From Mucosal to Pulmonary Involvement: A Case of C-ANCA-Associated Granulomatosis with Polyangiitis Presenting with Isolated Oral Ulceration

Nur Diyana Mohd Shukri[1,3]*, Syazwani Mohd Tajudin[1,3], Noor Suryani Mohd Ashari[1,3], Nurul Khaiza Yahya[1,3], Wan Syamimee Wan Ghazali[2,3]

[1]Department of Immunology, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan
[2]Department of Internal Medicine, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan
[3]Hospital Pakar Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan

***Corresponding author:** diyanashukri@usm.my

Introduction

Granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis is a rare yet potentially life-threatening autoimmune disease. It is characterised by necrotising granulomatous inflammation and vasculitis, primarily affecting small to medium-sized blood vessels and often associated with antineutrophil cytoplasmic antibodies (ANCA). GPA frequently involves the upper respiratory tract, the lung parenchyma and the kidneys, with the lungs being the most affected organs.

Case Report

A 42-year-old lady presented with a history of an oral ulcer over the left buccal mucosa. Autoimmune screening revealed a strong positive C-ANCA pattern, indicating ANCA directed towards proteinase 3 (PR3). Antinuclear antibody (ANA) and anti-double-stranded DNA (anti-dsDNA) were negative. Infective screening and cultures were unremarkable. Later, she developed a progressive cough, shortness of breath, haemoptysis and fever. Chest X-ray and computed tomography (CT) of the thorax revealed lung features consistent with granulomatous disease (Fig.1 and 2). Renal biopsy confirmed immune necrotising crescentic glomerulonephritis. A diagnosis of C-ANCA-associated GPA was made based on clinical presentation, imaging, and serology. She was treated with intravenous methylprednisolone followed by intravenous cyclophosphamide.

Discussion

Oral mucosal involvement in granulomatosis with polyangiitis (GPA) is relatively uncommon, occurring in approximately 6-13% of cases, and is most often seen in conjunction with other upper respiratory tract manifestations such as chronic sinusitis, nasal crusting, or epistaxis (1). These mucosal changes typically occur during an established disease and rarely precede involvement in other organs. In the present case, the patient presented with a solitary, non-healing oral ulcer without systemic or respiratory manifestations. This isolated mucosal manifestation, occurring before the emergence of more typical GPA features, is extremely rare and poses a diagnostic challenge. Such lesions may be readily misinterpreted as benign conditions, such as aphthous ulcers, traumatic injuries, or oral infections, thereby delaying the identification of the underlying systemic vasculitis. A study by Labrador et al. identified several cases in which gingival or mucosal changes were among the first clues to systemic vasculitis (2).

The diagnostic process in this case was further complicated by the absence of concurrent sinonasal or lower respiratory tract symptoms at initial presentation. However, the subsequent emergence of pulmonary manifestations, together with CT thorax findings demonstrating granulomatous changes, supports the diagnosis of GPA. The identification of C-ANCA, which targets PR3, was crucial in validating the diagnosis. PR3-ANCA positivity is associated with a higher probability of systemic involvement, more severe disease progression, and higher recurrence rates than MPO-ANCA positivity (3).

This example highlights the need to maintain a heightened index of suspicion for systemic vasculitis in patients with atypical or chronic oral lesions, particularly when these lesions do not respond to standard local treatments. In summary, a prompt evaluation of GPA in the differential diagnosis

augmented by early ANCA testing can enable timely action, thereby potentially reducing irreparable organ damage.

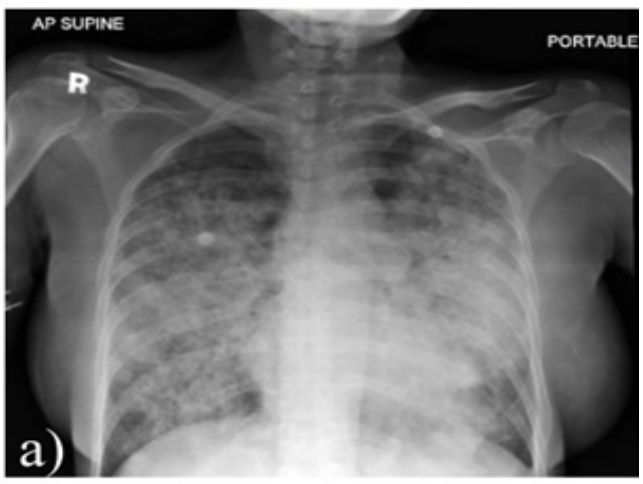

Figure 1. Antero-posterior view of the chest x-ray showing diffuse nodular opacities suggestive of pulmonary haemorrhage

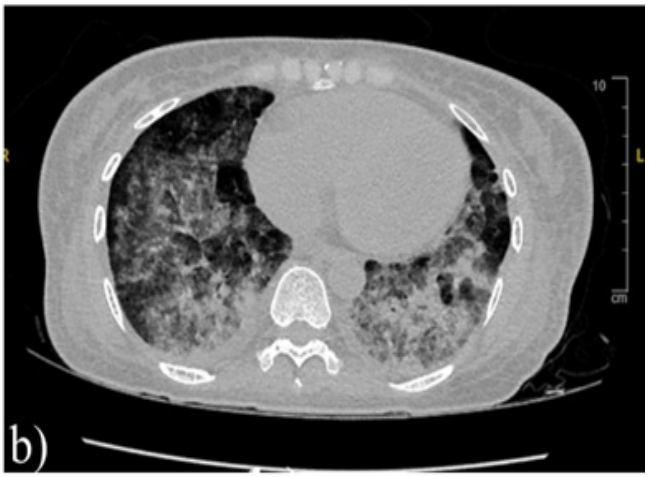

Figure 2. Axial computed tomography of the chest showing “crazy paving” of bilateral lower zones, in line with pulmonary haemorrhage

Keywords: Granulomatosis with polyangiitis; C-ANCA; PR3; oral ulcer

References

1. Lalla F, Vinciguerra A, Lissoni A, Danè G, Abati S. Oral lesions in Granulomatosis with polyangiitis (GPA): An updated overview. Journal of Osseointegration. 2020;12(4):736-42.
2. Labrador AJP, Valdez LH, Marin NRG, Ibazetta KA, Chacón JA, Fernandez AJ, et al. Oral granulomatosis with polyangiitis a systematic review. Clinical and Experimental Dental Research. 2023;9(1):100-11.
3. Chen DP, Aiello CP, McCoy D, Stamey T, Yang J, Hogan SL, et al. PRTN3 variant correlates with increased autoantigen levels and relapse risk in PR3-ANCA versus MPO-ANCA disease. JCI insight. 2023;8(4):e166107.