

Oral medicine case book 59:

Syphilis of the oral mucosa

SADJ May 2014, Vol 69 no 4 p172 - p173

BK Bunn¹, JC Marnewick², AW van Zyl³, WFP van Heerden⁴

CASE REPORT

A 35-year-old male patient presented to the Oral Medicine Clinic complaining of painful oral ulcers of six weeks duration. The patient was a non-smoker and did not report any additional medical history of clinical significance.

Extra-oral examination revealed mild cervical lymphadenopathy upon palpation of the neck. A widespread skin rash was present on the trunk and extremities (Figure 1). Intra-oral examination showed superficial erosions involving the buccal, labial and palatal mucosa. Some of the lesions had coalesced to form serpentine mucosal ulcers (Figure 2). Thickened white plaques, some focally fissured, were present on the tongue (Figure 3). An incisional biopsy was taken from the area of labial mucosal ulceration and was submitted for histology. Serological testing for human immunodeficiency virus (HIV) infection was also requested.

The clinical differential diagnosis included syphilis, medication-induced ulceration, recurrent aphthous stomatitis and immune-mediated vesiculo-ulcerative disorders. The patient was not on any form of chronic medication and the unusual mucocutaneous presentation prompted further histopathological investigation.

Microscopic examination of the incisional biopsy specimen showed a shallow area of ulceration surfaced by fibrinopurulent material. The adjacent stratified squamous parakeratinising epithelium was hyperplastic and showed areas of marked inflammatory exocytosis, spongiosis and acanthosis. In addition, focal superficial intra-epithelial micro-abscesses were observed (Figure 4a). The ulcer bed comprised granulation tissue with an extensive subjacent mixed acute and chronic inflammatory cell infiltrate. The infiltrate was composed of plasma cells, lymphocytes, histiocytes, eosinophils and occasional neutrophils. The plasma cells also showed an additional distinct perivascular distribution. The infiltrate extended to involve the deep submucosal connective tissue. Fungal elements were not morphologically recognised and their presence was excluded by means of a periodic acid-

ACRONYM

ELISA: Enzyme-linked immunosorbent assay

Schiff (PAS) special stain. A Warthin-Starry (WS) special stain was performed, which confirmed the presence of numerous coiled spirochetes within the epithelium between the keratinocytes, as well as within the submucosa in close association with blood vessels and the perivascular plasma cell infiltrates (Figure 4b). A diagnosis of secondary syphilis was made. This was confirmed with positive treponemal and non-treponemal serological assays. An ELISA test was negative for HIV. The patient was referred to his medical doctor for treatment. At follow-up ten days later, the oral mucosal and skin lesions had resolved completely.

DISCUSSION

Syphilis is a systemic infection caused by the anaerobic spirochete *Treponema pallidum*. It is principally acquired via sexual transmission but may be vertically transmitted resulting in congenital disease.¹ Humans are the only known vector of this spirochete infection.^{2,3} The widespread use of antibiotics and the implementation of successful prevention campaigns led to a rapid decline in the prevalence and incidence of the disease by the year 2000.³ There has been a notable resurgence in newly diagnosed and reported cases in the last decade. This has been attributed to several factors including a general lack of public knowledge regarding sexually transmitted infections (STIs), the perception that STIs are curable, a decline in the use of barrier protection particularly in anogenital sexual contact, the evolution of sexual liberation and a culture that endorses multiple sexual partners as well as the mistaken belief that oral sexual contact is safe practice.^{3,4} Moreover, the incidence of syphilis and HIV co-infection is increasing. Syphilis is seventy-seven times more prevalent in the HIV-infected population as compared with the general population. The underlying immune dysfunction in HIV positive patients may predispose to syphilis co-infection and conversely, the presence of active syphilitic lesions is known to facilitate HIV infection.^{3,5}

Syphilis is subdivided into four stages based on the activity and infectivity of the lesions as primary, secondary, latent (early and late) and tertiary. Oral involvement is reported at all stages but is most prevalent during the secondary stage of disease.¹

Primary syphilis is localised to the site of infection where contact with an active lesion occurs. The genital area is thus most frequently involved whilst oral mucosal involvement represents the most common extragenital site, being observed in 12 to 14% of cases.^{2,5} A painless papule develops at the inoculation site following an incubation period of two to three weeks. The papule becomes indurated and ulcerated with resultant formation of the classical syphilitic chancre. The occurrence of intra-oral chancres on the tongue and lips is well documented when oral sex is implicated in disease transmission.¹ A useful diagnostic

1. **BK Bunn:** BDS, MDent, FC Path(SA) Oral Path. Department of Oral Pathology and Oral Biology, School of Dentistry, Faculty of Health Sciences, University of Pretoria.
2. **JC Marnewick:** BChD, MDent. Department of Periodontics and Oral Medicine, School of Dentistry, Faculty of Health Sciences, University of Pretoria.
3. **AW van Zyl:** BChD, MChD. Department of Periodontics and Oral Medicine, School of Dentistry, Faculty of Health Sciences, University of Pretoria.
4. **WFP van Heerden:** BChD, MChD, FC Path(SA) Oral Path, PhD, DSc. Department of Oral Pathology and Oral Biology, School of Dentistry, Faculty of Health Sciences, University of Pretoria.

Corresponding author

WFP van Heerden:

Department of Oral Pathology and Oral Biology, University of Pretoria, Pretoria, South Africa, Tel: 012 319 2320, Fax: 012 321 2225. E-mail: willie.vanheerden@up.ac.za



Figure 1: The maculopapular skin rash involving the trunk. The rash was also present on the extremities as well as the palms and soles.



Figure 2: Mucous patches on the palate coalesced to form a snail track pattern.



Figure 3: Mucous patches on the tongue with focal fissuring.

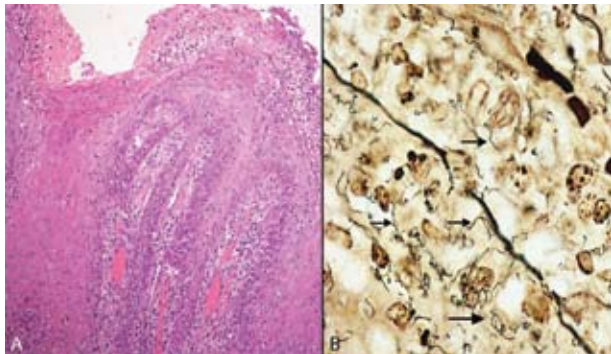


Figure 4: (A) Microscopic view of biopsy from the tongue showing epithelial hyperplasia with exocytosis and spongiosis and superficial intra-epithelial microabscesses (H&E X100). (B) Numerous coiled spirochetes (arrows) were present within the epithelium (Warthin-Starry stain, x400).

clue to primary syphilis is the frequent occurrence of regional lymphadenopathy. Chancres resolve spontaneously within four to six weeks and in some instances go unnoticed by patients.⁵

Secondary syphilis is characterised by generalised, disseminated disease following lymphovascular spread of the spirochetes from the primary site of involvement. This represents the most diagnostically challenging stage due to its diverse clinical presentation. Long regarded as the "great imitator", lesions of secondary syphilis are often misdiagnosed or overlooked as other disease processes.^{1,2} Clinical symptoms are usually non-specific. Patients may complain of headaches, low-grade fever, myalgia, generalised lymphadenopathy and a sore throat.² A consistent finding in up to 80% of cases is that of a mucocutaneous maculopapular rash located predominantly on the trunk and extremities and often with palmar and plantar involvement.⁵ In up to 60% of patients, oral mucosal lesions are present, the most frequent being multiple white patches and shallow erosions that may affect any mucosal surface. The ulcers characteristically coalesce to form confluent serpiginous zones termed "snail track ulcers".^{1,5} Less often, features include fissuring of the mucosa, condylomata lata and widespread mucosal sloughing. HIV co-infection may dramatically alter the clinical appearance and is associated with an aggressive course in which widespread destruction of tissue occurs.⁶

Progression to the latent and tertiary stages of disease occurs in up to a third of patients who do not receive treatment. Early latency is defined by an asymptomatic period of up to one year following infection. Patients are susceptible to mucocutaneous relapse at this time.⁵ Late latency spans periods of one year to three decades later at which time patients are asymptomatic and non-infectious. Tertiary syphilis is associated with the greatest morbidity and mortality due to the severe neurological and cardiovascular complications. The characteristic syphilitic lesion during this stage is the non-infective gumma, an area of necrotising granulomatous inflammation whose occurrence in the oral cavity is well documented. Gummatous foci involving the hard palate

and tongue are typical. The palatal lesions often result in destruction of bone with oro-antral communication, whilst the tongue lesions heal with pronounced scarring and muscular contracture.^{1,5} Atrophic glossitis is an additional feature of tertiary syphilis and was previously associated with a greater risk for the development of oral squamous cell carcinoma. The increased risk for cancer may in fact have been due to the arsenicals and heavy metals traditionally used in the treatment of syphilis rather than due to the infection itself.¹

The confirmation of suspected syphilis is based on serology. Two types of serological tests are employed: the non-treponemal and treponemal assays. The non-treponemal tests are cost effective and are useful for screening suspected patients, as well as for monitoring response to treatment. These tests detect IgM and IgG antibodies within sera, present in reaction to lipid-like substances released by damaged host cells. Treponemal tests are more specific and are of a qualitative nature. They are therefore useful to confirm the presence of disease following positive non-treponemal test results. Their qualitative nature however, precludes their use in evaluation of treatment response. Once a treponemal test is positive, it remains positive in a patient for life.^{2,5} The preferred treatment for syphilis remains benzathine penicillin G (2.4 million Units IM).

CONCLUSION

The increased prevalence and re-emergence of syphilis as an STI in the last decade necessitates renewed interest, awareness and education of this disease process. The mortality and morbidity, particularly in the setting of HIV/AIDS, as well as its facilitation of new HIV infections, is of clinical significance. The oral healthcare worker is likely to encounter the varied syphilitic lesions and therefore plays a crucial role in the early recognition and diagnosis of new infections. Furthermore, the oral lesions of syphilis are highly contagious. This case study emphasises the importance of considering syphilis in the clinical differential diagnosis of unusual forms of oral ulceration and confirms the imperative for appropriate referral and management.

Declaration: No conflict of interest declared.

References

1. Compilato D, Amato S, Campisi G. Resurgence of syphilis: a diagnosis based on unusual oral mucosa lesions. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009; 108: e45-9.
2. Kelner N, Rabelo GD, da Cruz Perez DE, *et al.* Analysis of non-specific oral mucosal and dermal lesions suggestive of syphilis: a report of 6 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2014; 117: 1-7.
3. Leuci S, Martina S, Adamo D, *et al.* Oral syphilis: a retrospective analysis of 12 cases and a review of the literature. *Oral Dis* 2013; 19: 738-46.
4. Hertel M, Matter D, Schmidt-Westhausen AM, Bornstein MM. Oral syphilis: a series of 5 cases. *J Oral Maxillofac Surg* 2014; 72: 338-45.
5. Little JW. Syphilis: an update. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2005; 100: 3-9.
6. Ortega KL, Rezende NP, Magalhaes MH. Diagnosing secondary syphilis in a patient with HIV. *Br J Oral Maxillofac Surg* 2009; 47: 169-70.