. In that case, treponemal tests are of extreme importance: once negative, despite a positive non-treponemal test, the diagnosis is unlikely; once positive, it confirms the reinfection, as described in Fig. 1^[1,2,7]. As for treatment, penicillin is the antibiotic of excellence, only varying its dose depending on clinical classification^[1,2].

CASE DESCRIPTION

A 30-year-old woman with previous diagnosis of migraine was admitted in the emergency department with a six-month history of painful neck lymph nodes with progressive enlargement, persistent headache with different characteristics than usual (intensity 8/10, difficult to subdue with analgesics), weight loss (8% of total body weight), myalgia and alopecia. The patient denied fever, travels abroad, animal exposure and high-risk sexual behaviour. At physical examination she showed two palpable tender painful anterior left jugular lymph nodes <1 cm. Neurological and skin examinations were normal. Initial blood work showed sedimentation rate 24 mm, C-reactive protein 0.7 mg/dl, and normal haemogram and lactate dehydrogenase (LDH). A neck CT showed several adenomegalias in the posterior and anterior cervical chains and supraclavicular chains (Fig. 2). A first investigation was made, and haematological neoplasms were excluded, given the absence of cytopenia or leukocytosis, abnormal findings on peripheral blood smear, LDH elevation and hepatosplenomegaly. A basic autoimmune panel turned out negative. Infectious serologies for HIV, cytomegalovirus and Epstein-Barr virus

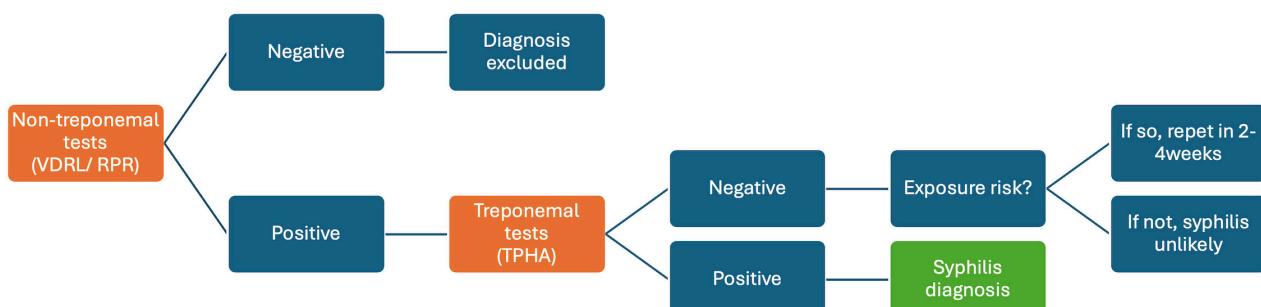


Figure 1. Diagnostic approach to a suspected syphilis infection.

were negative for acute infection. *T. pallidum* serology was positive (RPR 16 dils/ TPHA 1/20480). The diagnosis of syphilis was established; however, due to the persistent and disabling headache, after consulting with Neurology and Infectious Diseases, the hypothesis of CNS involvement was considered, and the patient was admitted for further study. At this time, the patient noted the appearance of *de novo* non-painful patchy tongue erosions (Fig. 3). Cerebral MRI showed absence of lesions, meningeal highlight or cerebral venous thrombosis. Additionally, a lumbar puncture depicted uncharacteristic cerebrospinal fluid, with negative VDRL, excluding CNS involvement. Thus, secondary syphilis was admitted, and the patient was treated with a single dose of 2.4 MIU of penicillin, with complete symptomatic resolution. Contact tracing was performed, and the patient's sexual partner turned out positive. Because he had no symptoms a diagnosis of latent syphilis was made and 2.4 MIU of penicillin was administered for three weeks. The patient maintained follow-up in Internal Medicine and RPR titration six months after treatment presented a significant titre reduction (2 dils). The patient's sexual partner was also evaluated with a similar RPR titre reduction six months after initial treatment.

DISCUSSION

The manifestations of syphilis are multiple and as a result it is known as the great imitator^[1,4]. Secondary syphilis can affect any organ, particularly skin and mucosal surfaces. Oral manifestations of syphilis are wide and multiple, mimicking a variety of infectious, neoplastic and immune-mediated processes, making diagnosis hard and challenging^[1,4,5].

This case highlights the non-specific presentation of secondary syphilis in a young patient, sexually active but without high-risk sexual behaviours, for instance unprotected sexual relationships with multiple partners. At presentation the leading symptoms were adenomegalias and weight loss. Hence, common and potentially severe lymph node enlargement aetiologies were initially excluded, such as haematological neoplasm, general autoimmune diseases and major infectious syndromes. Syphilis was diagnosed during this differential diagnosis, and secondary syphilis was considered. Because of the presence of neurological symptoms – a persistent and disabling headache, different than usual, that did not subside with analgesic medication – Neurology and Infectious Disease specialists were consulted, and the exclusion of CNS involvement was mandatory. The patient was admitted to our Internal Medicine ward and underwent brain MRI excluding major involvement of CNS structures and other causes for a headache differential. A lumbar puncture was performed and VDRL in cerebrospinal fluid was negative, ruling out CNS involvement. At the time of hospital admission, the patient noted *de novo* tongue erosions (Fig. 3), not previously presented, with a few days' evolution, well defined, non-painful, without wounds or elevated margins. A primary chancre was excluded given the absence of an ulcer with elevated margins and clean

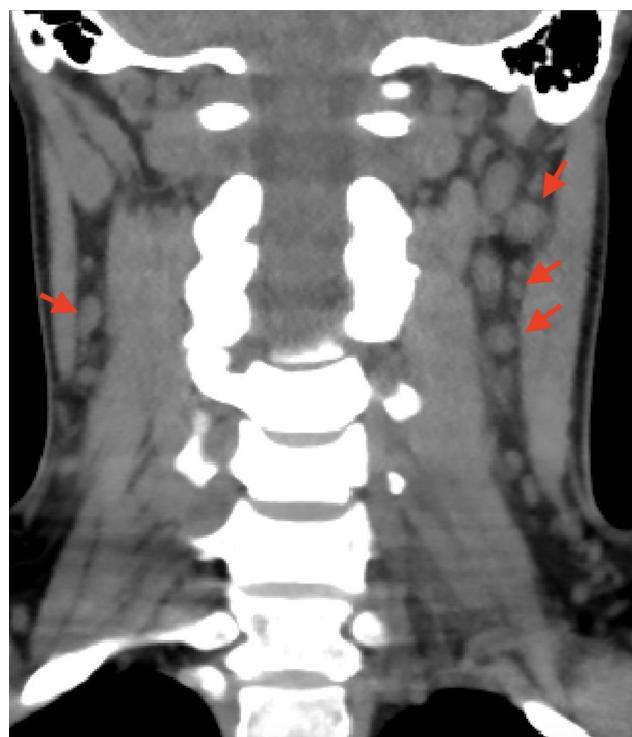


Figure 2. Neck CT scan showing multiple lymphadenopathies (arrows).



Figure 3. Tongue erosions.

base, typical presentation of these lesions. The stomatitis was identified to be a manifestation of secondary syphilis and treatment was given. The patient was rediscussed with a Stomatology specialist, and the stomatitis, although not pathognomonic, was extremely indicative of secondary syphilis.

As stated before, the oral mucosa is particularly susceptible to syphilis manifestations. In primary syphilis, chancre can appear anywhere on the oral mucosa as a solitary lesion, predominantly in the tongue and lips^[5]. In secondary syphilis lesions are often multiple, firming up the differential diagnosis. Mucous patches can be seen, in a white-pinkish

colour, normally in a serpentine or snail-like trail. Superficial necrosis of the epithelium can also occur, leaving exposed the underlying connective tissue. A small percentage of patients may instead present with raised papillary grey-whitish in colour – condyloma lata^[5]. Differential diagnosis includes traumatic lesions, drug-related ulcerations, aphthous ulcerations, geographic tongue, neoplastic, infectious and autoimmune diseases^[5].

Given the resurgence of syphilitic infections worldwide, reinforced awareness of this infection is particularly important. Because of its symptomatic pleomorphism, many cases of syphilis go undiagnosed and evolve through time to the tertiary stage of the disease, where complications and lifelong sequelae are more common. The case presented describes the non-specific generalised symptomatic presentation of secondary syphilis, easily misunderstood and misdiagnosed by clinicians. Although already described in the literature, tongue involvement is frequently unrecognised outside the scope of Dermatology and Stomatology. Therefore, the case presented reinforces such involvement and the need for attentive observation by internists, integrating a cornerstone speciality and able to manage and diagnose systemic diseases.

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