Annals of Diagnostic Pathology 19 (2015) 76–80

Contents lists available at ScienceDirect

Annals of Diagnostic Pathology

Oral syphilis: report of three cases and characterization of the inflammatory cells

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ARTICLE INFO

Keywords:
Infection disease
Treponema pallidum
Sexually transmitted diseases

ABSTRACT

Syphilis is a sexually transmitted infectious disease caused by *Treponema pallidum*. This study reports 3 cases of syphilis and highlights the importance of identifying oral lesions for its final diagnosis. Case 1: a 48-year-old male patient presented with a bleeding ulcer in the lower lip. Overall clinical examination revealed patchy alopecia and skin target lesions. Case 2: a 61-year-old male patient presented with white spots on the lateral tongue and nodules on the dorsum of the tongue. Overall clinical examination showed erythematous target lesions on the abdomen, forearm, palms of the hand, and soles of the feet. Case 3: a 17-year-old male patient presented with an ulcerated lesion on the tongue and lymph node involvement. The following serologic tests were requested: Venereal Disease Research Laboratory, fluorescent treponemal antibody–absorption, anti–HIV-1 and anti–HIV-2, and anti–hepatitis C virus. An incisional biopsy revealed epithelial hyperplasia associated with intense and diffuse mononuclear inflammatory cell infiltration consisting mainly of plasma cells, in a perivascular and perineural distribution. The final diagnosis in the 3 patients was syphilis. Treatment consisted of 1 weekly dose of penicillin (2.4 million units, intramuscular) for 2 or 3 weeks. Immunohistochemical reactions for XIIIa, CD3, CD20, CD68, CD163, S100, CD1a, CD11c, CD83, CD138, and CD208 were performed. Clinicians should be familiarized with oral syphilis lesions in order to be able to diagnose this emerging infectious disease of variable clinical presentation.

1. Introduction

Syphilis is an infectious disease caused by *Treponema pallidum*. Transmission of the disease occurs through sexual contact, vertical transmission, or, less frequently, blood transfusions or reused sharp objects [1,2]. Syphilis is an emerging disease, and an increase in the number of cases has been observed in recent years [3].

Syphilis can be divided into different stages: primary, secondary, latent, and tertiary [4]. The first sign of syphilis is a hard chancre, and the lips are the most affected extragenital site [1]. Oral lesions are observed in at least 30% of patients with secondary syphilis and appear as white plaques, papules, or nodules [3]. Involvement of the palms and soles is characteristic of this stage [2]. After the second stage, the disease enters long periods of latency that can last from 10 to 30 years [2,5]. In the third stage, there is involvement of the skin, mucosa, cardiovascular and central nervous systems [2,6], liver, spleen, and other organs [5]. Gingival lesions are characteristic of this stage and may perforate the palate and destroy the nasal septum [2].

The objectives of the present study were to report 3 cases of syphilis with variable clinical characteristics and to highlight the importance of identifying oral lesions for the definitive diagnosis and for establishing adequate therapeutic protocols.

2. Case report

2.1. Case 1

A 48-year-old male patient sought the stomatology outpatient clinic of Universidade Estadual Paulista "Júlio de Mesquita Filho", São José dos Campos, São Paulo, with a 5-month history of a wound in the lower lip, which spontaneously bleeds at night (Fig. 1A). During anamnesis, the patient reported that he had seen a physician who prescribed Neomicina ointment (30 g, betamethasone valerate + neomycin sulfate, Bunker Indústria Farmacêutica LTDA, São Paulo, Brazil), which did not result in improvement. The patient was submitted to a chest x-ray because of his chronic dry cough, but no pulmonary alterations were detected. The patient was a smoker and chronic drinker for 34 years and had worked as a stonemason under sun exposure without protection for decades. He also reported significant weight loss in the last months. Overall clinical examination revealed alopecia (Fig. 1B), erythematous lesions on the skin (Fig. 1C), and an ulcer with a hemorrhagic crust on the left side of the

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http://dx.doi.org/10.1016/j.anndiagpath.2015.01.003
1092-9134/

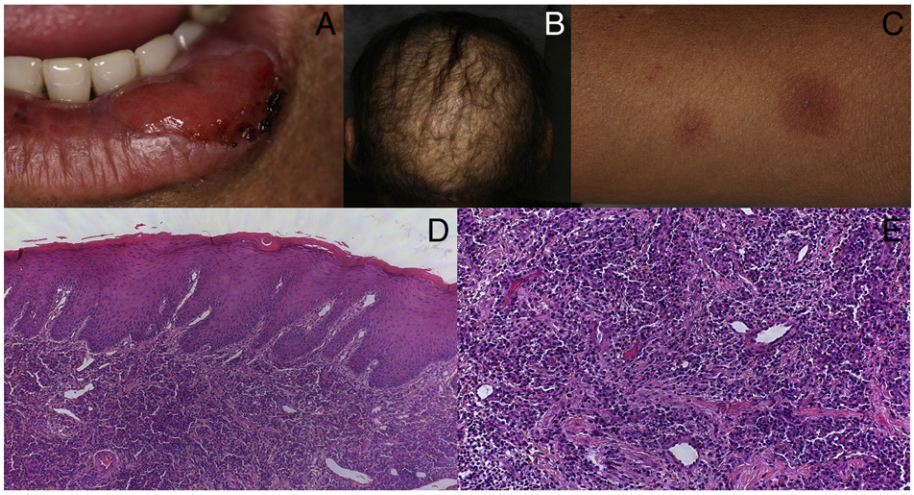

Fig. 1. Case 1. (A) Initial clinical appearance showing an ulcer in the lower lip. (B) Hair loss. (C) Skin target lesion. (D) Mucosal fragment exhibiting parakeratinized stratified epithelium with acanthosis and intense inflammation in the connective tissue (hematoxylin and eosin [H&E], magnification ×100). (E) Perivascular distribution of inflammatory cells, particularly plasma cells (hematoxylin and eosin, magnification ×400).

lower lip (Fig. 1A). No lesions on the palms and soles or interdigital condylomata were observed.

The clinical diagnostic hypotheses were immune-mediated diseases such as erythema multiforme and infectious diseases such as syphilis and tuberculosis. An incisional biopsy of the oral lesion was performed, which revealed a mucosal fragment covered with parakeratinized stratified pavement epithelium exhibiting areas of acanthosis, intracellular edema, and exocytosis associated with a focal area of superficial ulceration (Fig. 1D). There was an intense subepithelial inflammatory cell infiltrate consisting mainly of plasma cells, which exhibited a perivascular and perineural distribution pattern in the underlying connective tissue (Fig. 1E).

The following serologic tests were requested and the results are shown in Table 1: Venereal Disease Research Laboratory (VDRL), fluorescent treponemal antibody–absorption (FTA-Abs), anti–HIV-1 and anti–HIV-2, and anti–hepatitis C virus (HCV). The clinical and histopathologic findings and serologic tests confirmed the diagnosis of secondary syphilis.

The patient was referred to an infectologist and was treated with 1 weekly dose of penicillin (2.4 million units, intramuscular [IM]) for 3 weeks (Fig. 1F).

2.2. Case 2

A 61-year-old male patient was referred to our service because of a 2-month history of white spots on the tongue. Overall clinical examination revealed red target lesions on the abdomen, soles of the feet, and palms of the hands (Fig. 2A-C). On intraoral examination, nodular-papular lesions measuring approximately 1 cm were observed on the dorsum of the tongue (Fig. 2D) and erythematous lesions on the palate (Fig. 2E). Furthermore, a well-delimited white spot containing a small area of ulceration and showing no painful symptoms was noted on the ventral surface of the tongue (Fig. 2F). During anamnesis, the patient reported self-medication with fluconazole (150 mg/wk) for 3 weeks due to a lesion in the genital region, but without improvement.

In view of the differential diagnosis of secondary syphilis, a biopsy of the tongue lesion was performed. Microscopic analysis showed intense epithelial hyperplasia, exocytosis, and intraepithelial microabscesses, in addition to intense perivascular and perineural plasma cell infiltration (Fig. 2G-I). The results of the serologic tests (VDRL, FTA-Abs, anti-HIV, and anti-HCV) showed in Table 1 indicated secondary syphilis. The patient was referred to an infectologist and was treated with 1 weekly dose of penicillin (2.4 million units, IM) for 2 weeks.

Table 1
Serologic results of the 3 cases reported

Case	VDRL	FTA-Abs	HIV	HVC
1	1:1024	+	−	+
2	1:520	+	−	−
3	NA[a]	+	NA[a]	NA[a]

[a] Patient refused to inform.

2.3. Case 3

A 17-year-old male patient presented with a 2-month history of an ulcer on the lateral border of the tongue. During anamnesis, the patient reported the use of oral mouth rinse and Omcilon A Orabase ointment (triamcinolone acetonide, Bristol-Myers Squibb Farmacêutica S.A., Santo Amaro, São Paulo, Brazil), without satisfactory results. Extraoral clinical examination revealed a 4-cm nodule in the upper neck region that was mobile, tender to palpation, and asymptomatic (Fig. 3A). Intraoral examination showed a 3-cm asymptomatic ulcer on the right lateral border of the tongue (Fig. 3B).

The differential clinical diagnoses included neoplastic and infectious diseases. An incisional biopsy of the tongue lesion was performed, and microscopic analysis revealed pseudoepitheliomatous hyperplasia, exocytosis, and intraepithelial microabscesses (Fig. 3C). Moreover, there was a prominent subepithelial inflammatory infiltrate, as well as evident perivascular and perineural plasma cell infiltration (Fig. 3D). The final diagnosis of syphilis was made based on the serologic tests (VDRL, FTA-Abs, anti-HIV, and anti-HCV) whose results are summarized in Table 1. The patient was referred to an infectologist and treated with 1 weekly dose of penicillin (2.4 million units, IM) for 2 weeks.

3. Immunohistochemical analysis

All tissue specimens were fixed in 10% neutral-buffered formalin for 24 hours at room temperature, embedded in paraffin at 55°C, and cut into consecutive parallel 3-μm-thick sections. For immunohistochemistry, the slides were hydrated and treated with hydrogen peroxide.

For retrieval of the XIIIa, CD3, CD20, CD68, CD163, S100, CD1a, CD11c, CD83, CD138, and CD208 epitopes, the tissue specimens were pretreated with 10 mM sodium citrate buffer, pH 6.0, in a pressure cooker. The CD123, CD303, and CD207 epitopes were unmasked by pressure cooker pretreatment in 10 mM Tris/1 mM EDTA buffer, pH 9.0. The sections were then successively incubated with the primary antibodies (Table 2). Next, the sections were incubated with the secondary antibodies conjugated with streptavidin-biotin-peroxidase (K0690; Universal Dako LSAB + Kit, Peroxidase, Carpinteria, California). The reactions