BULLETIN OF STOMATOLOGY AND MAXILLOFACIAL SURGERY
Volume 21, Issue 8

DOI: 10.58240/1829006X-2025.21.8-140

ORIGINAL RESEARCH

RECURRENT APHTHOUS STOMATITIS IN A PATIENT WITH WILSON'S DISEASE: A CASE REPORT

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Received: *Jun 11, 2025;* ***Accepted:*** *Jul 21, 2025;* ***Published:*** *Aug 31, 2025*

ABSTRACT.

Background: Wilson's disease (WD) is a rare autosomal recessive disorder of copper metabolism caused by ATP7B gene mutations. Recurrent aphthous stomatitis (RAS) is a common, multifactorial oral mucosal disorder. Their coexistence is uncommon and has been scarcely reported in the literature**.**
Objectives: This case report aims to describe the clinical features, management, and possible association between RAS and WD, highlighting the importance of treatment adherence and interdisciplinary care.
Materials and Methods: A 26-year-old male with a known history of WD under zinc therapy presented with recurrent oral ulcerations and gingival bleeding. Detailed history, clinical examination, and follow-up assessments were performed to evaluate the nature of lesions and their correlation with treatment compliance**.**
Results: Clinical examination revealed two minor aphthous ulcers on the lower labial mucosa with associated generalized gingival erythema. Ulcer recurrences correlated with poor adherence to zinc therapy. Complete healing was observed after resuming therapy, with no recurrence at one-month follow-up.
Conclusion: This case highlights a possible link between WD and RAS, potentially mediated by micronutrient imbalance and immune dysregulation. Strict adherence to therapy and interdisciplinary management are crucial for preventing recurrences and maintaining oral health in WD patients.

Keywords: *Recurrent aphthous stomatitis, Wilson disease, copper metabolism, case report.*

INTRODUCTION

Recurrent aphthous stomatitis (RAS) Recurrent aphthous stomatitis (RAS) remains the most common ulcerative disease of the oral mucosa, presenting as painful round shallow ulcers with well-defined erythematous margins and yellowish-gray pseudomembranous centers. While the etiology of RAS is multifactorial, systemic diseases, nutritional deficiencies, and immunological factors have been implicated in its pathogenesis. RAS has a characteristic prodromal burning sensation that lasts from 2 to 48 hours before an ulcer appears. Lesions typically occur on non-keratinized mucosa (buccal mucosa, labial mucosa, floor of mouth, ventral tongue, soft palate). Keratinized mucosa (hard palate, attached gingiva, dorsal tongue) is less commonly involved.

RAS is classified into minor, major, and herpetiform ulcers. More than 85% of RAS presents as minor ulcers that are less than 1 cm in diameter and heal without scars. Ulcers classified as major RAS, also known as Sutton's disease or periadenitis mucosa necrotica recurrens, are larger than 1 cm in diameter, persist for weeks to months, and heal with scars. Herpetiform ulcers are clinically distinct because they appear as clusters of multiple ulcers scattered throughout the oral mucosa; despite the name, these lesions have no association with herpes simplex virus.[1]

Wilson Disease (WD) is an inherited disorder of copper metabolism that is both potentially serious and treatable. It is characterized by abnormal accumulation of copper in the body. The underlying cause is mutations in the ATP7B gene, which encodes a transmembrane copper-transporting ATPase. This genetic defect leads to progressive copper overload, particularly in the liver, brain, and other organs.[2]

The clinical course of WD can vary greatly in severity. However, progressive liver disease remains one of its most common and important features. In addition to hepatic involvement, patients may present with neurological symptoms such as tremors or movement disorders, as well as psychiatric manifestations including mood changes or cognitive disturbances.[3]

Diagnosis is based on structured algorithms that combine clinical signs and symptoms with laboratory measures of copper metabolism. Genetic testing for ATP7B mutations also plays an essential role in confirming the diagnosis and guiding family screening.[4]

Treatment focuses on reducing copper overload and preventing organ damage. Available therapies include copper-chelating agents, which promote urinary excretion of copper, and zinc salts, which block copper absorption in the intestine. These treatments work through different mechanisms but are effective in controlling disease progression when started early.[5]

This case report highlights the association between recurrent aphthous stomatitis and Wilson disease, emphasizing the need for clinicians to consider underlying systemic conditions in patients presenting with refractory or atypical RAS.

REPORT OF THE CASE

A 26-year-old male presented to the outpatient department (OPD) with a primary complaint of gingival bleeding during toothbrushing, persisting for the past year. He reported difficulty in maintaining oral hygiene but denied any episodes of spontaneous gingival bleeding. The patient had a known diagnosis of Wilson's disease, for which he was undergoing treatment.

Medical history was notable for recurrent oral ulcerations, which the patient reported were exacerbated by sleep deprivation and periods of non-compliance with zinc supplementation. There was no history of cutaneous lesions suggestive of systemic involvement.

Intraoral examination revealed two ovoid ulcers on the lower right labial mucosa, measuring approximately 3 × 2 mm and 2 × 1 mm (figure1), respectively.

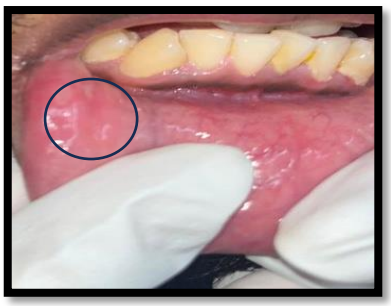

Figure 1. Two ovoid ulcers of approximately 3 × 2 mm and 2 × 1 mm

The ulcer bases were covered with whitish slough and surrounded by a well-defined erythematous halo. The gingiva demonstrated generalized marginal erythema (figure2) with brownish pigmentation along the attached gingiva.

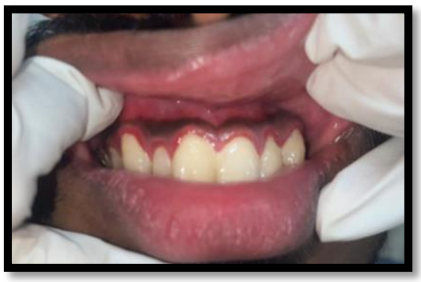

Figure 2. Erythmatous marginal gingiva

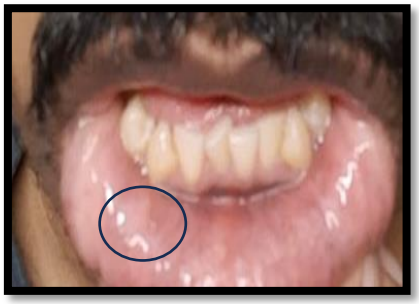

Figure 3. Healed ulcer at follow-up

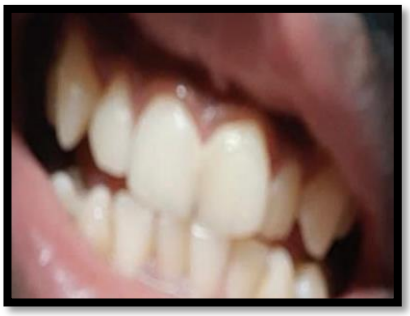

Figure 4. Normal marginal gingiva showing no erythematous areas

No extraoral manifestations of Wilson's disease were observed during the ulcerative episodes. The patient was advised to maintain strict oral hygiene measures and to continue zinc supplementation as prescribed. A follow-up visit was scheduled after one month to assess for complete healing (figure3,4) and to monitor for recurrence. At one-month follow-up, the ulcers demonstrated complete healing, correlating with improved compliance with zinc therapy. The patient remained asymptomatic, with no new ulcerative lesions observed on clinical examination.

DISCUSSION

Wilson's disease (WD) is an autosomal recessive disorder of copper metabolism caused by mutations in the ATP7B gene, resulting in pathological copper accumulation primarily in the liver, central nervous system, and other organs. The clinical presentation is heterogeneous, with hepatic, neurological, and psychiatric manifestations being most common. Oral manifestations, though less frequently reported, may reflect systemic disease activity or complications of therapy.[3]

In this case, the patient presented with chronic gingival bleeding during toothbrushing and recurrent oral ulcerations, which were temporally associated with non-adherence to zinc supplementation. Zinc salts remain a mainstay of WD treatment, acting by inducing intestinal metallothionein to reduce copper absorption. Discontinuation or irregular intake of zinc can lead to fluctuations in copper levels, potentially contributing to mucosal vulnerability and impaired wound healing.

Oral ulcerations in patients with WD may also be multifactorial, involving nutritional deficiencies, altered immune responses, or local trauma exacerbated by poor oral hygiene. In this patient, ulcers were observed as well-defined ovoid lesions with erythematous halos and slough-covered bases, consistent with minor aphthous ulcers. Notably, ulceration episodes coincided with periods of zinc therapy interruption and improved with restored compliance, suggesting a contributory role of zinc in mucosal integrity and healing.

Gingival findings of generalized marginal erythema with brownish pigmentation may reflect chronic inflammatory changes and melanin deposition, a known finding in chronic gingivitis. While WD itself is not classically associated with specific gingival pigmentation, systemic disease burden and oral hygiene challenges can exacerbate periodontal inflammation.

This case underscores the importance of interdisciplinary management in patients with WD, including dental practitioners, to monitor oral manifestations, reinforce treatment adherence, and maintain optimal oral hygiene. Early recognition and management of oral lesions can improve quality of life and prevent complications in this patient population.

This report highlights a potential association between Wilson's disease (WD) and recurrent aphthous stomatitis (RAS), but it is important to acknowledge several limitations inherent to case reports. As a single-patient observation, the findings lack generalizability, and the apparent relationship between WD and RAS may be coincidental rather than causal. Confounding factors and alternative etiologies for RAS may not have been fully excluded.

RAS is a common oral mucosal disorder characterized by recurrent, painful ulcers with a multifactorial etiology. Contributing factors include psychological stress, immune dysregulation, and nutritional deficiencies (e.g., zinc, iron, vitamin B12). Systemic conditions such as inflammatory bowel disease or Behçet's syndrome also warrant consideration. Without comprehensive exclusion of these alternative diagnoses, attributing the occurrence of RAS solely to WD remains speculative.

Wilson's disease is a rare autosomal recessive disorder caused by mutations in the ATP7B gene, leading to impaired copper homeostasis and toxic accumulation in the liver, brain, and cornea. Several pathophysiological mechanisms may plausibly link WD to RAS. Dysregulated copper metabolism in WD may induce immune system

dysfunction, a recognized contributor to RAS pathogenesis. Additionally, secondary deficiencies in essential micronutrients such as zinc or iron—whether due to the underlying disease or chelation therapy—may compromise mucosal integrity and immune competence, predisposing to ulcer formation.[6]

Oxidative stress is another potential mechanistic link. Excess free copper catalyzes the formation of reactive oxygen species (ROS), causing tissue injury that may predispose to oral mucosal ulceration. Furthermore, chronic systemic inflammation in WD, characterized by elevated pro-inflammatory cytokines such as TNF-α and IL-1, may contribute to the development or persistence of RAS lesions.[7]

Nevertheless, in the absence of mechanistic evidence or long-term follow-up data, the causal relationship between WD and RAS remains hypothetical. The current report does not provide direct evidence that treatment of WD, such as chelation therapy or zinc supplementation, directly alters the frequency or severity of RAS episodes over time. Future studies with larger patient cohorts, mechanistic investigations, and extended clinical observation will be necessary to clarify this potential association and its clinical implications.

CONCLUSION

This case underscores the importance of recognizing potential oral manifestations in patients with Wilson's disease, including recurrent aphthous stomatitis (RAS) and chronic gingival inflammation. While the observed improvement in oral ulceration with zinc supplementation suggests a possible contributory role of micronutrient deficiency or immune dysregulation secondary to WD, the relationship remains speculative given the multifactorial nature of RAS.(5)

Clinicians should maintain a high index of suspicion for oral mucosal lesions in patients with systemic diseases such as WD and ensure thorough assessment of contributing factors, including treatment adherence and nutritional status. Interdisciplinary management, involving medical and dental practitioners, is essential for optimizing patient outcomes.

DECLARATION

Funding

This research did not receive any specific grant or financial support from funding agencies in the public, commercial, or not-for-profit sectors.

Competing Interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

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