Secondary Syphilis-Related Oral Ulcers: Report of Four Cases

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Establishing a diagnosis of syphilis, whatever the stage of the disease, can be difficult because syphilis is a great mimic in clinical morphology and histology. Many patients infected with venereal diseases have oral manifestations, but very few dentists and physicians have the proper experience to diagnose syphilis or other STDs from oral lesions. Oral secondary syphilis appears to be very uncommon, and few cases have been reported over the recent past. We present 4 patients who developed secondary syphilis-related oral lesions of moist ulcers, irregular linear erosions termed 'snail-track' ulcers, or erythematous mucous patches on the labial mucosa, buccal mucosa, palate, or tongue. Concurrent human immunodeficiency virus (HIV) infection was diagnosed in 1 patient. The histological examination in 2 patients showed dense subepithelial inflammatory cell infiltration comprised predominantly of plasma cells, and it was of practical help in the diagnosis of syphilis. The diagnostic value of a histological examination, serologic tests, and treatment of syphilis are discussed. Obviously, coinfection with HIV will complicate the clinical presentation, diagnosis, and management of syphilis. Concurrent HIV infection should be considered in any patient with a sexually transmitted disease including syphilis. *(Chang Gung Med J 2002;25: 683-8)*

Key words: sexually transmitted disease, syphilis, oral ulcer, HIV.

Present trends show a dramatic increase in sexually transmitted diseases (STDs) in Taiwan, including herpes simplex virus types 1 and 2, syphilis, gonorrhea, chlamydia, and HIV. A great challenge to the dental profession is that many patients infected with venereal diseases have oral manifestations. Unfortunately very few dentists and physicians have the proper experience to diagnose syphilis or other STDs from oral lesions. A person with an STD is also at a high risk of HIV infection. In addition the increased susceptibility to HIV infection, persons coinfected with HIV and a STD are theoretically more likely to transmit HIV to others. One reason for that is an increase in vaginal and urethral discharge that occurs in many patients with STDs. These discharges contain large numbers of HIV-infected T-cells, which may make transmission of HIV easier. In this study, we report on 4 patients with secondary syphilis-related oral lesions, including 1 coinfected with HIV.

CASE REPORTS

Case 1

A 58-year-old married man complained of a 4-week history of ulceration of the lower labial mucosa on the left buccal mucosa. The ulcers persisted despite treatment by other otorhinolaryngologists and dentists. He developed a maculopapular skin rash close to the external genitals at the same time. There was no other relevant medical history.

Oral examination revealed moist ulcers on the

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lower labial mucosa, irregular serpiginous linear erosions and ulcers with a 'snail-track' appearance along the left buccal mucosa, and an erythematous patch on the left border of the tongue (Figs. 1, 2). The lesions showed numerous small nodules below the surface of the ulcers on palpation. He had cervical lymph node enlargement on the left side and was afebrile. The histological study revealed ulcers with superficial, bandlike, deeply perivascular, diffuse, dense inflammatory infiltrate composed mainly of plasma cells (Fig. 3A, B). This aroused suspicion of syphilis, and the serological tests showed a positive venereal disease research laboratory test (VDRL) (1:256) and Treponema pallidum hemagglutination test (TPHA) (1:5120). This was consistent with a diagnosis of secondary syphilis. The patient was referred to the Division of Infectious Diseases, and his wife also received penicillin treatment. Because of the social stigma in dealing with venereal diseases and poor patient compliance, he defaulted from follow-up after initial treatment.

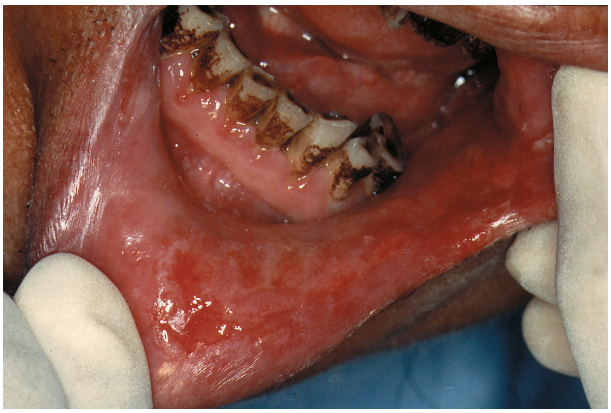

Fig. 1 Moist ulcers on the lower labial mucosa and irregular linear erosions with a 'snail-track' appearance extending to the left buccal mucosa.

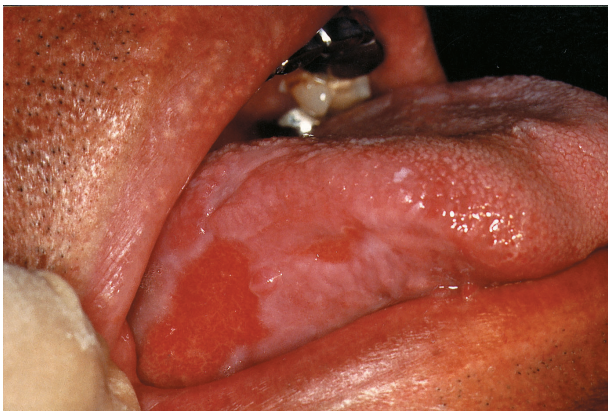

Fig. 2 Erythematous patch on the right border of the tongue.

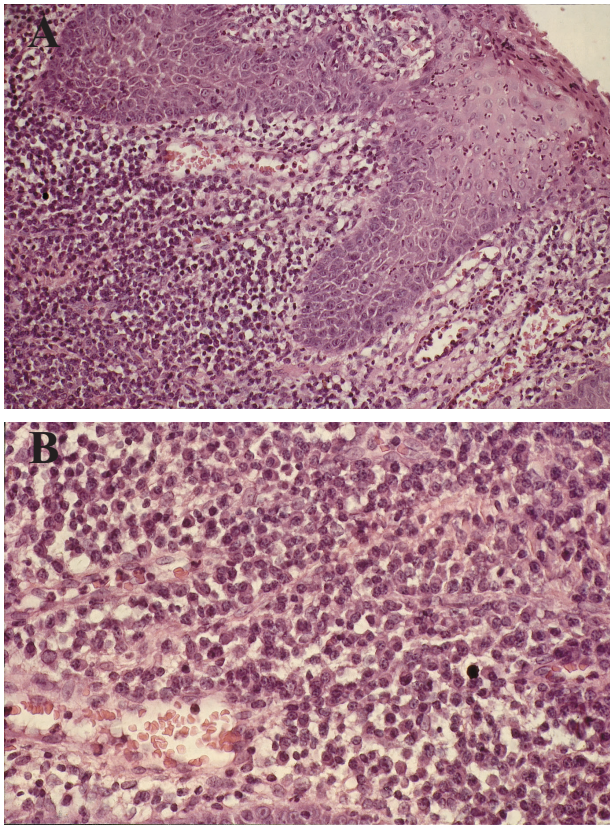

Fig. 3 Epithelial hyperplasia with surface erosion and dense superficial inflammatory cell infiltration comprised predominantly of plasma cells. (H & E stain; A, 100¡ ; B, 400¡).

Case 2

A 30-year-old unmarried man complained of a 1-year history of recurrent erythematous mucous patches on the left buccal mucosa and received many treatments without permanent relief. He denied any systemic diseases. Both palms showed a deep-red skin rash. He served as a bartender in a pub and had once experienced unprotected sexual intercourse.

An oral biopsy was done with dense subepithelial inflammatory cell infiltration comprised predominantly of plasma cells. Serological tests of syphilis

(STS) were positive by VDRL (1:64) and TPHA (1:640). A secondary syphilis-related oral lesion was diagnosed. He was referred to the Division of Infectious Diseases. The oral lesion and skin rash resolved 2 months later after weekly injections of 2.4 ¡ 10^6 units of Benzathine penicillin G (BZN-PCN) for a total of 3 doses.

Case 3

A 38-year-old married woman complained of recurrent sore throat and erythematous patches on the palate for several months. She suffered from syphilis and had received an initial treatment of 3 doses of 2.4 ¡ 10^6 units BZN-PCN by intramuscular injection 8 months previous. Another 2 courses of 3-week oral erythromycin (250 mg 4 times daily) were given 4 and 6 months later due to relapse of clinical symptoms and increased VDRL titer.

The STS showed positive VDRL (1:32) and TPHA (1:640) at that point. She was referred to the Division of Infectious Diseases to restart the entire 3-week course of BZN-PCN injections. The oral lesions and sore throat resolved, with the VDRL declining to 1:4 after 1 month.

Case 4

A 35-year-old man complained of a 5-month history of recurrent oral ulcers and intermittent fever and diarrhea. Oral findings showed irregular erythematous patches on the palate and left buccal mucosa, linear erosion on the right buccal mucosa with superinfection by miliary candidiasis, and heavy thrush on the dorsal surface of the tongue. Herpes zoster on the left thigh had been noted for several days.

He denied any previous systemic diseases. He had visited Chang Gung Memorial Hospital due to pneumonia 7 months previous, when atypical pneumonia was diagnosed. At that time, clarithromycin was given, and his fever had subsided for several weeks. But the fever recurred afterwards, and oral ulcers and thrush bothered him very much during that period. He usually went to local clinics for help, and a common cold was diagnosed. Then he was referred to the Department of Oral Medicine of Chang Gung Memorial Hospital. STDs were highly suspected. He used to live in Japan and had had unprotected sexual exposure with many prostitutes there. The laboratory tests were positive for HIV, VDRL (1:8), and TPHA (1:160). Blood tests showed mild anemia, mild leukopenia, low CD4 counts of 59 cells/mm^3, and a very low CD4/CD8 ratio of 0.08. A diagnosis of AIDS with syphilis was made. He was referred to the Division of Infectious Diseases for antiretroviral therapy and BZN-PCN injection. We recommended that his wife and previous sexual partners be screened for possible HIV and syphilis infection.

After treatment, the oral lesions resolved, but oral candidiasis recurred whenever the antifungal therapy was discontinued. He is now hospitalized for further management.

DISCUSSION

The 4 cases illustrate the need for vigilance with suspected STDs in the differential diagnosis of oral ulceration. It is also important to exclude the possibility of more than 1 STD presenting at the same time. Other STDs often have a much shorter period between infection and symptoms than HIV, and they can serve as a marker for those more vulnerable to HIV infection. Coinfection with HIV will complicate the oral features of syphilis or other STDs and make a diagnosis more difficult.[1-3] Oral health providers should have an understanding of the natural history, oral manifestations, and management of syphilis and HIV infection.

After initial exposure to infection with Treponema pallidum, the primary chancre develops at the site of entry after an incubation period of about 3 to 4 weeks. The chancre is a round or oval ulcer with an indurated base which spontaneously heals 1 to 5 weeks after appearing. Secondary syphilis-related oral lesions usually manifest 6 to 8 weeks after disappearance of the primary chancre and are often accompanied by systemic symptoms and signs including fever, sore throat, anorexia, headache, generalized lymphadenopathy, and a maculopapular skin rash. It can be recurrent during a period of 8 weeks to 3 years after initial infection if treatment is not sufficient. Then it becomes latent and enters the tertiary syphilis or neurosyphilis stage. The oral features of secondary syphilis can be painless or painful erythematous lesions, grayish-white mucous patches, or irregular linear erosions termed 'snail-track' ulcers.[4-7] They are often confused with aphthous ulcers, infectious diseases, or nonspecific erosions and ulcers. Secondary syphilis-related oral lesions

are highly contagious. It is wise for clinicians to wear protective rubber gloves while examining patients presenting with undiagnosed oral lesions in order to avoid not only syphilis, but also other infections including AIDS. The common oral features of HIV infection are oral candidiasis, hairy leukoplakia, HIV-associated gingivitis/periodontitis, and Kaposi's sarcoma. In this report, case 4 presented with recurrent erosion on the bilateral buccal mucosa and erythematous patches on the palatal mucosa, which were superinfected with Candida, leading to a diagnosis of coinfection of HIV.

A diagnosis of syphilis, at whatever stage of the disease, might not be easy because it is a great mimic clinically and histologically. Alessi et al. reported that there was an excellent correlation among histologic findings, clinical appearance, and duration of syphilis in their 33 cases.[8] In the early stage, plasma cells were absent, and there was only sparse superficial infiltrate; but as the disease progressed, dense superficial and deep infiltrate with abundant plasma cells became predominant.[9] The pathological findings of the 2 patients in that study illustrated the importance of oral biopsy in the diagnosis of secondary syphilis.

STS are absolutely necessary to establish a diagnosis of syphilis at any clinical stage. But a diagnosis of syphilis cannot be made on the basis of only 1 set of STS alone. Which of these tests appears positive depends on the clinical stage of syphilis. The STS are either non-specific (nontreponemal test) or specific (treponemal test). Commonly used for nonspecific tests is VDRL and the Rapid Plasma Reagin (RPR) test. The specific tests include TPHA and the fluorescent treponemal antibody absorption (FTA-ABS) test. The best combination of tests for screening of syphilis is VDRL/RPR plus TPHA or VDRL/RPR plus TPHA and FTA-ABS once per month for at least 4 months, because 35% latent syphilis shows a negative VDRL test, and primary syphilis often is seronegative except FTA-ABS.[10-13] A rising titer of VDRL or RPR may be indicative of a recently acquired infection, a reinfection, a relapse in sero-fast individuals, or late syphilis. The findings of a clinically suspicious lesion and a reactive nontreponemal test are sufficiently specific for syphilis that a routine confirmation test is not necessary. Following therapy, the VDRL or RPR titer tends to become negative and is useful for monitoring treatment. However, unlike the VDRL test, the specific tests often stay positive for life in spite of adequate treatment and cannot be used to monitor response to treatment. This condition is called a serological scar. Therefore, a definite diagnosis of syphilis will depend on correlating all the historical, clinical, and STS results and histological findings if possible. In this study, the variable values of VDRL and TPHA accompanied by different degrees of clinical symptoms in these 4 patients were compatible with a diagnosis of secondary syphilis.

The category "early syphilis" includes primary, secondary, and latent syphilis of less than 1-year's duration.[14] Treatment failure in early syphilis is defined as failure of the nontreponemal test to decline 4-fold (equivalent to 2 dilutions; for example, from 1:16 to 1:4, or from 1:64 to 1:16) within 6 to 12 months after treatment, or a 4-fold increase in titer at any time; a patient with this situation should undergo serologic follow-up at 6, 12, 18, and 24 months after completion of treatment. Many retrospective studies on the results of treatment with BZN-PCN in patients with primary or secondary syphilis cited a failure rate of 5.0%.[15-17] HIV-infected persons with early syphilis should receive the same therapy as an HIV-seronegative individual.[18-20] A stable or rising titer during the observation period may suggest inadequate therapy, reinfection, or a false-positive serology. However, patients treated for latent or late syphilis may be sero-fast, so that failure to observe a titer fall in these patients does not indicate a need for retreatment except when clinical symptoms recur, as with patient 3 in this study.

Syphilis is well known for its diversity of clinical manifestations. For this reason oral syphilis needs to be considered and investigated in any patient who presents with what might at first look like a common clinical problem, such as a nonspecific oral ulceration or rash. Furthermore, it is emphasized that coinfection with HIV is not uncommon in patients with other STDs.

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與二期梅毒相關口腔潰瘍的診斷與治療：四例報告

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近年來國人感染性病人數倍增，加上梅毒、淋病與愛滋病等都會出現口腔症狀，對牙醫師是一很大的挑戰，但很少牙醫師與其他科別的醫師有從口腔特徵診斷性病的能力。本文報告4例病人因口腔潰瘍而診斷梅毒，其中一例因合併感染口腔念珠菌而診斷出愛滋病。梅毒的口腔病變常位於唇、舌、頰黏膜或上顎黏膜，原發性梅毒的口腔表徵爲一淺表性潰瘍，上覆蓋以一層灰白色膜，常因口腔細菌之繼發感染而表現急性炎症反應，腫脹顯著之後成褐色結痂外觀，不治療也會在2至4週內自行癒合，此時會讓病人誤以爲病已痊癒。實際狀況卻是在原發病變6至8週後產生第二期梅毒症狀，梅毒螺旋菌侵入血行蔓延全身侵犯任何組織器官，以皮膚出疹及粘膜病變爲特徵，口腔病變呈不規則形狀或橢圓形淺潰瘍，灰白或紅色粘膜斑，潰瘍表面發亮如snail-track ulcers，內含大量的梅毒螺旋菌傳染力很高，可持續數月至3年之間反覆發作。鏡檢之下可看到潰瘍表皮下數量不等的形質細胞浸潤，因爲梅毒臨床表現與病理特徵多變，不論梅毒的那一個階段，建立診斷並不容易。本文特別討論梅毒的口腔表徵、診斷與治療，並提醒多種性病出現口腔潰瘍的可能，包括應合理懷疑病人可能是愛滋病的高危險群，應提高診斷的警覺性。(長庚醫誌 2002;25:683-8)

關鍵字：性病，梅毒，口腔潰瘍，愛滋病。

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