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Case Report

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ANCA-associated Leucocytoclastic Vasculitis presenting with Bronchiectasis, GI Involvement and Hypertensive Urgency: A Complex Case without Renal Involvement

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ABSTRACT

Introduction: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) are autoimmune diseases characterized by inflammation of small to medium blood vessels. This case explores AAV pathophysiology, its link to bronchiectasis and leucocytoclasia, ANCA positivity, and current treatment guidelines. **Case Presentation**: A 48-year-old with abdominal pain, rash, hypertensive urgency, and respiratory symptoms was diagnosed with AAV, confirmed by skin biopsy and positive C-ANCA, stool occult blood with negative abdominal imaging along with bronchiectasis on HRCT. The patient initially failed to respond to broad-spectrum antibiotics but improved with high-dose corticosteroids. **Conclusion**: We highlight an atypical presentation of AAV, showing the importance of timely immunosuppressive therapy for favorable outcomes.

Keywords: ANCA Associated Vasculitis, , Bronchiectasis, Leucocytoclastic vasculitis

INTRODUCTION

This case report describes a challenging diagnostic scenario involving ANCA-associated vasculitis (AAV) with bronchiectasis and gastrointestinal (GI) involvement, ultimately managed through immunosuppression and steroid tapering. AAV is a rare autoimmune condition marked by inflammation of small blood vessels, often affecting multiple systems (1). No similar cases are reported in Sri Lanka. In this case report, we are discussing the clinical features, pathophysiology and along with standard guideline-based treatments.

CASE REPORT

Mr. R presented with severe abdominal cramps, and a generalized non-itchy maculopapular rash involving both upper and lower limbs and the trunk. Two weeks before the current admission, he had been evaluated in a surgical ward for similar abdominal pain but was discharged with normal investigations (except for unexplained high CRP) without a diagnosis, though he continued to experience recurrent abdominal pain. Shortly before his second admission, he developed a mild

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fever, worsening cough, and a rash. His symptoms included severe abdominal pain occurring in frequent paroxysms intermittently associated with meals, episodes of fresh per rectal bleeding, cough with whitish sputum, and fever responsive to paracetamol. He had no significant history of cardiac issues, constitutional symptoms, hematuria or reduced urine output and contact history of TB. He had a past medical history of mild intermittent asthma controlled with inhalers, but no significant recent exacerbations. He was not recently on any medications except for analgesics and ciprofloxacin for 3 days and anti-peptic treatment while being in the surgical ward. He had no history of smoking, alcohol consumption, or sexual promiscuity.

Upon examination, he appeared generally ill, mildly dyspneic, and in abdominal discomfort. He had a maculopapular non-blanching rash with pigmented nodules and pustules on the limbs and trunk (Figure 1). Neither oral nor genital ulcers were noted. His blood pressure was significantly elevated at 240/135 mmHg without pulse delays, and respiratory examination revealed coarse crepitations in the lower lungs. His abdominal and neurological exams were unremarkable, aside from abdominal tenderness.

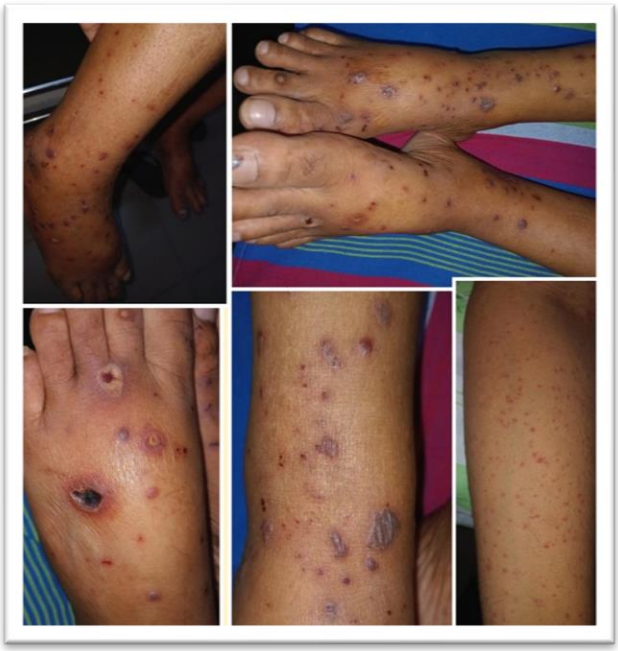

Figure 1: Rash distribution

The investigations revealed neutrophil leukocytosis and elevated CRP (140 mg/L) and ESR (45). He had normal Serum amylase, renal function, serum electrolytes, ECG, and troponin I with mild elevation of bilirubin levels. The blood picture was suggestive of sepsis without evidence of hemolysis. UFR was normal. Stool full report revealed the presence of RBC (50-60/hpf), pus cells (2-3/hpf), and occult blood positivity. Serum cryoglobulins, ANA, Mycoplasma antigen, CMV, EBV, Hepatitis B and C markers, and HIV tests were all negative. A skin biopsy (Figure 2) revealed leukocytoclastic vasculitis, with dermal vessel neutrophil infiltration, fibrinoid necrosis, and red cell extravasation without granuloma formation. 2D echocardiogram revealed was normal without evidence of aortic dissection or valve thrombosis or hypertrophy. C-ANCA was positive, while P-ANCA and ASOT were negative. Upper and lower GI studies were unremarkable, as was Abdominal CT angiogram and venogram. Chest X-ray showed bilateral lower lobar hazy shadows and HRCT of the chest (Figure 3) was significant for cystic and cylindrical bronchiectasis in both lungs, predominantly in the lower lobes along with possible ongoing infection.

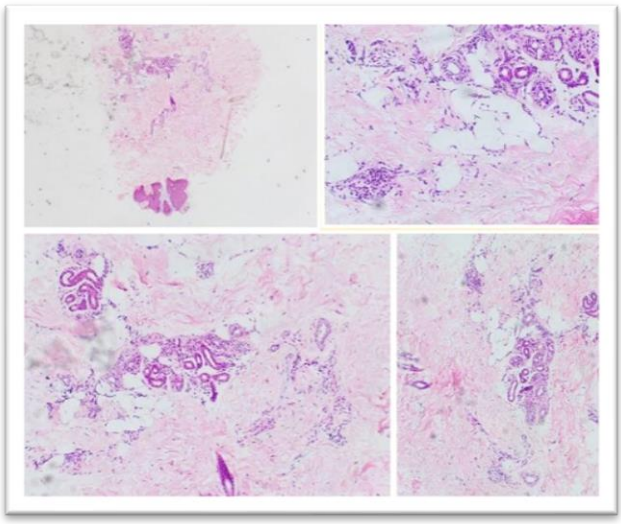

Figure 2: Skin Biopsy Histology

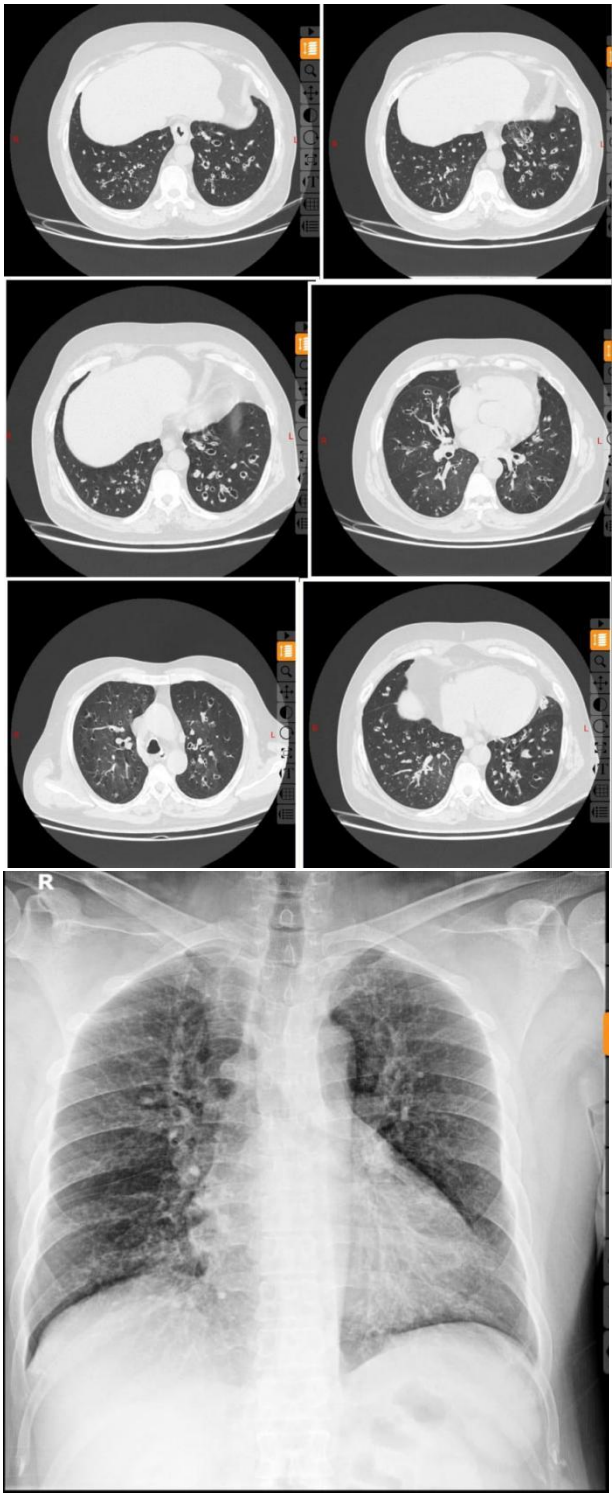

Figure 3: Chest X-Ray and HRCT Chest

Management: He was initially managed for hypertensive urgency and possible atypical pneumonia, given his respiratory involvement. Despite broad-spectrum antibiotics and supportive care, his condition did not improve, prompting a multidisciplinary team approach to consider vasculitis. High-dose corticosteroids (prednisolone 1 mg/kg daily) were initiated, resulting in rapid clinical improvement. The patient's C-ANCA results were positive, and he was diagnosed with ANCA-associated leukocytoclastic vasculitis, affecting the respiratory, dermatological, GI, and cardiovascular systems but sparing the kidneys. Steroids were gradually tapered, and follow-up with rheumatology was arranged. This case highlights the complexity of diagnosing and managing AAV, particularly when multiple systems are involved without renal manifestations.

DISCUSSION

ANCA-associated vasculitis (AAV) is a group of rare autoimmune diseases and are three main types which are granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA). These conditions have a range of clinical manifestations, some overlapping and others distinct, as in our case in which we couldn't differentiate exactly among these. GPA and MPA share similarities in presentation and treatment. Accurate interpretation of ANCA test results is crucial for diagnosing and managing these vasculitides effectively (1). The systemic involvement of these vasculitides summarized is shown in the table (Table 1) which is derived from an epidemiological study (2). Anti-neutrophil cytoplasmic antibodies (ANCAs) with specificity for proteinase-3 (PR3 or C ANCA) or myeloperoxidase (MPO or P ANCA) are hallmarks of AAV and have an important role in pathogenesis. In addition to ANCA, the cellular immune system contributes to the pathogenesis of the disease. ANCA-mediated degranulation of neutrophils causes vasculitic damage; T cells drive granuloma formation, promote vasculitic damage by several different pathways, and enhance autoantibody production by B cells. Recently, complementary PR3 and lysosomal membrane protein-2 were suggested as novel autoantigens in AAV. Novel pathophysiological findings also highlight the importance of complement, danger-associated molecular patterns, and dendritic cells in AAV (3).

AAV and bronchiectasis

We investigated this association as our patient had AAV along with severe respiratory and GI involvement which mandated us to perform advanced imaging of the chest and abdomen. This extensive evaluation ruled out other autoimmune causes, infective causes, mesenteric atherosclerosis and thrombosis and viral-related etiologies. Recent studies indicate that approximately 19-40% of AAV patients exhibit bronchiectasis, with a notable association with myeloperoxidase (MPO)-ANCA positivity (4,5). Female sex and peripheral neuropathy are risk factors for developing bronchiectasis in AAV patients. Patients with bronchiectasis often present with lower proteinuria levels and a better renal prognosis compared to those without bronchiectasis (5, 6). Despite the presence of bronchiectasis, overall survival rates do not significantly differ between AAV patients with and without this condition. While bronchiectasis is seen in AAV, its pathophysiological relationship remains unclear, warranting further research.

Table 1: Clinical Features in ANCA Associated vasculitis

Organs involved	WG	MPA	CSS	PAN
ENT	+++	+	++ polypi	–
Kidney	++	+++	+	+/HT
Nervous system	++	+	+++	+++
Lungs	++ noduli	+(+) diffuse	+ transient	–
Eyes	++	+	(+)	–
GI-tractus	+(+)	+(+)	++	+++
Heart	+	(+)	++	–
Skin	++	++	++	++
Muscle/joint	++	++	++	++
ANCA	PR3	MPO	MPO	negative

ENT: ear-nose and throat, GI: gastrointestinal, WG: Wegener's granulomatosis
MPA: microscopic polyangiitis, CSS: Churg Strauss syndrome,
PAN: polyarteritis nodosa, HT: arterial hypertension,
ANCA: anti neutrphil cytoplasmic antibody, PR3: proteinasis 3, MPO: myeloperoxidasis.

Source: (2)

Leucocytoclastic vasculitis (LCV) and C ANCA Positivity

C-ANCA positivity can occur in LCV and LCV typically presents as palpable purpura, primarily on the lower extremities, and is confirmed through skin biopsy showing leukocytoclasia (7). In a similar case in a pediatric patient, Henoch-Schoenlein purpura which is an IgA-mediated ANCA-negative vasculitis should be ruled out. In cases where LCV is accompanied by C-ANCA positivity, it is crucial to correlate clinical and pathological findings to determine the underlying etiology (8, 9) in which case skin biopsy would be of great value. Some cases of LCV with C-ANCA positivity have been linked to secondary causes, which we had to rule out even in a resource-poor setting (1).

Standard Treatments related to AAV Glucocorticoids remain the cornerstone of AAV treatment, often used in high doses in conjunction with other Immunosuppressants. Immunosuppressants such as Cyclophosphamide, azathioprine, methotrexate, and mycophenolate mofetil are commonly employed to induce and maintain remission. For remission induction in life-threatening or organ-threatening AAV, EULAR recommend a combination of high-dose glucocorticoids (GCs) in combination with either rituximab or cyclophosphamide. Also, recommend tapering the GCs dose to a target of 5 mg prednisolone equivalent/day within 4-5 months (10, 11, 12). Avacopan may be considered as part of a strategy to reduce exposure to GC in GPA or MPA (12). Among biologics, Rituximab (B cell depletion) in maintenance of remission and mepolizumab (IL-

5 inhibition) In patients with relapsing or refractory eosinophilic GPA have shown efficacy. Azathioprine and methotrexate are alternatives to biologics for remission maintenance in AAV (12, 13). Newer agents targeting the complement system are being integrated into treatment protocols (11). Plasma Exchange is recommended for severe cases, particularly in rapidly progressive glomerulonephritis. Despite advancements, challenges remain, particularly in resource-limited settings where access to these therapies can be restricted (12, 13, 14, 15).

Author declaration

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Authors' contributions:
Conceptualization and Design: NMMR; Data Collection and Patient Care: NMMR, IKJ, NA, EMCBE, SH; Literature Review: NMMR, JFS; Manuscript Writing: NMMR; Critical Review and Editing: NMMR, IKJ, NA, EMCBE, SH, JFS.

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Statement on data availability:
All data generated during this study are included in this published article.

REFERENCES

1. National Institutes of Health. ANCA-Associated Vasculitis [Internet]. https://www.ncbi.nlm.nih.gov/books/NBK554372/
2. Koldingsnes W, Nossent HC. Epidemiology of ANCA associated vasculitis. Norsk Epidemiologi. 2009;18(1). https://doi.org/10.5324/nje.v18i1.62
3. Wilde B, van Paassen P, Witzke O, Tervaert JW. New pathophysiological insights and treatment of ANCA-associated vasculitis. Kidney Int. 2011;79(6):599-612. https://pubmed.ncbi.nlm.nih.gov/21150876/
4. Yu G, Zhang T, Zhu W, Han Y, Shi J. Prevalence and characteristics of bronchiectasis in ANCA-associated vasculitis: A systematic review and meta-analysis. Arch Rheumatol. 2024. https://doi.org/10.46497/archrheumatol.2024.10352
5. Ren J, Ding Y, Zhao J, Sun YC. Bronchiectasis in patients with antineutrophil cytoplasmic antibody-associated vasculitis: a case control study on clinical features and prognosis. Expert Rev Respir Med. 2022;16(6):697-705. https://doi.org/10.1080/17476348.2022.2088512
6. Luo L, Li H, Tang J, et al. Clinical characteristics and outcomes of MPO-ANCA-associated glomerulonephritis with bronchiectasis: A retrospective case-control study. Semin Arthritis Rheum. 2022;57:152082-152082. https://doi.org/10.1016/j.semarthrit.2022.152082
7. Beltrami JC, Basso S, Chiodini RL, et al. ANCA positive leukocytoclastic vasculitis: a case report. Int J Sci Res. 2024. https://doi.org/10.36106/ijsr/2125120
8. Bettacchioli E, Foulquier JB, Chevet B, et al. Dual MPO/PR3 ANCA positivity and vasculitis: insights from a 7-case study and an AI-powered literature review. Rheumatology (Oxford). 2024;63(9):2557-2568. doi: 10.1093/rheumatology/keae170. https://doi.org/10.1093/rheumatology/keae170
9. Xiong M, Singer H, Bae E, et al. IgA Vasculitis With Concurrent ANCA-Positivity in the Setting of Bacterial Endocarditis. R I Med J (2013). 2022 Dec;105(10):52-55. PMID: 36413453. https://pubmed.ncbi.nlm.nih.gov/36413453/
10. Chalkia A, Jayne D. ANCA-associated vasculitis - Treatment Standard. Nephrol Dial Transplant. 2023. doi: 10.1093/ndt/gfad237. https://doi.org/10.1093/ndt/gfad237
11. Reggiani F, Stella M, Calatroni M, Sinico RA. Treatment strategies for ANCA-associated vasculitides: from standard protocols to future horizons. Expert Rev Clin Immunol.2024;1-16. https://doi.org/10.1080/1744666x.2024.2326628
12. Hellmich B, Sanchez-Alamo B, Schirmer JH, et al. EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update. Ann Rheum Dis. 2024 Jan;83(1):30-47. https://doi.org/10.1136/ard-2022-223764
13. Kronbichler A, Bajema IM, Bruchfeld A, et al. Diagnosis and management of ANCA-associated vasculitis. Lancet. 2024;403:683-698. https://doi.org/10.1016/s0140-6736(23)01736-1
14. Pimentel-Quiroz VR, Alarcón GS. Role of plasma exchange in ANCA-associated vasculitis. Lancet Rheumatol. 2023;5(10):e579-e580. https://doi.org/10.1016/s2665-9913(23)00234-5
15. Magri S, Ugarte-Gil MF, Brance ML, et al. Pan American League of Associations for Rheumatology Guidelines for the treatment of ANCA-associated vasculitis. Lancet Rheumatol. 2023. https://doi.org/10.1016/S2665-9913(23)00128-5