

Case-report

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Atypical Verrucous Gingival Lesion in a Patient with Syphilis Ultimately Confirmed as Verrucous Carcinoma: A Case Report

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Abstract

Syphilis is a chronic systemic infection with diverse oral manifestations that can mimic inflammatory, potentially malignant, and malignant disease. We present a case of an 80-year-old woman with recently diagnosed late latent syphilis referred for a painful, friable white verrucous lesion of the anterior maxillary gingiva, associated with dental mobility and feeding difficulty. Initial incisional biopsy showed verrucous epithelial hyperplasia with parakeratosis, acanthosis, chronic inflammation, and spirochetes demonstrated by immunohistochemistry for *Treponema pallidum*. Despite intramuscular benzathine penicillin G and an appropriate serological response, the lesion persisted. A repeat biopsy showed atypical keratinizing squamous epithelial proliferation with lichenoid inflammation, raising concern for malignancy. Staging imaging showed localized maxillary gingival disease without suspicious cervical lymphadenopathy or thoracic metastases. Surgical excision with multiple dental extractions and reconstruction was performed. The resection specimen confirmed a 30 mm, well-differentiated verrucous carcinoma with 1 mm depth of invasion, expansile growth, no lymphovascular or perineural invasion, and pathological stage pT2. The sequential findings do not establish syphilis-related malignant transformation; lesion heterogeneity and sampling variability remain plausible. Persistent verrucous oral lesions require deep, representative biopsy, close clinicopathological correlation, and continued surveillance.

Highlights

- Persistent verrucous gingival lesion occurred in an older patient with late latent syphilis.
- Initial histology showed verrucous epithelial hyperplasia with *Treponema pallidum* spirochetes.
- The lesion persisted despite penicillin therapy and an appropriate serological response.
- Sequential biopsies highlight sampling variability and the need for deep, representative tissue assessment.
- Surgical resection confirmed a well-differentiated verrucous carcinoma, pT2.

1. Introduction

Syphilis is a systemic infection caused by the spirochete *Treponema pallidum* (*T. pallidum*) and is conventionally classified into primary, secondary, latent, and tertiary stages. Primary syphilis typically develops at the site of inoculation, whereas secondary syphilis reflects systemic dissemination and is the stage most commonly associated with oral mucosal lesions, including mucous patches, plaques, and ulcers. Latent syphilis is characterized by reactive serological tests in the absence of clinical manifestations, while tertiary disease may include late cardiovascular or gummatous complications.[1–3] Oral manifestations are clinically heterogeneous and may mimic inflammatory, infectious, potentially malignant, and malignant disorders.[1]

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Persistent oral white lesions with a verrucous or ulcerated surface raise concern for an oral potentially malignant disorder or squamous cell carcinoma, particularly in older patients. Verrucous carcinoma is a well-differentiated, low-grade variant of squamous cell carcinoma that may show deceptively bland cytology and considerable clinical and histological overlap with verrucous hyperplasia.[4–6] Chronic inflammation has been implicated in carcinogenesis in other infectious settings;[7, 8] however, there is no established evidence supporting a direct carcinogenic role for *T. pallidum* in the oral cavity. In the present case, the patient had been clinically classified as having late latent syphilis. Subsequent demonstration of spirochetes within the gingival lesion supported local treponemal involvement but did not establish a causal relationship with neoplasia.

This case report describes a persistent verrucous gingival lesion in a patient with serologically confirmed late latent syphilis. The initial biopsy demonstrated spirochetes and verrucous epithelial hyperplasia, whereas complete surgical assessment ultimately confirmed verrucous carcinoma. The aim of this case report is to highlight the clinicopathological overlap between infection and malignancy and the limitations of small incisional biopsies in oral verrucous lesions.

2. Case Report

An 80-year-old woman was referred to the Stomatology consultation in June 2024 for evaluation of a painful, bleeding white gingival lesion associated with progressive dental mobility and difficulty eating. The patient's medical history included an ischemic stroke in March 2024. The patient was partially edentulous, with few remaining teeth. On clinical examination, a white verrucous lesion was noted involving the buccal attached gingiva around tooth 12, extending across the residual alveoli of absent teeth 11 and 21, and continuing, to a lesser extent, along the attached gingiva mesial to tooth 23. Teeth 22 and 23 exhibited grade 3 mobility in all planes. Painful ulcerative lesions were also present on the lower lip and right buccal mucosa. An asymptomatic ulcerated area was observed on the ventral surface of the tongue. No additional white plaques or suspicious lesions were identified in the remaining oral mucosa.

Both teeth were extracted at the initial appointment because of their poor prognosis and the white tissue was curetted and the sockets thoroughly cleaned, revealing persistent verrucous tissue within the residual sockets (Fig. 1).

During the March 2024 hospitalization for ischemic stroke, a Venereal Disease Research Laboratory (VDRL) test was positive at a titre of 1:16. Cerebrospinal fluid analysis excluded neurosyphilis. The patient was diagnosed with late latent syphilis, and treatment with intramuscular benzathine penicillin G was initiated.

An incisional biopsy of the maxillary gingival lesion

was performed. Histopathological examination revealed verrucous epithelial hyperplasia with parakeratosis and acanthosis, accompanied by a chronic inflammatory infiltrate in the lamina propria. Immunohistochemistry for *Treponema pallidum* demonstrated spirochetes, supporting local treponemal involvement. Additional immunohistochemical studies showed a non-increased Ki-67 proliferation index and a wild-type p53 expression pattern (Fig. 2).

Serological follow-up showed a decline in VDRL titres to 1:8 in June and 1:4 in November 2024, consistent with an appropriate response to treatment. Nevertheless, the gingival lesion persisted without clinical regression. A repeat incisional biopsy in April 2025 showed atypical keratinizing squamous epithelial proliferation with nuclear pleomorphism, mitotic activity, and lichenoid interface inflammation. The findings were considered suggestive of malignant transformation but were not definitive in the limited sample (Fig. 3).

Computed tomography (CT) of the maxillofacial region and neck demonstrated a lesion of the left maxillary gingiva in the second quadrant, adjacent to the alveolar arch and involving the incisor-to-canine region. Although the lesion crossed the midline clinically, the radiologically identifiable component was predominantly left-sided. It measured approximately 18 mm in transverse diameter and 5 mm in thickness, with permeative and erosive changes in the adjacent alveolar ridge. No suspicious cervical lymph nodes were identified. Thoracic computed tomography showed no suspicious pulmonary lesions or mediastinal, hilar, or axillary lymphadenopathy.

The case was discussed at a multidisciplinary meeting, and surgical treatment was recommended. The patient was admitted on 8 May 2025 and, on 9 May 2025, underwent surgical excision of the maxillary gingival lesion, multiple dental extractions, and reconstruction of the resulting defect with a dermal matrix under general anesthesia. The procedure and immediate postoperative course were uneventful.

Histopathological examination of the resection specimen confirmed a unifocal, well-differentiated verrucous carcinoma of the maxillary gingiva, centered at the midline. The tumor measured 30 mm in greatest dimension, had a depth of invasion of 1 mm, and showed an expansile growth pattern (Fig. 4). The discrepancy with the 18 mm CT measurement likely reflects differences between radiological and pathological delineation, with CT not fully depicting the superficial extent of the lesion. Ulceration, necrosis, lymphovascular invasion, angioinvasion, and perineural invasion were not identified. The lesion was staged as pT2 according to the eighth edition of the American Joint Committee on Cancer staging system. No lymph nodes were identified. The surgical margins intersected the neoplasm, and the radial and deep planes were described as tangential to it.

After multidisciplinary discussion the patient was submitted to widening of surgical margins. The sample



Figure 1. Clinical appearance at the initial assessment (A) showing a white verrucous lesion on the attached gingiva of the anterior maxilla before tooth extraction. (B) Following tooth extraction and alveolar debridement, showing the underlying persistent verrucous lesion.

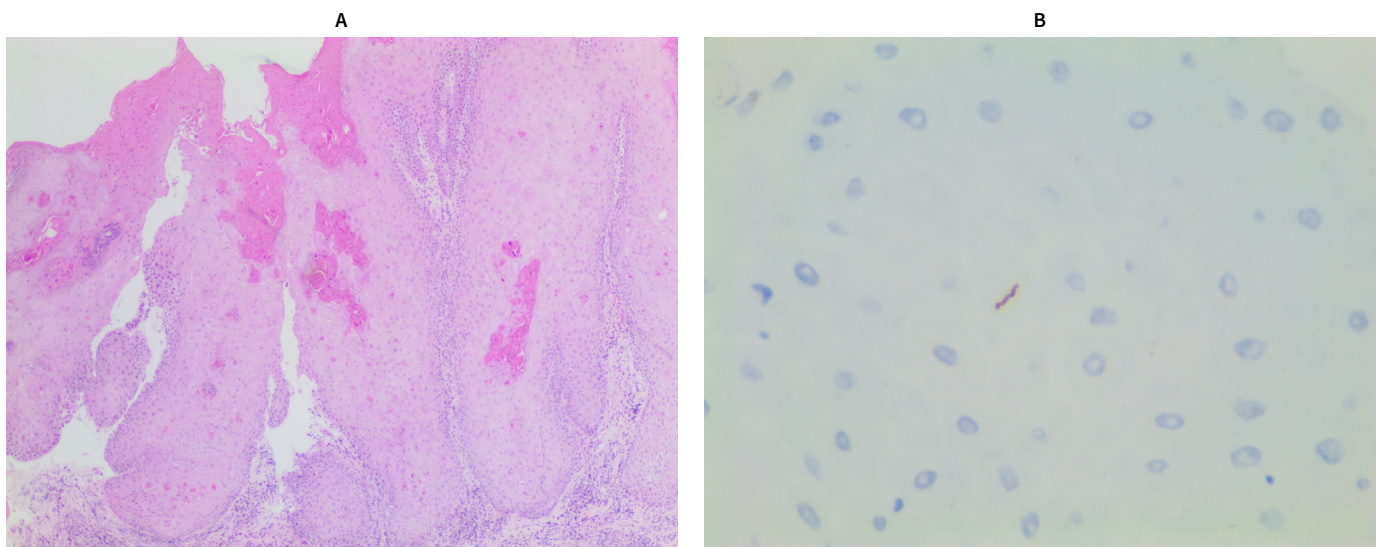


Figure 2. Initial incisional biopsy. (A) Verrucous epithelial hyperplasia with parakeratosis and acanthosis (H&E, original magnification $\times 4$). (B) Immunohistochemistry for *Treponema pallidum* highlighting spirochetes within the tissue (anti-*T. pallidum*, original magnification $\times 40$).

showed high-grade squamous dysplasia with no invasive malignancy identified in these specimens.

The decision of the multidisciplinary team was to keep the patient under surveillance without adjuvant therapy.

At the most recent follow-up in July 2026, approximately 14 months after the initial surgical excision, the patient remained clinically well and pain-free, with post-operative fibrosis, under surveillance and awaiting prosthetic oral rehabilitation.

3. Discussion

Oral syphilis can reproduce a broad spectrum of clinical appearances and may mimic inflammatory, infectious, potentially malignant, and malignant disorders.[1] In this patient, the initial presence of spirochetes within a verrucous hyperplastic lesion, together with positive serology, supported syphilitic involvement. However, persistence of the lesion despite appropriate antimicrobial treatment and a fourfold serological decline required renewed clinicopathological assessment.

The final resection diagnosis resolves the primary ambiguity inherent in the initial report: the lesion was a well-

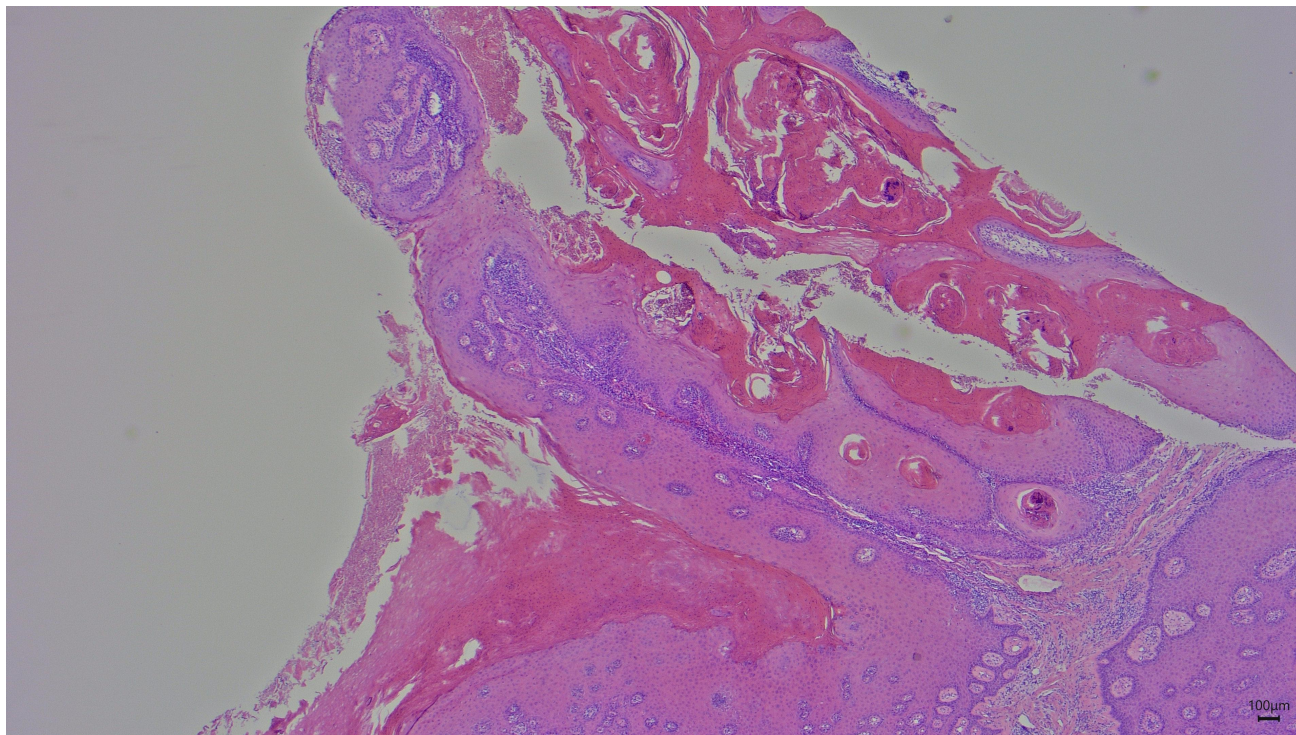


Figure 3. Repeat incisional biopsy demonstrating atypical keratinizing squamous epithelial proliferation with nuclear pleomorphism, mitotic activity, and lichenoid interface inflammation, suggestive of malignant transformation (H&E, original magnification $\times 2.5$).

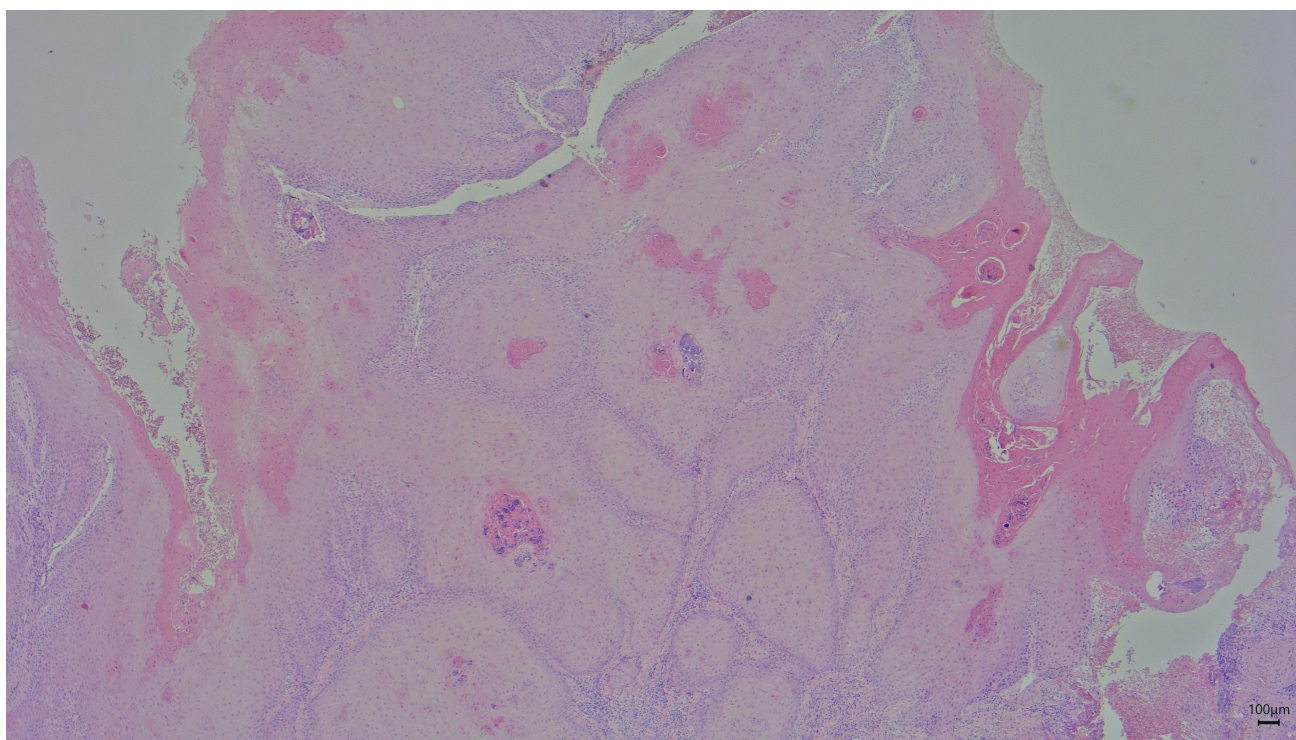


Figure 4. Low-power view of the surgical resection specimen showing well-differentiated verrucous carcinoma with an expansile growth pattern (H&E, original magnification $\times 2.5$).

differentiated verrucous carcinoma. Verrucous carcinoma is characterized by well-differentiated epithelium and a

broad pushing invasive front, which may not be represented in superficial or small incisional samples. Studies

of oral verrucous lesions have demonstrated substantial disagreement between incisional biopsy and resection findings and emphasize the need to sample the epithelial-connective tissue interface adequately.[4–6] Therefore, an initial under-sampled pre-existing carcinoma and lesion heterogeneity are plausible explanations for the different histological findings in this case.

The lichenoid inflammatory pattern in the repeat biopsy further complicated interpretation. Lichenoid inflammation may occur in immune-mediated mucosal disorders but can also accompany epithelial dysplasia and carcinoma.[9] Accordingly, this pattern should be interpreted together with the epithelial architecture, depth of the specimen, clinical morphology, and imaging findings rather than as evidence of a purely inflammatory process.

Although chronic inflammation can contribute to epithelial carcinogenesis in other infectious settings,[7, 8] no direct carcinogenic role of *T. pallidum* in the oral cavity has been established. In the present case, treponemal infection may have coexisted with the neoplasm and increased the inflammatory and diagnostic complexity, but causation cannot be inferred from a single observation.

The patient's advanced age, poor dentition, severe dental mobility, and subsequent alveolar ridge deficit also complicated clinical assessment and rehabilitation. These factors may encourage attribution of pain and feeding difficulty to dental disease alone. Persistent verrucous tissue, failure to regress after treatment of an identified infection, or discordance between clinical and histological findings should therefore prompt repeat and sufficiently deep biopsy, imaging when indicated, and multidisciplinary review.

4. Conclusion

This case illustrates the diagnostic complexity of a persistent verrucous gingival lesion in a patient with serologically confirmed late latent syphilis. The initial biopsy demonstrated spirochetes and verrucous epithelial hyperplasia, whereas complete surgical assessment confirmed a pT2 verrucous carcinoma. The chronology does not establish syphilis-related malignant transformation; sampling variability and lesion heterogeneity remain plausible. Persistent verrucous oral lesions require deep, representative biopsy, close clinicopathological correlation, and multidisciplinary follow-up. Ongoing surveillance is essential when margin involvement or postoperative epithelial dysplasia is present.

Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used OpenAI ChatGPT to improve readability and language. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Author Contributions

Vânia Pinto: Initial clinical assessment and follow-up in the Stomatology Department, diagnostic investigation, performance of diagnostic biopsies, data collection and analysis, literature review, conceptualization, and preparation of the entire original manuscript.

Nuno Durão: Supervision of the initial clinical assessment and subsequent follow-up in the Stomatology Department, contribution to the diagnostic investigation, and performance of diagnostic biopsies.

Sara Santos: Participation in the initial surgical intervention and subsequent surgical margin widening, data collection and analysis.

Maria Mexia and Ricardo Brandão: Histopathological examination, interpretation of pathological findings, and selection and preparation of histopathological images.

All authors critically reviewed the manuscript and approved its final version.

Competing Interests: The authors declare no competing interests.

Patient Informed Consent

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Notes

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