



## Syphilis of the oropharynx: Case series of “The Great Masquerader”<sup>☆,☆☆</sup>

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### ABSTRACT

**Objective:** Syphilis is a sexually transmitted infection with various presentations. Although, oropharyngeal manifestations are known to occur, the purpose of this study is to present the first case series in which the lesions were initially mistaken for human-papillomavirus (HPV)-related oropharyngeal squamous cell carcinoma (OPSCC).

**Methods:** A multi-institutional retrospective review.

**Results:** Six cases of oropharyngeal syphilis were initially thought to be secondary to OPSCC due to presentation. Symptoms were vague and exam findings consisted of either a tonsillar or base of tongue mass, or lymphadenopathy. Biopsies were negative for OPSCC. Further workup diagnosed syphilis, with resolution of symptoms and lesions after antibiotic treatment.

**Conclusions:** Head and neck manifestations of syphilis have been reported in the literature. However, this is the first series reporting on oropharyngeal syphilis masquerading as HPV-related OPSCC. Ultimately, otolaryngologists must maintain a high suspicion for syphilis in order to ensure prompt diagnosis and treatment.

## 1. Introduction

Syphilis is a sexually transmitted infection caused by the spirochete *Treponema pallidum*. It has been described as a human pathogen since ancient times [1]. Its incidence has dropped dramatically with the discovery of antibiotics; however, there has been a recent resurgence in the disease [2]. Syphilis has often been described as the great imitator given its myriad of presentations and systemic involvement. Syphilis remains a diagnosis relevant to otolaryngologists, as it is known to present with head and neck manifestations [2,3].

Oropharyngeal manifestations of all three stages of syphilis are known to occur. These range from oropharyngeal manifestations of secondary syphilis to gummas from tertiary syphilis. While syphilis is known to mimic various diseases, there is little in the literature describing oropharyngeal spirochete infections that were initially misdiagnosed as HPV-related oropharyngeal squamous cell carcinoma (OSCC).

Distinguishing syphilis from carcinoma is especially relevant today

given the rising rates of spirochete infection and the current epidemic of HPV-related OPSCC. Here, we present six cases in which *Treponema pallidum* lesions resembled squamous cell carcinoma of the oropharynx. To the best of our knowledge this represents the only case series in the literature of syphilis presenting in the oropharynx in a manner similar to oropharyngeal carcinoma. Ultimately our case series highlights the importance of syphilis in the differential diagnosis for the oropharyngeal mass.

## 2. Methods

Six cases of oropharyngeal syphilis were identified in records of Mount Sinai Beth Israel and Westchester Medical Center. Clinical records for the selected patients were reviewed using the Prism (General Electric Corporation, Boston MA) electronic medical record, and the A2K AllScripts (Allscripts Healthcare Solutions, Chicago IL) system. The records of each identified patient were reviewed for radiologic and pathologic data. Radiology records were reviewed using the GE

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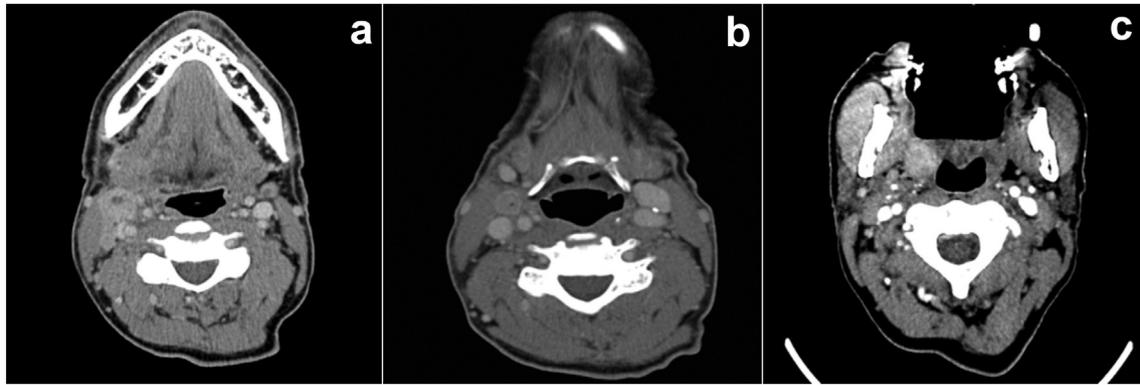
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**Fig. 1.** (a–c). Axial sections of a CT scan of the neck for the patient in case 4 demonstrating multiple bilateral lymph nodes as well as a tonsillar mass involving the lateral soft palate and inferior aspect of the lateral wall of the right nasopharynx.

Centricity Picture Archival and Communications System (General Electric Corporation, Boston MA) by a head and neck radiologist (AK).

Retrospective chart review was done to obtain demographic data, past medical history, physical examination findings, operative reports, and any available follow-up information. As a retrospective review, this study was exempted from review by the Icahn School of Medicine at Mount Sinai Institutional Review Board.

### 3. Results

#### 3.1. Case 1

An otherwise healthy 51-year-old male presented with persistent right sided throat pain for 1 month that was refractory to treatment with antibiotics. HIV status was unknown. Physical exam was significant for a large, firm mass measuring 6–8 cm in diameter in the right tonsillar fossa with a central crater. There was a 2 cm right level IIA lymph node in the neck. The remainder of the head and neck exam, including flexible fiberoptic laryngoscopy examination, was normal. Biopsy of the tonsillar mass was performed twice, both failing to show any evidence of lymphoma or carcinoma within the specimen obtained. Fine needle aspiration of the cervical lymph node was also performed and was non-diagnostic. On subsequent follow up, it was noted that the patient also had macular lesions on his hands. Fluorescent Treponemal Antibody Absorption (FTA-ABS) and a reactive rapid plasma regain (RPR) were obtained and were positive, thus confirming the diagnosis of syphilis. Ultimately, the patient was successfully treated with antibiotics for his disease.

#### 3.2. Case 2

A 35-year-old male presented with several days of left sided throat pain and swelling of the left neck. HIV status was unknown. Social history was significant for being sexually active with a same-sex partner, and a vague history of an unknown sexually transmitted disease as a child without known treatment. Physical examination was positive for a necrotic ulcer in the superior pole of the left tonsil surrounded by extensive white, fibrinous exudate. The left neck had marked matted adenopathy in levels II–III. The remainder of the head and neck exam, including fiberoptic flexible laryngoscopy examination, was normal. Biopsy of the mass was performed. On histopathological analysis, the mass was determined to have acute and chronic inflammation with focal necrosis, compatible with spirochete infection. The patient was treated for syphilis and symptoms and physical examination findings subsequently resolved.

#### 3.3. Case 3

A 41-year-old male presented with a three-month history of foreign body sensation of the throat. The patient denied frank dysphagia, odynophagia or other aero-digestive tract symptoms besides minor reflux-related symptoms. He also complained of left tonsillar irritation during the same time period. The rest of his history was unremarkable. HIV status was unknown. Physical exam revealed an ulcerative lesion in the middle of the left tonsil that was felt to be suspicious for squamous cell carcinoma. Flexible fiberoptic laryngoscopy revealed erythema of the arytenoids bilaterally but was otherwise normal. The remainder of the head and neck examination was normal. Subsequent discussion with the patient revealed that he had been recently diagnosed with syphilis at the time of the visit and had received the first of 3 doses of intramuscular penicillin. The diagnosis of laryngopharyngeal reflux and syphilitic chancre in the left tonsil was then made. Upon follow up in 4 weeks, the patient had received all 3 doses of intramuscular penicillin. At this time, his tonsil and throat symptoms had resolved and the physical examination had normalized.

#### 3.4. Case 4

A 67-year-old male presented with three weeks of a tender right-sided neck mass. The patient also reported an oral lesion that was previously biopsied by another physician six months prior which suggested a diagnosis of papilloma. The rest of the history was unremarkable. His HIV status was unknown. On physical examination, a firm right-sided submucosal mass was palpable within the superior pole of the palatine tonsil. Neck examination revealed a 3 cm firm mass in level IIA of the right neck. The rest of the head and neck exam, including flexible fiberoptic laryngoscopy, was normal. Computed tomography imaging (CT) of the neck with intravenous contrast revealed multiple bilateral lymph nodes as well as symmetrical enhancement of the pharynx occupying the superior half of the right palatine tonsil with questionable mucosal ulceration (Fig. 1). There was also asymmetrical enhancement of the ipsilateral soft palate and the lateral nasopharyngeal wall. Inferiorly the pyriform apex was spared; however, there was potential extension into the central third of the right retro-molar trigone. Laterally, there was enhancement into the parapharyngeal space. There was also noted to be multiple heterogenous appearing lymph nodes in the right neck within levels IIA, IIB, and III. The largest node was 2.5 cm in greatest dimension. Several of these nodes were noted to have surrounding edematous change.

The tonsillar pole mass was biopsied and the neck mass was needle aspirated. The results of the fine needle aspiration showed a reactive lymph node and no evidence of lymphoma or carcinoma. The results of the tonsil biopsy also showed reactive tissue without malignancy. The patient was then evaluated by an infectious disease doctor and found to

be positive to EBV, CMV and syphilis. At two weeks follow up from the initial visit and following initiation of antibiotic treatment for syphilis, the patient's symptoms had markedly improved and physical examination findings had resolved.

### 3.5. Case 5

A 52-year-old male with a past medical history significant for HIV and smoking, presented with a four day history of a sore throat. The pain was worse when speaking and swallowing. There were no voice changes, dyspnea, stridor, or weight loss. Physical examination of the head and neck, including flexible fiberoptic laryngoscopy examination, was normal. The patient was treated with a course of antibiotics, which resulted in resolution of his symptoms. At a 4-month follow up visit, the patient noted new left neck and throat pain. On physical exam, a mass was seen in the left base of tongue. A CT neck with intravenous contrast was then obtained and demonstrated a 15 mm × 15 mm × 10 mm enhancing base of tongue lesion without involvement of the epiglottis, oral tongue, or glossotonsillar sulcus. Bilateral lymphadenopathy was noted, including a necrotic left lymph node in level III ipsilateral to the base of tongue lesion that measured 2.8 × 1.7 × 1.5 cm. Significant right sided lymphadenopathy was also noted that extended from levels II–IV. There was no evidence of extracapsular extension. These findings were felt to be essentially pathognomonic for base of tongue squamous cell carcinoma. Subsequently, the patient was taken to the operating room for a formal direct laryngoscopy and examination under anesthesia. Multiple directed biopsies of the base of tongue mass were negative for carcinoma on both frozen section and permanent analysis. Multiple ultrasound guided fine needle aspirates showed reactive lymphadenopathy with caseating granulomatous lymphadenitis. Flow cytometry was negative for lymphoma. All cultures were also negative. Upon referral to infectious disease, the patient was found to be positive for syphilis and received intramuscular penicillin. He subsequently had complete resolution of both symptoms and physical exam findings on one month follow-up in the office.

### 3.6. Case 6

A 55-year-old male non-smoker with a past medical history of hypertension was referred by his primary care physician due to a one month history of sore throat and tonsillar asymmetry. He was noted to be allergic to penicillin. The patient's symptoms began one month prior to his visit and were precipitated by an upper respiratory infection, which was treated with azithromycin without improvement. A CT neck with intravenous contrast was significant for marked right tonsillar asymmetry and ipsilateral cervical lymphadenopathy. On examination, the right tonsil was enlarged without evidence of a mass, erosion or ulceration. On palpation of the neck, the patient was found to have an enlarged, non-tender right level IIA lymph node. The remainder of his physical examination, including flexible fiberoptic laryngoscopy, was unremarkable. The examination and imaging findings were felt to be highly suspicious for right tonsillar squamous cell carcinoma.

A fine needle aspiration of the right neck lymph node was performed and was nondiagnostic. A repeat biopsy of the tonsil and neck node was then performed, which demonstrated only benign lymphocytes. Given the inconclusive biopsy results, a formal examination under anesthesia with right tonsil biopsy was performed in the operating room. Final surgical pathology with Warthin-Starry and spirochete staining was positive for spirochetes and negative for malignancy (Figs. 2–3). Rapid plasma reagin confirmed the diagnosis of syphilis and the patient underwent penicillin desensitization before treatment with intramuscular penicillin. This ultimately led to complete resolution of his symptoms.

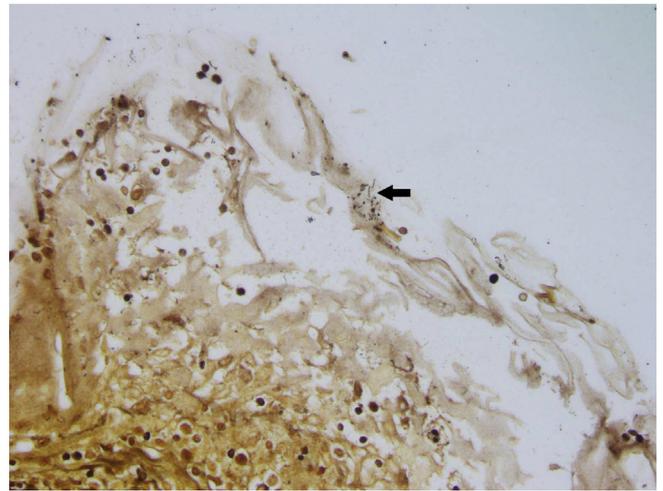


Fig. 2. Warthin-Starry or Silver Stain section of patient in case 6 showing spirochetes (arrow).

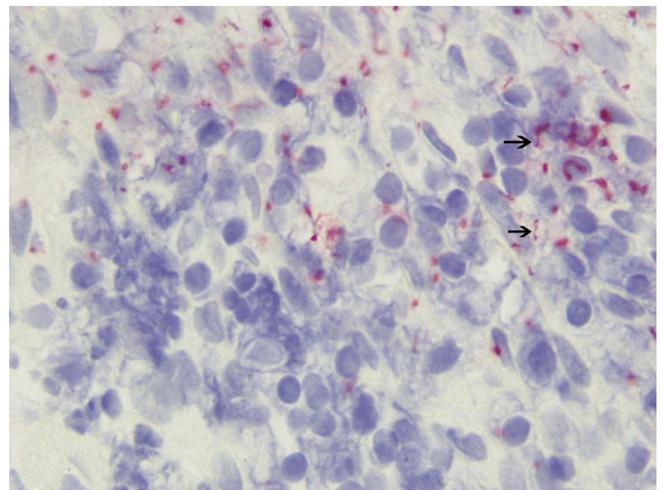


Fig. 3. Spirochete stained section of biopsy from the patient in case 6 with *Treponema pallidum* organisms stained pink (arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

## 4. Discussion

Syphilis is a highly infectious disease caused by the bacterium *Treponema pallidum*. It has been described as a human pathogen for centuries and can manifest in numerous ways [1]. The spirochete infection of syphilis progresses in stages after an initial incubation period, beginning with the chance of primary syphilis and finally tertiary syphilis characterized by systemic signs and symptoms, the hallmark of which are gummata. Following the Second World War, the discovery of penicillin led to a tremendous decrease in the prevalence of the syphilis, making syphilitic infections a rarity by the end of the 20th century [2,4]. However, a re-emergence of this historical disease has been steadily on the rise. This is felt to be due to a variety of factors including changing sexual practices and lack of awareness of the disease. Recent data shows there has been a doubling of the rate of syphilis in the United States since the turn of the 21st century [4]. The diagnosis of syphilis is often delayed due to the non-specific nature of the findings of a spirochete infection. In the head and neck, examination and radiographic findings of syphilis can be highly variable and can present as oropharyngeal masses and necrotic lymphadenopathy [3]. Given the recent surge and awareness of HPV-related OPSCC, these findings can

easily be initially misdiagnosed as carcinoma. Here, we highlight the importance of considering *Treponema pallidum* infections by presenting the largest case series of syphilis mimicking oropharyngeal squamous cell carcinoma in the literature.

Following the genitalia, the most common site for the chancre of primary syphilis is the oral cavity. Lip involvement is the most common, followed by tongue and tonsil in decreasing frequency [5–8]. Secondary syphilis has been shown to manifest in the oral cavity as aphthous or pseudomembranous lesions or leukoplakia [5,6]. Gummata of the hard/soft palate are known head/neck manifestations of tertiary syphilis [9,10]. Our review of the English language literature yielded fewer than 15 reports of oropharyngeal syphilis. The majority of these reports describe unusual cases of tonsillitis. In only 3 of these reports was a malignancy work-up even considered. In a case series by Hamlyn et al. including three patients with syphilitic tonsillitis, only one patient had concurrent cervical lymphadenopathy that was initially felt to be suspicious for lymphoma [11]. Ikenberg et al. reported five patients with syphilis who had cervical lymphadenopathy. Two of these patients also had oropharyngeal lesions that were suspicious for carcinoma [12]. Lastly, Tamura et al. described a patient with oropharyngeal and gastric manifestations of syphilis who was noted to have hypermetabolic lesions on positron emission tomography imaging within the neck and base of tongue [13]. Oropharyngeal carcinoma was initially considered until biopsies confirmed syphilis.

There are several shortcomings to our study. One major limitation to our study is the lack of HIV status on several of the patients. It is known that syphilis and the HIV infection can be synergistic. Patients with syphilis and HIV tend to have more aggressive and atypical presentations of the spirochete infection [14,15]. Unfortunately given the lack of defined HIV status in several of the cases reported, we can make no comment on any role of the AIDS virus on the oropharyngeal course of the spirochete infection. Another weakness of our study is lack of follow-up imaging. While all of the patients presented here noted resolution of their symptoms and all physical exam findings, radiographic evidence of successful treatment could have added to the utility of this report.

Often, the diagnosis of syphilis is delayed due to its unusual presentation and imitation of other conditions. Syphilitic lesions may often be confused for neoplastic or malignant processes. Given the surge in HPV-related OPSCC, unsurprisingly oropharyngeal carcinoma is often much higher on the differential diagnosis than syphilis. However, as the incidence of syphilis has steadily increased over the last decade, it is important to consider the oropharyngeal manifestations of early and late stage spirochete infections. In each of these cases the working diagnosis by the treating otolaryngologist was squamous carcinoma before spirochete infection was confirmed. Ultimately, otolaryngologists must maintain a high index of suspicion for syphilis amongst patients with atypical oropharyngeal findings in order to initiate the appropriate

work-up and treatment.

## 5. Conclusion

Syphilis, an infection caused by the *Treponema pallidum* spirochete, has been referred to as the “great masquerader” or “great imitator” as infection can have systemic signs and symptoms that are often non-specific. Head and neck manifestations can be present in all stages of the infection. Oropharyngeal manifestations of syphilis, such as those presented here, can mimic those of oropharyngeal malignancy. Given the recent resurgence of syphilis, otolaryngologists must maintain a high index of suspicion for *Treponema pallidum* infections when evaluating oropharyngeal masses.

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