Int J Clin Exp Med 2017;10(9):13916-13919
www.ijcem.com /ISSN:1940-5901/IJCEM0059814

Case Report

Primary syphilis of the tonsil: a case report and literature review

Cheng-Han Yang[1], Ting-Yi Su[2], Kai-Ping Chang[3], Li-Yu Lee[1]

Departments of [1]Pathology, [2]Internal Medicine (Division of Infectious Diseases), [3]Otolaryngology, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kwei San, Taoyuan, Taiwan

Received April 15, 2017; Accepted August 31, 2017; Epub September 15, 2017; Published September 30, 2017

Abstract: We report here a case of a 30-year-old man with primary syphilis of the tonsil diagnosed by light microscopy; he presented with a tonsillar ulcer and pain on swallowing. As a new case report of primary tonsillar syphilis, the pathological diagnosis was challenging due to insufficient clinical information. We here describe the detailed microscopic findings and compare the differences with the 12 previously reported cases.

Keywords: Sexually transmitted disease, syphilis, tonsil, *Treponema pallidum*

Introduction

Syphilis is a chronic infectious disease caused by *Treponema pallidum*, a bacterium from the order Spirochaetales. The transmission of *T. pallidum* usually occurs via sexual behaviors. Syphilis infection can also be acquired by passage through the placenta or, rarely, by blood transfusion. A diagnosis of syphilis can be made by demonstration of *T. pallidum* in clinical specimens by dark field microscopy, polymerase chain reaction (PCR), or equivalent direct molecular methods.

The natural history of untreated syphilis includes primary, secondary, early latent, late latent and late syphilis. Primary syphilis is usually manifested by a chancre at the site of inoculation. A classic chancre is a painless ulcer with a raised and indurated margin. Primary syphilis usually appears on the genitalia, but may present on other sites, such as the anus or oral cavity. The lips are the most common site of primary syphilis of the oral cavity, followed by the tongue and then the tonsillar area [1].

To the best of our knowledge, there have been 12 cases of tonsillar primary syphilis published in the English-language literature [1-8]. Most of them had sufficient clinical information prior to the diagnostic tests, and detailed pathological information was not provided. In only one case, the patient was thought to have a tonsillar tumor, and the diagnosis was based on the excised tonsillar tissue [6]. We describe here an additional case with challenging pathological diagnosis due to a lack of clinical information.

Case report

A 30-year-old male came to the otorhinolaryngology clinic at our center with the chief complaint of a sore throat for one week. He also complained of pain on swallowing. He had no fever, dysphagia, or recent weight loss. His past medical history was negative for immunodeficiency or malignancy and was otherwise unremarkable.

On examination, his right tonsil showed grade IV swelling with an ulcerative surface. Enlarged lymph nodes at right neck levels II and IV were also noted. The results of a complete blood count test were all within normal limits. Then, a biopsy of the right tonsil was performed.

Microscopically, the tonsillar tissue showed an ulcerated stratified squamous epithelium with fibrinopurulent exudates and reactive keratinocytic atypia. The underlying connective tissue and lymphoid nodules showed heavy infiltrations of plasma cells, as well as lymphocytes and histocytes (**Figure 1**). Perivascular plasma-lymphocytic infiltrations and endarteritis were

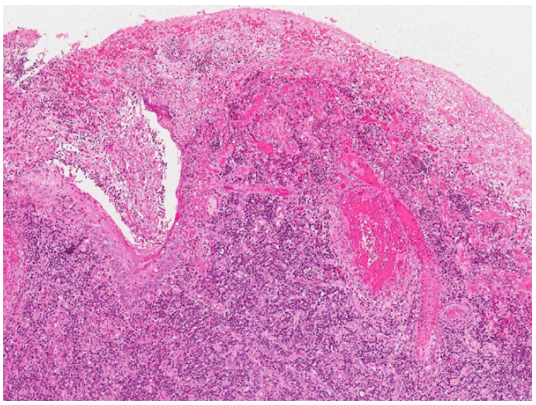

Figure 1. Heavy infiltrations of plasma cells in the squamous mucosa and submucosa of the biopsy specimen. Original magnification 50x, hematoxylin and eosin.

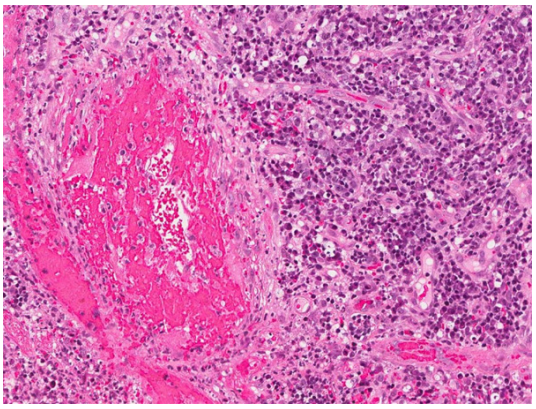

Figure 2. Perivascular plasmalymphocytic infiltrations and endarteritis. Original magnification 200x, hematoxylin and eosin.

also seen (**Figure 2**). Immunohistochemically, there was no light chain restriction by kappa and lambda immunostains; thus, plasma cell neoplasms and lymphoma were excluded. The plasma cells were diffusely positive for IgG, but only focally positive for IgG4, so IgG4-related sclerosing disease was excluded. Periodic acid-Schiff (PAS) stain and acid-fast stains were also performed, which showed no fungal or mycobacterial infection. Finally, numerous *Treponema pallidum* were detected by use of anti-*T. pallidum* antibody in the squamous epithelium, submucosa, and vessel walls (**Figure 3**).

After a pathologic diagnosis of primary syphilis was made, serologic tests were performed. The Rapid Plasma Reagin (RPR) test was reactive at 1:128, and the *Treponema Pallidum* Particle Agglutination (TPPA) test also showed reactivity

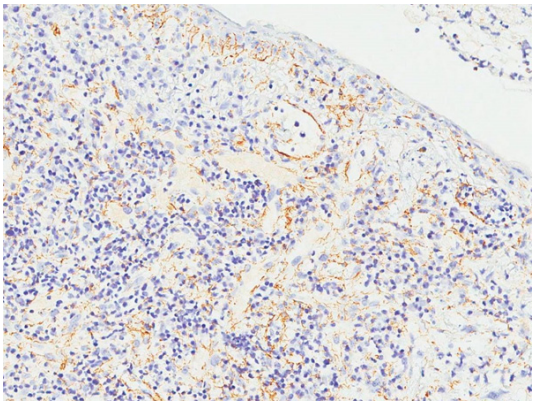

Figure 3. *Treponema pallidum* detected in the squamous epithelium, submucosa, and vessel walls. Original magnification 200x, immunohistochemical stain.

in a dilution of > 1:1280. The patient had no other ulcers on the oral mucosa, genitalia, or anus. As a result, a diagnosis of primary syphilis was confirmed. However, further history taking failed to obtain the patient's previous sexual contact history. The patient was then treated with a single dose of benzathine penicillin G (2.4 million units IM). Three months later, the follow-up RPR test result was 1:64, which then reduced to 1:2 six months after treatment. Thereafter, the patient was lost to follow-up.

Discussion

Since the successful usage of Penicillin in treating syphilis in 1940s, its incidence has obviously decreased in developed countries. However, syphilis remains one of the most common sexually transmitted diseases worldwide. In 2013, the rate of reported primary and secondary syphilis in the United States was 5.3 cases per 100,000 population, more than double the lowest-ever rate of 2.1 in 2000 [9]. The increases have occurred primarily among men and particularly among men who have sex with men (MSM). The increasing incidence of syphilis among MSM is due in part to risky sexual behaviors, such as anonymous sex, unprotected sex (oral and anal), sex with multiple partners, and/or sex under the influence of drugs. In Taiwan, there were 5915 cases of reported syphilis in 2012, compared with 4158 cases in 2001. The incidence of syphilis in men was higher than in women every year; the men-to-women ratio increased from 1.4 in 2001 to 3.5 in 2012.

Table 1. The 12 previously reported cases of tonsillar primary syphilis

Case/Reference	Age/Sex	Sexual orientation	Contact history	Diagnostic test
1. Vincenti [2]	17/M	N/A	Oral sex	W. R. and Kahn tests
2. Fiumara et al. [3]	24/M	Homosexual	With a friend with secondary syphilis	RPR and FTA-ABS tests
3. Fiumara et al. [3]	28/M	Homosexual	With a secondary syphilis patient	N/A
4. Viers [1]	22/F	N/A	Oral sex	Dark field microscopy
5. Viers [1]	20/F	N/A	Oral sex	Dark field microscopy
6. Viers1	19/F	N/A	Oral sex	Dark field microscopy
7. Viers [1]	18/F	N/A	Oral sex	Dark field microscopy
8. Fiumara et al. [4]	40/M	Homosexual	Sexual contact with 4 people in the previous 3 months	RPR-CT test
9. Ishimaru et al. [5]	43/M	Heterosexual	Oral sex	RPR and TPHA tests
10. Oddó et al. [6]	49/M	N/A	N/A	Light microscopy and Warthin-Starry stain
11. Barbee et al. [7]	34/M	Homosexual	Oral sex	RPR test
12. Lobato-Berezo et al. [8]	24/F	Heterosexual	Oral sex	RPR and TPHA tests
13. Present case	30/M	N/A	N/A	Light microscopy and IHC stain using anti-*T. pallidum* antibody

F: female; FTA-ABS test: fluorescent treponemal antibody absorption test; IHC: immunohistochemistry; M: male; N/A: not available; RPR-CT: rapid plasma reagin circle card test; RPR test: rapid plasma reagin test; TPHA test: *Treponema pallidum* hemagglutination test; W.R.: Wassermann reaction.

Primary syphilis is characterized by a chancre at the site of inoculation, which is typically a painless ulcer with a raised and indurated margin. It usually appears on the genitalia. However, extra-genital lesions have become more common, especially oral manifestations. This may be due in part to the increasing popularity of oral sex in recent years. The lips are the most common site of primary syphilis of the oral cavity, followed by the tongue and then the tonsillar or palatal area. In the 12 previously reported cases of primary syphilis of the tonsil [1-8], 10 presented with a tonsillar ulcer, one with an ulcerated tonsillar tumor [6], and one with an enlarged tonsil [7]. In cases whose specific contact history was obtained, all had had previous oral sexual contact (n = 8). Sexual orientation was noted in six previously reported cases; four were homosexual and two were heterosexual (**Table 1**). As a result, an ulcerated tonsil or an enlarged tonsil with or without regional lymphadenopathy may be the typical presentation of tonsillar primary syphilis. Patients may complain of a sore throat and painful swallowing. Then, detailed history taking, including recent sexual contact, is needed for further differential diagnosis, especially in sexually active individuals.

Among the 12 cases, 10 were diagnosed clinically after thorough history taking and sufficient information was obtained. In the case reported by Barbee et al. [7], the diagnosis was not established initially until the patient developed the signs and symptoms of secondary syphilis (i.e. a diffuse maculopapular rash on the trunk, arms, and legs, with a solitary scaly lesion on the left palm). In our case, because there was limited clinical information and dark field microscopy is not available in our institute, the diagnosis of syphilis by light microscopy was challenging. The final diagnosis was made via an immunohistochemical stain of *Treponema pallidum* polyclonal antibody. The subsequent serologic tests also confirmed the diagnosis. The case reported by Barbee et al. [7] and our case once again underscore the importance of taking a thorough sexual history.

The microscopic features of our case include heavy plasma cell infiltration in a diffuse and perivascular pattern and endarteritis, which are in part compatible with the reported features of syphilis. However, several diseases should also be considered based on these findings, including infections caused by other

organisms, IgG4-related sclerosing disease, and plasma cell neoplasms. In the study of A. W. Barrett et al., the microscopic features of primary oral syphilis included unusual epithelial hyperplasia, infiltrates of plasma cells in a diffuse and/or perivascular pattern extending into and disrupting submucosal structures, endarteritis, and neuritis [10]. Each of the features is not specific to syphilis. As a result, it is suggested that the combination of microscopic features as well as clinical information be considered together and then serologic tests are performed for definitive diagnosis. Additionally, an accurate and timely diagnosis not only helps patients to receive proper treatment, but also improves public health.

In summary, we present a case of tonsillar primary syphilis with initial presentation of a tonsillar ulcer with pain on swallowing. Pathological diagnosis would be challenging without sufficient clinical information, because the microscopic features of primary syphilis are not specific. A tentative diagnosis of syphilis can be made through the combination of clinical information and microscopic findings, followed by serologic tests for confirmation.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Li-Yu Lee, Department of Pathology, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, 5 Fu Hsin Street, Kwei San, Taoyuan, Taiwan. Tel: +886-3-328-1200, Ext. 2722; Fax: +886-3-328-014; E-mail: r22068@cgmh.org.tw

References

[1] Viers WA. Primary syphilis of the tonsil: presentation of four cases. Laryngoscope 1981; 91: 1507-11.

[2] Vincenti NH. A case of sero-positive primary syphilis of the tonsil. J Laryngol Otol 1971; 85: 869-70.

[3] Fiumara NJ and Berg M. Primary syphilis in the oral cavity. Br J Vener Dis 1974; 50: 463-4.

[4] Fiumara NJ and Walker EA. Primary syphilis of the tonsil. Arch Otolaryngol 1982; 108: 43-4.

[5] Ishimaru T, Mizuno Y, Shiga H, Nagayama I and Furukawa M. Patient with primary tonsillar and gastric syphilis. J Laryngol Otol 1997; 111: 766-8.

[6] Oddó D, Carrasco G, Capdeville F and Ayala MF. Syphilitic tonsillitis presenting as an ulcerated tonsillar tumor with ipsilateral lymphadenopathy. Ann Diagn Pathol 2007; 11: 353-7.

[7] Barbee LA, Centor RM, Goldberger ZD, Saint S and Dhanireddy S. Clinical problem-solving. A history lesson. N Engl J Med 2015; 372: 1360-4.

[8] Lobato-Berezo A, Imbernon-Moya A, Martinez-Perez M, Churruca-Grijelmo M, Vargas-Laguna ME, Fernandez-Cogolludo E, Aguilar-Martinez A and Gallego-Valdes MA. Tonsillar chancre as unusual manifestation of primary syphilis. Dermatol Online J 2015; 21.

[9] Patton ME, Su JR, Nelson R, Weinstock H and Centers for Disease Control and Prevention (CDC). Primary and secondary syphilis--United States, 2005–2013. MMWR Morb Mortal Wkly Rep 2014; 63: 402-6.

[10] Barrett AW, Villarroel Dorrego M, Hodgson TA, Porter SR, Hopper C, Argiriadou AS and Speight PM. The histopathology of syphilis of the oral mucosa. J Oral Pathol Med 2004; 33: 286-91.