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Photo vignette

Whitish oral lesions in a heavy pipe smoker

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Abstract

Classically known as the "Great Imitator", the diagnosis of syphilis continues to be an enormous challenge. We describe a case of isolated oral lesions as the sole presentation of secondary syphilis and the only clinical clue to previously undiagnosed human immunodeficiency virus infection. The current increase in new cases of syphilis should stimulate physicians to consider this disease in daily practice.

Keywords: Syphilis, oral cavity, mucosal lesions

Case synopsis

A 55-year-old, heavy pipe smoking man presented to our department with a painful easily-bleeding lesion over his lower lip, which had begun as a whitish progressively growing plaque two months before.

On physical examination, a 2 centimeter, grayish-white, thickened plaque with an irregular and friable surface was observed on the left region of the lower lip mucosa (Figure 1). Oral cavity inspection revealed the presence of another two smaller, but clinically similar, lesions near both buccal commissures (Figure 2). No other cutaneous or mucosal lesions were identified. There was neither regional lymphadenopathy nor systemic involvement.

Microscopy of a punch-biopsy specimen showed an oral mucosa with acanthosis, irregular epithelial



Figure 1. Grayish-white infiltrated plaque on the lower lip

hyperplasia and moderate keratinocyte atypia, accompanied by a densely band-like inflammatory infiltrate of plasma cells within the lamina propria (Figures 3 and 4). Immunohistochemistry for *T. pallidum* demonstrated numerous spirochetes spreading throughout the epithelium (Figure 5). Rapid plasma reagin (RPR) serology was positive (1/512) as well as the more specific *T. pallidum* haemagglutination assay (TPHA) and fluorescent treponemal antibody absorbed (FTA-abs) tests, which had been all negative nine months before. An extended serological workup revealed a previously undiagnosed HIV infection, with a 300 CD4 cell count and more than 10^7 viral copies/ml. Cerebrospinal fluid examination dismissed underlying neurosyphilis.

Figure 2. Mucous patches symmetrically located near both buccal commissures.

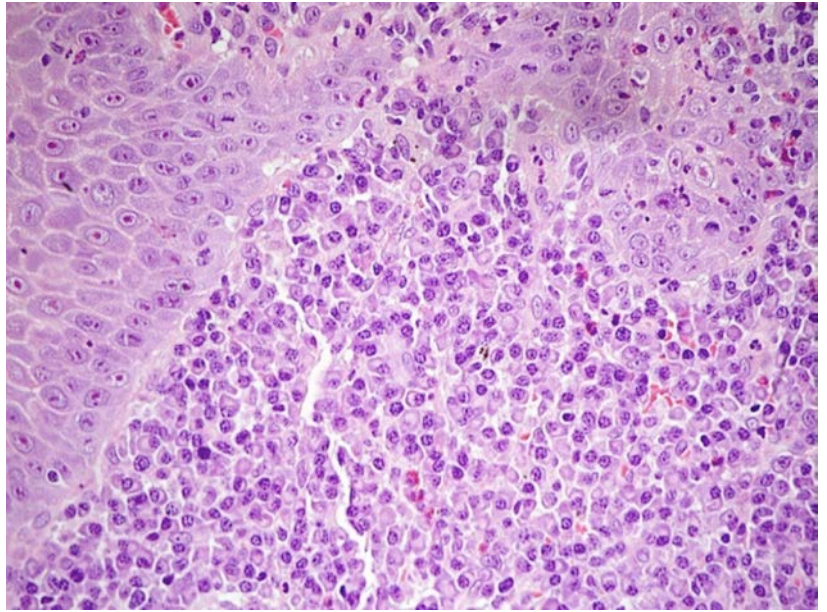
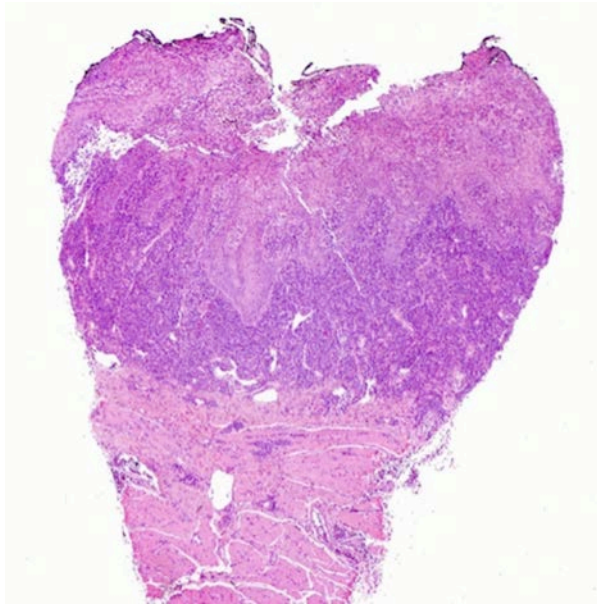
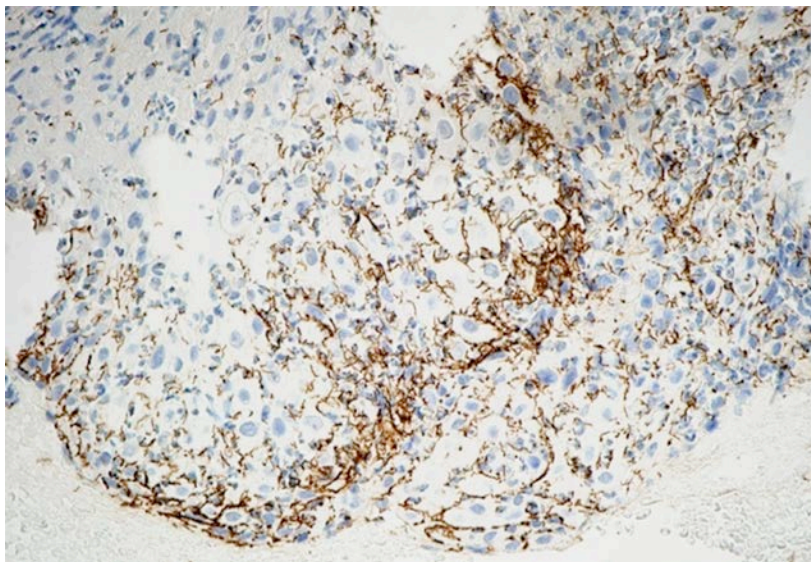


Figure 3. Partially ulcerated epithelium with irregular hyperplasia and a dense band-like inflammatory infiltrate (H&E original magnification, x 1.25).

Figure 4. Hematoxylin-eosin (H&E)-stained sections of mixed inflammatory infiltrate primarily composed of plasma cells (original magnification, x 40).

Figure 5. Immunohistochemical staining for *T. pallidum* (original magnification, x 40).



Diagnosis

Based on clinical, pathological, and microbiological findings, a diagnosis of early secondary syphilis in a HIV-seropositive patient was made. A good clinical and

serological response was observed after a single-dose treatment with benzathine penicillin G (2.4 million units, intramuscularly).

Discussion

Syphilis is an ancient sexually transmitted infection currently rising among the homosexual male HIV-seropositive population of developed countries [1,2,3]. Traditionally defined as “the Great Imitator” because of its wide spectrum of dermatological and systemic signs, unusual and misleading presentations may remain an important cause of underdiagnosis. The oral cavity has traditionally been considered the most common extragenital site of infection [3]. However, only a few cases of oral

syphilis have recently been reported worldwide, even when the fraction of transmission attributed to oral sex has significantly increased for the last years [2]. Probably confused with other more common oral mucosal disorders, such as lichen, candidiasis oral, aphthous stomatitis, erythema multiforme, or actinic cheilitis, the diagnosis of oral syphilis requires a high index of suspicion, both for pathologists and dermatologists, especially when solitary oral lesions occur.

According to published data, oral involvement is primarily seen in secondary syphilis [1,2,3,4,5,6]. Although lesions may affect almost any part of the oral cavity, they are most commonly found on the dorsal region of the tongue, followed by gingivae, buccal mucosa, and less frequently, lips and palate. Morphologically, lesions maintain the characteristic polymorphic picture of secondary syphilis, ranging from an erosive-ulcerative nature or whitish soft plaques as we saw in our patient, to a tumoral or nodular appearance. Typically, they are multiple, painful, and usually accompanied by other cutaneous or systemic signs that lead to the correct diagnosis. Unusual hypertrophic, serpiginous, and pemphigus-like presentations have also been described [3,7]. In contrast, syphilitic chancre is more rarely located in the oral cavity and appears most commonly over the tongue or hard palate as a solitary painless ulcer without other concomitant manifestations [1,2,3,5]. Nevertheless, Duarte et al. reported a case of nodular oral chancre and Flynn et al. described an erythematous rash on the lower limbs of a patient with primary syphilis [8,9]. Oral lesions in tertiary syphilis seem to be extremely rare [1,2,3,4,5,6]. Tertiary lesions clinically are often consistent with solitary, progressively growing, painless palatal masses, although Leuci et al. studied a patient with extensive necrosis of the dorsum of the tongue as a highly atypical presentation of third-stage syphilis [3].

Diagnosis of oral syphilis may be also quite challenging for dermatopathologists owing to the absence of a single microscopic feature specific by itself. However, the confluence of several suggestive findings, such as an unusual epithelial hyperplasia, endarteritis, neuritis, or a prominent inflammatory infiltrate primarily composed of plasma cells may be strongly indicative of syphilis [10]. As proposed by Ficarra et al, there are three important histological clues to suggest syphilis: epithelial changes, plasma cell infiltrate, and identification of *T. pallidum* within the oral mucosa assessed by immunohistochemistry [2]. Our patient presented the typical histological picture of secondary syphilis, characterized by psoriasiform or pseudoepitheliomatous hyperplasia, a dense superficial and deep inflammatory infiltrate, often in a band-like distribution, and multiple spirochetes throughout the epithelium [4]. On the other hand, an ulcerated epithelium with superficial perivascular dermatitis and spirochetes limited to the basal layer or dermal-epidermal junction is suggestive of primary syphilis [2]. Third-stage syphilis is defined by gumma formation (central necrosis surrounded by a mixed infiltrate of plasma cells, lymphocytes, and histiocytes), variable endarteritis, and scarring [2,4,10].

The progressive increase in new cases of syphilis over the last years is leading to reemergence of currently forgotten old scenarios of this polymorphous entity. Oral syphilis may present serious diagnostic problems in daily clinical practice, especially in cases of uncommon isolated presentations. Therefore, physicians should consider this possibility in patients with solitary painless ulcers or multiple grayish-white plaques in the oral cavity, especially if a conspicuous inflammatory infiltrate of plasma cells is found on histological examination.

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