Dysphonia and odynophagia: a presentation of late syphilis

Clinical Case

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Abstract

Syphilis is known to be "the great imitator", as the clinical history is often treacherous and the clinical spectrum of signs and symptoms is extremely extensive, making diagnosis particularly challenging.

We present the case of a 69-year-old man with symptoms of hearing loss, dysphonia and odynophagia for 3 months. Associated with this, he had pruritus with generalized erythema and cutaneous desquamation, changes in visual acuity and nocturnal hypersudoresis. He had a history of smoking and alcoholism and had denied unprotected sexual contact for 10 years.

In the oropharynx, flat, whitish lesions were observed on the soft palate. Laryngoscopy showed alterations, with areas of leukoplakia in both vocal cords, ventricular bands and posterior commissure. The analytical study was compatible with the diagnosis of syphilis. The patient complied with the recommended treatment and presented resolution of the complaints and lesions observed.

Keywords: syphilis; dysphonia; hearing loss; leukoplakia; otosyphilis.

Introduction

Syphilis is a chronic bacterial infection caused by the spirochete *Treponema pallidum*[1]. It develops in several stages: the early stage, which includes primary and secondary syphilis and evolves to an asymptomatic latent stage if untreated; the late stage, which also includes a latent stage; and tertiary syphilis[1].

It is associated with substantial morbidity and mortality[2,3]. It can affect multiple organs and the central nervous system at any stage of the disease[1,4]. In 1928, Alexander Fleming (1881–1955) discovered penicillin, which became the treatment of choice for syphilis from 1943 until today[5]. The number of confirmed cases of syphilis is increasing in Portugal and Europe[6]. In 2019, the mean incidence of syphilis in Europe was 7.4 cases per 100,000 people, while

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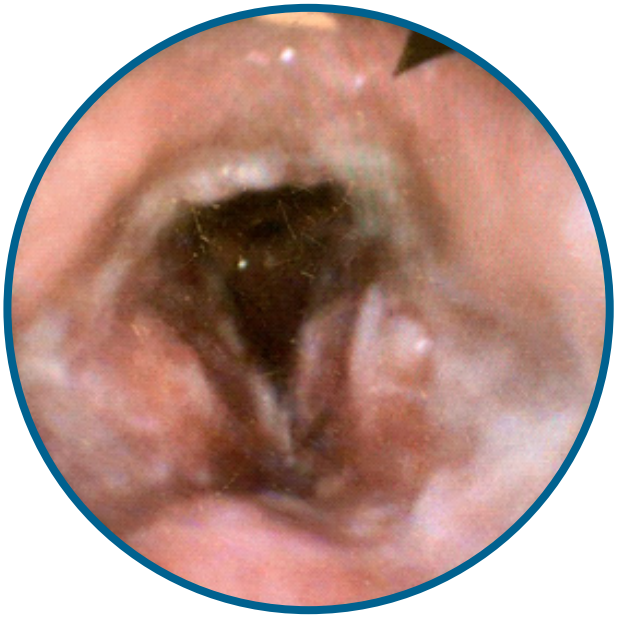
in Portugal it was 4.1 cases per 100,000 people[6]. In Portugal, this number has been increasing since 2015; the total number of cases declared in 2015 was 43, which increased to 419 in 2019[6]. The objective of the present study was not to report on a rare disease but on a disease with an atypical presentation whose incidence has been increasing in recent years, a disease which otorhinolaryngology specialists should always keep in mind.

Case description

We present the case of a 69-year old man who was referred to the otorhinolaryngology (ORL) clinic with a three-month history of hypoacusis, dysphonia, and odynophagia. During this time, he also developed a papulosquamous rash with pruritus, generalized erythema (limbs and trunk), and flaking skin, and was being followed-up by a dermatologist. In addition, he reported a non-productive cough, changes in the visual acuity, and excessive sweating at night. He denied having a fever, dysphagia, dyspnea, tinnitus, vertigo, or other ORL symptoms. The patient had a history of smoking (60 PY) and alcohol consumption. He denied having unprotected sex in the last 10 years. On objective ORL examination, there was bilateral impacted cerumen associated with scaling in the external auditory canals. His hearing improved after the cerumen was removed and the tympanic membranes were normal. Flat and whitish lesions in the soft palate were seen on oropharyngeal examination. The remaining mucosa of the oropharynx and oral cavity was erythematous with no other changes. Flexible nasopharyngolaryngoscopy showed hypertrophy of the nasopharyngeal lymphoid tissue and laryngeal changes, namely areas of leukoplakia in both the vocal cords, ventricular bands, and posterior commissure (Figure 1).

The initial complaint of hypoacusis was associated with obstruction of the auditory canals, exacerbated by the flaking skin. The audiogram obtained after removal of the impacted cerumen and flaked skin revealed a mean tone threshold of 20 dB bilaterally.

Figure 1
Areas of leukoplakia in both the vocal cords, ventricular bands, and posterior commissure

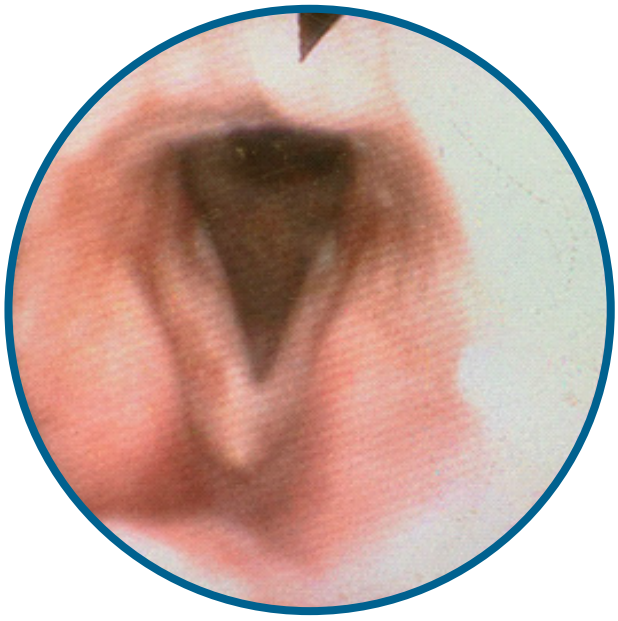


Biopsies of the oro- and nasopharyngeal lesions were performed and the anatomopathology showed reactive hyperplasia of the mucosa-associated lymphoid tissue, without signs of malignancy. Magnetic resonance imaging was compatible with a penetrating ulcer in the thoracic aorta. Laryngeal tuberculosis was ruled out through direct bacilloscopy and culture of a sputum sample. In view of this presentation of extensive symptoms, which included odynophagia, dysphonia, changes in the visual acuity, papulosquamous rash, and cough, as well as constitutional symptoms such as excessive sweating at night, a multisystemic autoimmune or infectious disease was suspected. Laboratory investigations showed positive nontreponemal and treponemal serological tests: venereal disease research laboratory (VDRL) test and *Treponema pallidum* hemagglutination assay (TPHA).

He was assessed by an ophthalmologist and diagnosed with panuveitis. The analysis of the cerebrospinal fluid, collected by a lumbar puncture, yielded a positive TPHA test, although the patient did not exhibit signs or symptoms of involvement of the central nervous system (CNS).

The result of the serological analysis, combined with the presenting signs and symptoms, led to a diagnosis of syphilis. Considering that the disease had progressed over at least ten years, the diagnosis was late syphilis with muco-cutaneous, ocular, cardiovascular, and CNS involvement. On account of the diagnosis of late syphilis with involvement of the CNS, the patient was treated with benzylpenicillin, 24 MU/day for 14 days, following which all his complaints and lesions disappeared (Figure 2). Moreover, the patient was referred to vascular surgery for evaluation and monitoring of the aortitis.

Figure 2
Resolution of the laryngeal lesions after treatment



Discussion

Syphilis is a multisystemic disease that develops in three stages. Typically, primary syphilis is characterized by the presence of a painless lesion at the site of inoculation. Secondary syphilis is classically described as a generalized rash, affecting the palms of the hands and soles of the feet; however, the presentation varies widely[1]. Tertiary syphilis classically manifests as late neurosyphilis, with cardiovascular involvement or the appearance of syphilitic gummas, which are granulomas that can appear in any part of the body[1]. Syphilis with ocular involvement can occur at any stage of the disease[3,7,8]. Despite these classic descriptions, the clinical presentation of syphilis is extremely variable and sometimes there is an overlap between presentations typical of different stages of the disease[9]. Syphilis is known as "the great mimicker," because the patient's clinical history is often misleading and the clinical spectrum of signs and symptoms is very wide with atypical clinical presentations; consequently, diagnosing the disease is especially challenging[4].

The changes observed in the mucosa often lead to biopsy; however, it does not show specific abnormalities unless dark field microscopy or other techniques for direct detection of treponema are used, but these tests are not widely available[10]. Nevertheless, biopsy is valuable for the exclusion of other suspected diseases. In ORL, syphilis manifests as a wide spectrum of symptoms that are described below. It is important to take a detailed clinical history and review the symptoms using devices and systems. It is the overall state of the patient, rather than an isolated ORL symptom, that will raise the suspicion of a multisystemic disease like syphilis. Otosyphilis can occur at any stage of the disease, regardless of other symptoms[3,8,11]. The patients may present with complaints of unilateral or bilateral hypoacusis, tinnitus, imbalance, or vertigo, which are sometimes the only symptoms, and this leads to a low index of suspicion of the disease, delaying its diagnosis by several weeks, years, or even decades[11]. Hypoacusis is usually sensorineural but can also involve the ossicles or middle ear, thereby causing conduction hypoacusis[3]. In such cases, an audiogram can exclude hypoacusis after the auditory canals are cleaned and otosyphilis can be ruled out. Some authors advocate screening for otosyphilis in all newly diagnosed cases of syphilis[3,8].

The involvement of the mucosa may present as a wide variety of lesions that clinically mimic conditions ranging from benign lesions, such as fibrous/epithelial hyperplasia,

hyperkeratosis, autoimmune diseases, and lymphoid hyperplasia or papillomas, to malignant lesions, such as squamous carcinoma or salivary gland carcinoma[12]. In ORL, syphilis should be considered as a differential diagnosis in cases of these types of lesions. Mucocutaneous involvement is described mainly in secondary syphilis[13] but also occurs in primary syphilis, with the appearance of a hard chancre, which is the lesion that occurs at the primary site of inoculation[12].

Hard chancre occurs mainly in the genital region but can also occur in the oral cavity and oropharynx. Approximately 4%–12% of patients with primary syphilis have a hard chancre in the oral mucosa[12,14]. It is typically a single, firm, asymptomatic lesion, although in rare cases it presents with multiple lesions or pain[12,14]. It can affect any part of the oral mucosa, including the lips, tongue, jugal mucosa, palate, gums, and even tonsillar or oropharyngeal pillars.

The involvement of the mucosa in secondary syphilis is extremely variable, and it usually presents with multiple lesions[12]. The mucosal lesions are typically well-defined erythematous or leukoplakic lesions over an erythematous base, with raised and occasionally ulcerated borders[12,13]. Superficial lesions such as mouth ulcers, irregular and serpiginous lesions, and leukoplakic adherent plaques can also be observed[13], as well as condylomas associated with syphilis (condylomata lata), which are raised grayish-white lesions of papillary appearance[12,15] that can easily be confused with condylomata acuminata associated with the human papillomavirus[13].

The sinonasal mucosa may also be affected and exhibit ulcers or septal perforations[16].

The existing laboratory tests for the diagnosis of syphilis include tests for the direct detection of treponema and serological tests[2].

Dark field microscopy is one of the direct detection methods. It requires fast and careful transportation of the sample to the laboratory, as well as specific materials and highly trained specialists. This method allows observation of the shape and motility of the treponema. It is a highly specific diagnostic test, but its sensitivity is only 50%; therefore, a negative test does not exclude the diagnosis[2]. Another method of direct detection is direct immunofluorescence, in which antibodies to treponema are stained with fluorescein to subsequently detect the spirochete using fluorescence microscopy. This method is more sensitive than dark field microscopy, but it also requires equipment and reagents that are not available in most countries[2]. In addition, direct detection can be performed with treponema DNA amplification tests; however, there are no commercial tests available in the market and it is thus very expensive[2].

Serological tests are the most widely available tests and are either treponemal or nontreponemal. They are used in blood samples and sometimes in the CSF for the diagnosis of congenital or tertiary syphilis[2]. The nontreponemal tests are not specific for syphilis and can give rise to false positives. The treponemal tests are highly specific but can remain positive for life in up to 85% of the patients, regardless of the treatment, and, as such, they do not differentiate between active and previously treated disease[2]. Confirmation of a syphilis diagnosis requires positivity in both the serological tests, in addition to the clinical presentation; if only one of the tests is positive, syphilis can only be assumed[2].

In view of the confirmed diagnosis and disease duration of at least ten years, the present case was deemed tertiary syphilis with mucocutaneous, ocular, cardiovascular, and CNS involvement.

The recommended treatment depends on the stage of the disease. In the case of early syphilis (primary, secondary, and first two years of the latent stage), a single intramuscular dose of 2.4 MU of benzathine penicillin is recommended[1,2,17]. For late syphilis (latent stage lasting more than two years or tertiary without involvement of the CSF), the recommended treatment is 2.4 MU of intramuscular benzathine penicillin once a week for three consecutive weeks[1,2,17]. In the special case of neurosyphilis, otosyphilis, or ocular syphilis, the treatment involves higher

doses and consists of 18 MU to 24 MU of penicillin per day, administered for 10 to 14 consecutive days[17].
After treatment, all of the patient's complaints and lesions were resolved.

Conclusion

We have described a case of late syphilis with CNS involvement, probable syphilitic aortitis, and ocular and mucocutaneous involvement. In ORL, this is a diagnosis to consider when there are flat whitish lesions in the oral cavity and oropharynx and as a differential diagnosis of leukoplakia on the vocal cords, even without a recent history of unsafe sexual behavior. It is important to ask the patient about other ORL symptoms and perform a review using devices and systems because this is a multiorgan disease. Furthermore, hearing tests should be performed in all newly diagnosed cases of syphilis. The treatment and follow-up of these patients requires a multidisciplinary team, which in the present case comprised infectious diseases, dermatology, ophthalmology, ORL, and vascular surgery.

Conflicts of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Data Confidentiality

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the 2013 Helsinki Declaration of the World Medical Association.

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Availability of scientific data

There are no datasets available, publicly related to this work.

Bibliographic references

1.Hook EW 3rd. Syphilis. Lancet. 2017 Apr 15;389(10078):1550-1557. doi: 10.1016/S0140-6736(16)32411-4.

2.WHO Guidelines for the Treatment of Treponema pallidum (Syphilis). 2016. [consultado 2021 nov 18] Disponível em: https://www.who.int/publications/i/item/9789241549714

3.Ramchandani MS, Litvack JR, Marra CM. Otosyphilis: a review of the literature. Sex Transm Dis. 2020 May;47(5):296-300. doi: 10.1097/OLQ.0000000000001155.

4.Hanlon CL, Galoosian A, Ali S, Edson RS. Painful rash with hoarseness: an atypical presentation of syphilis. BMJ Case Rep. 2018 Dec 27;11(1):e226892. doi: 10.1136/bcr-2018-226892.

5.Tampa M, Sarbu I, Matei C, Benea V, Georgescu SR. Brief history of syphilis. J Med Lif. 2014 Mar 15;7(1):4-10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3956094/

6.European Centre for Disease Prevention and Control. Syphilis. In: ECDC. Annual epidemiological report for 2019. Stockholm: ECDC; 2022. Disponível em: https://www.ecdc.europa.eu/en/publications-data/syphilis-annual-epidemiological-report-2019

7.Dutta Majumder P, Chen EJ, Shah J, Ching Wen Ho D, Biswas J, See Yin L. et al. Ocular syphilis: an update. Ocul Immunol Inflamm. 2019;27(1):117-125. doi: 10.1080/09273948.2017.1371765.

8.Theeuwen H, Whipple M, Litvack JR. Otosyphilis: resurgence of an old disease. Laryngoscope. 2019 Jul;129(7):1680-1684. doi: 10.1002/lary.27635.

9.Ivars Lleó M, Clavo Escribano P, Menéndez Prieto B. Atypical cutaneous manifestations in syphilis. Actas Dermosifiliogr. 2016 May;107(4):275-83. doi: 10.1016/j.ad.2015.11.002.

10.Satyaputra F, Hendry S, Braddick M, Sivabalan P, Norton R. The laboratory diagnosis of syphilis. J Clin Microbiol. 2021 Sep 20;59(10):e0010021. doi: 10.1128/JCM.00100-21.

11.Witt LS, Wendy Fujita A, Ho J, Shin YM, Kobaidze K, Workowski K. Otosyphilis. Open Forum Infect Dis. 2022 Dec 21;10(2):ofac685. doi: 10.1093/ofid/ofac685

12.Smith MH, Vargo RJ, Bilodeau EA, Anderson KM, Trzcinska A, Canterbury CR. et al. Oral manifestations of syphilis: a review of the clinical and histopathologic characteristics of a reemerging entity with report of 19 new cases. Head Neck Pathol. 2021 Sep;15(3):787-795. doi: 10.1007/s12105-020-01283-4.

13.Cakmak SK, Tamer E, Karadag AS, Waugh M. Syphilis: a great imitator. Clin Dermatol. 2019 May-Jun;37(3):182-191. doi: 10.1016/j.clindermatol.2019.01.007..

14.Ficarra G, Carlos R. Syphilis: the renaissance of an old disease with oral implications. Head Neck Pathol. 2009 Sep;3(3):195-206. doi: 10.1007/s12105-009-0127-0.

15.Carbone PN, Capra GG, Nelson BL. Oral Secondary Syphilis. Head Neck Pathol. 2016 Jun;10(2):206-8. doi: 10.1007/s12105-015-0623-3.

16.Sardana K, Goel K. Nasal septal ulceration. Clin Dermatol. 2014 Nov-Dec;32(6):817-26. doi: 10.1016/j.

clindermatol.2014.02.022.
17.Workowski KA, Bachmann LH, Chan PA, Johnston CM, Muzny CA, Park I. et al. Sexually transmitted infections treatment guidelines, 2021. MMWR Recomm Rep. 2021 Jul 23;70(4):1-187. doi: 10.15585/mmwr.rr7004a1