









Late diagnosis and oral rehabilitation in a patient with Cowden syndrome: case report

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Abstract:

Cowden syndrome is a rare autosomal dominant disorder associated with germline mutations in the PTEN gene and characterized by multiple hamartomas and an increased risk of malignancy. A 64-year-old woman was referred for evaluation of papillomatous lesions in the oral cavity. Clinical examination revealed verrucous lesions, macrocephaly, acral keratoses, and facial trichilemmomas. Complementary examinations showed benign breast nodules and gastrointestinal polyposis without malignant transformation. Based on clinical, histopathological, and imaging findings, a diagnosis of Cowden syndrome was established according to the criteria of the International Cowden Syndrome Consortium. The patient underwent surgical excision of the oral papillomatous lesions followed by prosthetic rehabilitation with complete removable dentures, which restored function and aesthetics. This report emphasizes the essential role of dentists in the recognition of Cowden syndrome and in the multidisciplinary management required for affected patients.

Keywords: Cowden Syndrome; PTEN Tumor Suppressor Gene; Oral Manifestations; Case Report; Oral Rehabilitation.

INTRODUCTION

Cowden syndrome (CS) is a rare autosomal dominant disorder associated with germline mutations in the PTEN gene, which functions as a tumor suppressor regulating cell growth and division¹. The estimated incidence of CS is approximately 1 in 200,000–250,000 individuals, making it a rare multisystemic condition². Clinically, it is characterized by macrocephaly, acral keratoses, facial trichilemmomas, and papillomatous oral lesions, in addition to an increased lifetime risk of malignant neoplasms, particularly of the breast, endometrium, and thyroid³. Oral and mucocutaneous findings are frequent and may be early diagnostic markers, including cobblestone-like papules, papillomatosis and gingival overgrowth⁴⁻⁷. Recent case reports and reviews highlight the role of dentists in early recognition and referral⁴⁻⁶.

The diagnosis of CS is established using the major and minor criteria proposed by the International Cowden Syndrome Consortium⁸. Although genetic testing for PTEN mutations can improve diagnostic accuracy, it does not always identify pathogenic variants⁹. Recent guidelines

Statement of Clinical Significance

Recognizing oral manifestations of Cowden syndrome is essential for early diagnosis and prevention of malignant complications. This case emphasizes the dentist's role in identifying characteristic lesions and providing functional and aesthetic rehabilitation that improves patient quality of life.

emphasize the practical application of these criteria, the usefulness of clinical scoring systems, and the importance of cancer surveillance¹⁰⁻¹³. Therefore, comprehensive clinical evaluation remains crucial, regardless of the availability or results of molecular testing¹⁴.

This case report describes the late diagnosis and oral rehabilitation of a patient with CS, highlighting the essential role of dentists in the early recognition and multidisciplinary management of this syndrome.

CASE REPORT

A 64-year-old woman was referred to the Stomatology Service of the Federal University of Alfnas

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(UNIFAL-MG), School of Dentistry, with complaints of pain during mastication and poor adaptation of her complete removable dentures. Her medical history included heart disease treated with a cardiac valve and a previous episode of anemia. Extraoral examination revealed verrucous lesions bilaterally at the labial commissures, macrocephaly, facial trichilemmomas, and acral keratoses on the hands and feet (Figure 1). Intraoral examination demonstrated multiple nodules and confluent papules on the gingiva, lips, and tongue, associated with candidiasis (Figure 2). Complementary laboratory and imaging investigations

were requested, including complete blood count (CBC), mammography, colonoscopy, and endoscopy (Figure 3).

Biopsies of the papillomatous lesions confirmed fibroepithelial papillomatous hyperplasia (Figure 4). Mammography revealed benign breast nodules, while colonoscopy and endoscopy identified gastrointestinal polyposis without malignant transformation. Based on the clinical, microscopic, and complementary findings, a diagnosis of Cowden syndrome was established.

The patient underwent preprosthetic surgery with surgical excision of the oral papillomatous lesions,



Figure 1. Extraoral examination. (A) verrucous lesions. (B) facial trichilemmomas. (C) acral keratosis on the hands.



Figure 2. Oral manifestations of CS. (A-B), multiple sessile, confluent, normochromic nodules and papules on the alveolar ridge, tongue, and buccal mucosa. Detachable creamy white plaques are visible, consistent with candidiasis.

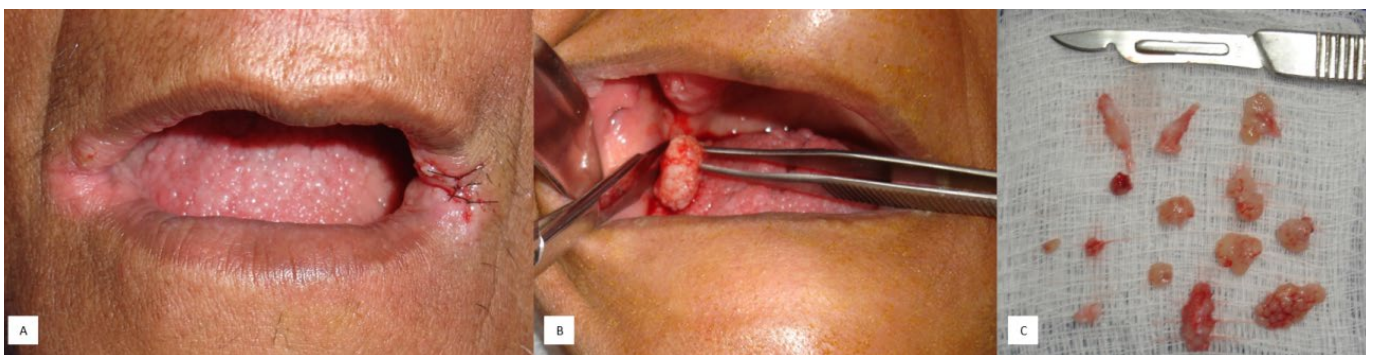


Figure 3. Pre-prosthetic surgical procedure. (A) Clinical aspect showing lesions at the labial commissures during surgical removal. (B) Intraoral view demonstrating the surgical excision of the lesions. (C) Excised tissue fragments obtained during the procedure and submitted for microscopic analysis.

followed by prosthetic rehabilitation using complete removable dentures. Functional impressions, occlusal registration, and articulation procedures were performed, resulting in the delivery of well-adapted dentures (Figure 5). The patient remains under follow-up with semiannual appointments for monitoring of lesion recurrence and prosthesis adaptation.

DISCUSSION

Cowden syndrome (CS) shows a higher prevalence in females, with a reported female-to-male ratio of approximately 2.3:1¹⁵. Oral and mucocutaneous lesions are among the earliest and most frequent manifestations, often appearing by the second decade of life, and are therefore considered valuable diagnostic markers^{16,17}.

Studies consistently report that gingival hypertrophy, papillomatosis and palatal abnormalities are present in the majority of adult patients with PTEN hamartoma tumor syndrome (PHTS)^{18,19}. Case series and reports emphasize that oral lesions often provide the first clue to diagnosis, later confirmed by histopathology and/or genetic testing^{4-7,20,21}. Despite this, delayed diagnoses are still common, frequently because these manifestations are overlooked by healthcare providers, which reinforces the importance of clinical awareness among dentists and physicians^{2,15}.

Pathogenetically, CS is linked to germline mutations in the PTEN gene, which encodes a tumor suppressor protein involved in cell cycle regulation, apoptosis, and DNA repair^{1,9}. Loss of PTEN function results in dysregulated cell growth and differentiation,

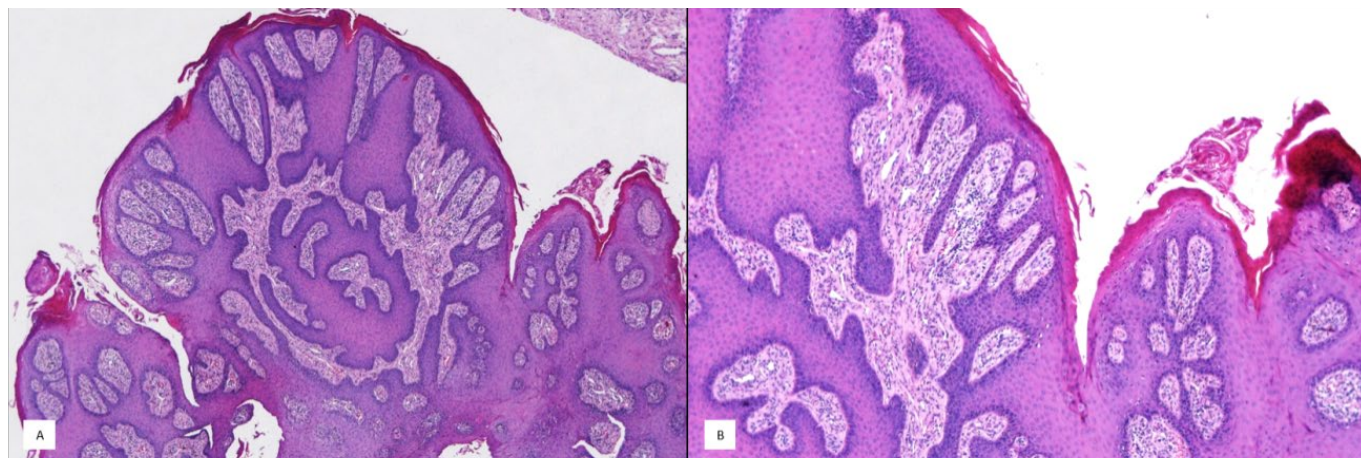


Figure 4. Histopathological aspects of oral papillomatosis. (A) papillomatous fibroepithelial hyperplasia (H&E, ×5). (B) mononuclear inflammatory infiltrate (H&E, ×10).



Figure 5. Upper and lower removable complete dentures in place. (A) patient without the prosthesis. (B) patient with the prosthesis.

predisposing patients to a broad spectrum of benign and malignant lesions across multiple organ systems^{3,8}. Genotype–phenotype studies and clinical cohorts show wide variability in expression, reinforcing the need for directed surveillance of breast, thyroid, endometrium, kidney, colon, melanoma and other neoplasms^{10–12,22,23}. Malignant neoplasms most frequently associated with CS include breast, endometrial, thyroid, and colorectal carcinomas, while benign conditions such as gastrointestinal polyposis, cutaneous hamartomas, and thyroid nodules are also prevalent^{3,24,25}. In the present case, the patient exhibited breast nodules and gastrointestinal polyposis, but without evidence of malignant transformation, consistent with previous observations that not all patients with PTEN mutations develop cancer during follow-up^{3,24,25}.

Oral manifestations, particularly papillomatous lesions, are common in CS and may occur in up to 80–100% of cases^{15,26}. Although they usually lack intrinsic morbidity, they can interfere with mastication, oral hygiene, phonation, and aesthetics, significantly impacting quality of life. Different therapeutic approaches have been described, including conventional excision, CO₂/Er:YAG laser ablation, and even topical sirolimus^{12,27,28}. In this report, sequential excision of the lesions was chosen to allow better healing and reduce surgical morbidity, which facilitated subsequent prosthetic rehabilitation.

Reports addressing oral rehabilitation in CS patients are limited. Case series emphasize the role of dentistry in functional and esthetic rehabilitation after lesion control^{4–7,28}. The present case demonstrates that, when combined with adequate surgical control of lesions, conventional removable dentures can restore oral function and aesthetics, contributing to improved patient well-being. This highlights the need for multidisciplinary collaboration between dentists, dermatologists, gastroenterologists, and oncologists for long-term management of affected individuals^{10–13}.

CONCLUSION

This case illustrates the challenges of late diagnosis of Cowden syndrome and reinforces the importance of recognizing its oral manifestations in clinical practice. Dentists are in a privileged position to identify early signs of this condition, contributing to timely referral, diagnosis, and multidisciplinary care. Furthermore, the successful surgical and prosthetic management described here underscores the role of dentistry in improving

function, aesthetics, and quality of life for patients with this rare syndrome.

AUTHORS' CONTRIBUTIONS

LAT: Data curation, Investigation, Writing – original draft. GMOA: Investigation, Resources, Writing – review & editing. LMC: Investigation, Resources, Writing – review & editing. CMP: Investigation, Resources, Writing – review & editing. AGS: Methodology, Validation, Writing – review & editing. CEO: Methodology, Validation, Writing – review & editing. MFH: Formal analysis, Visualization, Writing – review & editing. LAR: Conceptualization, Project administration, Supervision, Writing – original draft, Writing – review & editing.

CONFLICT OF INTEREST STATEMENT

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