

## A RARE CASE REPORT OF SYPHILIS MIMICKING AN OROPHARYNGEAL NEOPLASM

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### ABSTRACT

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**Aim** Syphilis is a widely spread, sexually transmitted disease that is often considered archaic, but it has been on the rise in recent years. The oropharyngeal region is an uncommon location for *treponema pallidum* to present itself. It is even more uncommon when, on a radiological evaluation, it is diagnosed as a neoplasm or squamous cell carcinoma. This case report discusses a rare case of syphilis that mimics an oropharyngeal carcinoma.

**Summary** The patient presented himself initially with cervical lymphadenopathies and an oropharyngeal lesion. On the MRI scan, the lesion was suspicious for an oropharyngeal squamous cell carcinoma. Multiple negative biopsies (2X) urged the search for an alternative diagnosis. After serologic testing, it became clear the patient was suffering from syphilis. Syphilis is known as the “great pretender” and can present in a non-specific manner.

### Key learning points

- i) Syphilis is known as the “great pretender”.
- ii) *Treponema pallidum* infections need to be taken into account as a differential diagnosis in patients with an oropharyngeal lesion.
- iii) Syphilis is on the rise.
- iv) Syphilis has the ability to mimic a malignancy upon clinical presentation.
- v) Syphilis has the ability to mimic a malignancy on CT and MRI-imaging.

### KEYWORDS

Syphilis; Cervical Lymph Node; Oropharyngeal Ulceration; Carcinoma; Mimicking.

### 1. INTRODUCTION

An increasing incidence of syphilis is inherently related to an increasing number of atypical presentations of the disease. Syphilis is on the rise and, with the increase in cases, there has been an increase in different and unusual presentations of the disease.

Since 2010, reports of syphilis incidence rates in the European Union (EU) have been ever increasing. This trend seems to be accelerating, predominantly amongst male homosexuals [1]. Syphilis is a sexually transmitted infection caused by *Treponema pallidum*, a well-known pathogen that can cause pathology in the maxillofacial area. Although there is little



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literature describing oropharyngeal treponema pallidum infections as mimicking an oropharyngeal squamous cell carcinoma (OPSCC), it has been described in rare cases [2]. This case report presents such a case.

Ulcers of the oral cavity and the oropharynx are frequently encountered in maxillofacial practices around the world. Consequently, the differential diagnosis of oral and oropharyngeal ulcers is an important one. A wide range of causes for oral or oropharyngeal ulcers are reported, such as aphthous, traumatic, malignant, tuberculosis, HIV and AIDS (Table 1).

Ulcers can also present associated with skin lesions [3]. Most of these ulcers are promptly diagnosed and treated because the oral or oropharyngeal subsite and the anamnesis are often positive indicators for diagnosis. An important differential diagnostic criterium for traumatic ulcerations is if healing occurs after removal of the probable cause. It is important however to distinguish innocent solitary ulcerations from malignant lesions, such as squamous cell carcinomas. Lesions that persist longer than 3 weeks should be considered as malignant until proven otherwise.

A tuberculous ulcer is rare, almost always secondary to lung tuberculosis and preferably located on the tongue (or lips). It is often not painful and regional lymphadenopathy is usually present. A rare cause of chronic solitary ulcers is syphilitic ulceration. Ulcer usually develops on the lips and, rarely, on the tongue, the pharynx, or the tonsils [4]. In even more rare cases, the ulcer will present itself mimicking a neoplasm in the oropharynx on a clinical and a radiological basis. Hence, it has been named "the great pretender" [5].

## 2. CASE REPORT

A 35-year-old male with no significant medical history was referred to the Cranio-Maxillo-Facial department of the University Hospital of Antwerp, Belgium with swallowing difficulty and minor pain in the throat for the last two months. He suffered from significant fatigue and unexplained weight loss of 10 kg in the previous months. He noticed a swelling of the left oropharynx and multiple bilateral lumps in his neck. There was no history of smoking, oncological disorders, or a familial predisposition to cancer. The patient claimed to have no risk factors for sexually transmitted diseases and no sexual contact for a longer period of time.

Clinical examination revealed an ulcerative mass of 30 mm by 50 mm in size in the left oropharynx (Fig. 1). The ulceration was associated with moderate pain complaints.

The patient had multiple swollen cervical lymph nodes, which were painless. No facial deformities or any neurological abnormalities were noted. The thyroid gland presented normal upon swallowing and was not enlarged. Further intra-oral examination

of the tonsils, mucosa, hard and soft palate, floor of the mouth, dentition, and tongue showed no abnormalities.

## 3. RADIOGRAPHIC EXAMINATION

A multi-slice computerized tomography scan (CT) with iodine contrast revealed an irregular lining on the left of the posterior wall of the oropharynx (Fig. 2). Furthermore, the scan showed a slight retropharyngeal gray area without any collection or fluid build-up.

There were multiple lymphadenopathies in the neck, at levels II to III on the left side and on level II on the right side. In addition, a magnetic resonance imaging (MRI) scan was performed to further investigate this soft tissue lesion. The MRI scan showed an oropharyngeal lesion compatible with an oropharyngeal carcinoma (Fig. 3). There was no extranodal extension in the neck. As an oropharyngeal squamous cell carcinoma was suspected, a diagnostic biopsy was performed.

## 4. PATHOLOGY

Two negative biopsies were taken by an ENT surgeon before referral. Because the clinical presentation was very suggestive for malignancy, a fiberoptic inspection under general anesthesia with biopsies was performed at our center.

The biopsy showed mucosal ulceration and a dense chronic inflammation with mixed lymphoplasmacytic infiltrate. No monoclonal cell population was detectable, and there was no evidence of dysplasia or epithelial malignancy.

## 5. DIAGNOSIS

Although the clinical and radiologic presentation was very suspect for an oropharyngeal carcinoma, multiple negative biopsies ruled out a malignancy. Alternative diagnoses were investigated and a differential diagnosis was made. After performing extensive laboratory tests, the diagnosis of an active syphilis was confirmed.

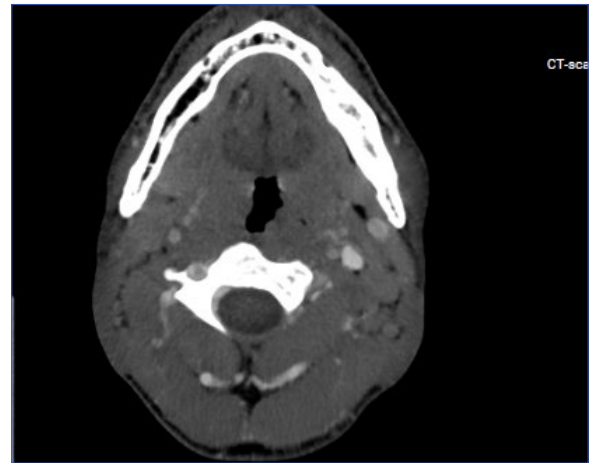
Blood tests showed a positive Treponema pallidum RPR (Rapid Plasma Regain) in combination with highly elevated titers in the Treponema Pallidum particle Hemagglutination Assay (TPHA). The TPHA test is a very sensitive treponemal test (sensitivity >95% and specificity >99%, qualitative mean accuracy, 91.4%; range, 56.1 to 98.2%; quantitative mean accuracy, 75.4; range, 55.5 to 95.5%) [6].

In this case, the TPHA was >20280 which indicated the presence of treponema pallidum. In addition to the TPPA result, a RPR (Rapid Plasma Regain, nontreponemal test) was performed, with a positive result (titer 2).

The results of this nontreponemal test is semiquantitative, reflecting the activity of the



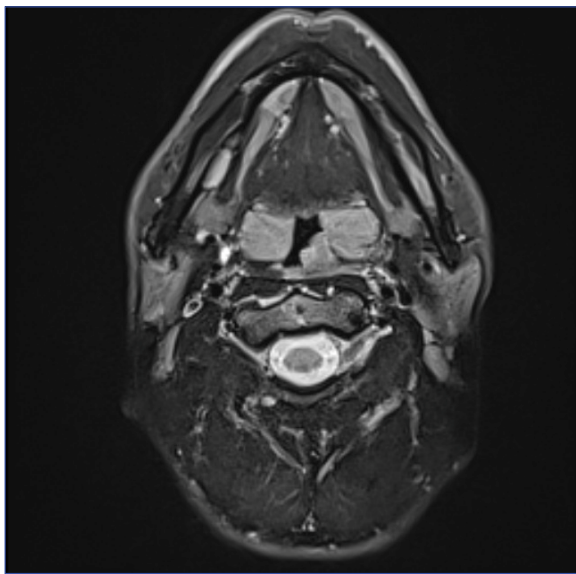
**Figure 1.** Ulcerative lesion seen in the left oropharynx.



**Figure 2.** Axial section of a CT scan of the head and neck showing an irregular posterior wall of the oropharynx.

**Table 1.** Differential diagnosis for oral/oropharyngeal ulcers.

<b>Traumatic</b>	<b>Syphilis</b>
Malignant	Tuberculosis
Iatrogenic (radiotherapy, chemotherapy, antiresorptive medication, etc.)	Recurrent, painful ulcerations (Behçet's disease, chemotherapy, radiotherapy, herpetic, aphthous, etc.)



**Figure 3.** Axial section of an MRI scan of the head and neck showing an oropharyngeal lesion compatible with an oropharyngeal carcinoma.

infection [7]. Given the clinical presentation and serologic testing, the diagnosis of a primary/early secondary active syphilis was made. HIV testing was negative, as was the screening for Chlamydia, Hepatitis B and C, and gonorrhea.

## 6. TREATMENT

The patient was referred to the infectious disease specialist and his general practitioner (GP) for treatment with benzathine penicillin intramuscular (2.4 million IE, one day treatment) [8].

After 3 weeks the patient was seen on consultation, and the lesion and the discomfort had disappeared.

## 7. DISCUSSION

Due to the rising number of cases of syphilis, syphilitic lymphadenitis is an important differential diagnosis for patients presenting with cervical lymphadenopathy and oropharyngeal lesions [9]. Clinicians should be aware that syphilis can also present as a squamous cell carcinoma-like lesion in most oral subsites [10]. In this case, the patient presented with weight loss, fatigue, cervical lymphadenopathies, an oropharyngeal lesion, and an MRI scan that suggested a possible oropharyngeal squamous cell carcinoma. Because multiple biopsies were negative for malignancy, an alternative diagnosis was eventually made.

It has to be mentioned, that there are different techniques to obtain an oropharyngeal biopsy, and a false-negative result may be possible if the technique employed is not optimal. In case of doubt, a new biopsy should be taken and retaken by the same surgeon, taking into account that an incision biopsy at the exact location of the lesion is the most sensitive. We advise against fine-needle aspiration cytology of ulcerative lesions because of its lower sensitivity and specificity, which are respectively 71.4% and 97.8% [11]. Syphilis can evolve into four stages, each with certain characteristics (Table 2). Given the absence of mucous patches or maculopapular lesions, and the local presentation, a working diagnosis of primary syphilis was made [12].

Tamura et al. (2008) described a case similar to the one presented in this report [13]. His patient presented with an oropharyngeal tumor and a cervical lymphadenopathy with the primary lesion being

**Table 2.** Most important characteristics of the four syphilitic stages.

Stages	Timing	Characteristics
Primary	3-4 weeks incubation	Painless chancre at the site of infection
Secondary	4-10 weeks after infection	Rash, systemic symptoms (fever, weight loss, fatigue), headache, mucous membrane lesions throughout body
Latent	Early latent (< 1 year after infection) Late latent (> 1 year after infection)	Asymptomatic, diagnosis through serologic testing
Tertiary	1-10 years after infection	Gummatous lesions, Cardiovascular issues, CNS disorders

strongly suggestive for oropharyngeal cancer. Eventually this case was diagnosed with oropharyngeal syphilis. As a FDG-PET scan was performed as part of a staging procedure, their work-up slightly differed from ours. Since FDG is not specific for malignancy, it will also accumulate in many benign processes such as inflammatory, post-traumatic or benign tumours. Preferably incisional qualitative biopsy should be taken before imaging FDG-PET scan is considered.

## 8. CONCLUSION

*Treponema pallidum* infections need to be taken into account as a differential diagnosis in patients with an oropharyngeal lesion when histopathological results exclude malignancy. Syphilis is known as

the 'great pretender', in their ability to mimic a malignancy upon clinical presentation and on CT and MRI-imaging.

### CONFLICT OF INTEREST

The authors declare that they have no competing interest.

### ACKNOWLEDGMENTS

There are no conflicts of interest and no financial interests to be disclosed.

### AUTHOR CONTRIBUTIONS

SK, CP, HV wrote the manuscript in consultation with WD and GV. All authors provided critical feedback and helped shape the research and the manuscript. SS and MV aided in interpreting the results.

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### CV

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### Questions

#### 1. Syphilis is a sexually transmitted infection caused by

- a. Treponema pallidum;
- b. Actinomyces;
- c. Streptococcus salivarius;
- d. Neisseria gonorrhoeae.

#### 2. Primary syphilis has an incubation time of

- a. 6 months;
- b. 3-4 weeks;
- c. 4-10 weeks;
- d. 1 day.

#### 3. Syphilis has the ability to mimic

- a. Dental caries;
- b. Periodontal disease;
- c. Neuropathic pain;
- d. A malignancy on CT- and MRI-imaging.

#### 4. An oral/oropharyngeal ulcer cannot be one of the following

- a. Syphilis;
- b. Traumatic ulcer;
- c. Malignant;
- d. Hemangioma.