# The Dilemma of Vasculitis: A Rare Overlap of ANCA-Associated Vasculitis and Behçet-like Features with IgA Nephropathy

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## ABSTRACT

Antineutrophil cytoplasmic antibody-associated vasculitis (AAV) is an uncommon autoimmune small-vessel condition that may coexist with other immune-mediated disorders, resulting in intricate clinical manifestations. We present a 39-year-old female with poorly managed diabetes mellitus for 16 years, who had non-healing ulcers on feet, anterior chest discomfort, and recurrent oral ulcers. Laboratory investigations indicated increased ESR and CRP levels, urine routine showed proteinuria and glucosuria,c-ANCAby Immunofluorescence positive (PR3-ANCA 153 U/mL),HLA-B51 and pathergy positivity. Renal biopsy confirmed IgA nephropathy, sternal biopsy revealed non-granulomatous small-vessel vasculitis, and CT thorax showed cavitary pulmonary nodules. A diagnosis of overlapping vasculitis, with ANCA-associated vasculitis and Behçet-like characteristics with IgA nephropathy was established. The patient received intravenous pulse methylprednisolone, followed by oral corticosteroids, azathioprine, and colchicineresulting in ulcer healing, normalization of inflammatory markers, and radiographic resolution with stable renal function at six months. Timely diagnosis and personalized immunosuppressive treatment resulted in a positive outcome in this uncommon overlap vasculitis manifestation.

**KEYWORDS**: ANCA-associated vasculitis, IgA nephropathy, Behçet's disease, overlap of vasculitidis, HLA-B51, immunosuppression, azathioprine, methylprednisolone, colchicine

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## INTRODUCTION

Antineutrophil cytoplasmic antibody-associated vasculitides (AAV) represent a rare group of systemic, necrotizing inflammatory disorders affecting small vessels, which include microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA). The estimated prevalence of AAV is approximately 42 per 100,000 individuals globally, with MPA and GPA occurring more commonly than EGPA (1–3). AAV frequently influences the respiratory system and kidneys, however it can affect nearly any organ. This results in a diverse array of clinical manifestations, including skin ulcers, rapidly deteriorating glomerulonephritis, and pulmonary hemorrhage (2,3).

The pathophysiology of AAV involves autoantibody formation, neutrophil activation, endothelial injury, and dysregulated immune responses. Genetic and environmental factors significantly contribute to AAV, accounting for approximately 20% of disease risk (5). The syndrome is serologically characterized by the presence of ANCAs directed against proteinase-3 (PR3) or myeloperoxidase (MPO), which provoke neutrophil degranulation and vascular necrosis (6).

IgA nephropathy (IgAN) is an immune-mediated renal disorder characterized by the deposition of IgA-containing immune complexes in the glomerular mesangium, leading to inflammation and subsequent renal dysfunction. Although AAV and IgAN

are distinct pathologies, an increasing number of cases with overlap are documented, revealing the coexistence of necrotizing glomerulonephritis with mesangial IgA deposits, suggesting shared immunological mechanisms (7,8). This form of dual pathology typically severely affects the kidneys and needs aggressive management.

Behçet's disease (BD), a variable vessel vasculitis is characterized by recurrent oral and genital ulcers, skin lesions, ocular inflammation, and vascular manifestations. It exhibits a strong correlation with HLA-B51, which augments neutrophil chemotaxis and endothelial activation (9,10). While ANCA positivity is uncommon in Behçet's disease (BD), a small subset of patients may exhibit both traits, complicating the diagnostic differentiation between Behçet's vasculitis and ANCA-associated vasculitis (AAV) (11).

Case series and reports of AAV with various autoimmune disorders are documented. Masiak et al. (2024) reported more than 14% of AAV patients with thyroiditis, rheumatoid arthritis, and psoriasis, which altered their disease presentation and clinical course (12).

This case exemplifies an unusual convergence of AAV withBehçet-like disease and IgA nephropathy in a middle-aged woman with a history of inadequately controlled diabetes mellitus. This case illustrates the convergence of autoantibody-mediated necrotizing vasculitis, immune complex deposition, and a familial predisposition to mucocutaneous inflammation. This presentation underscores the importance of comprehensive serological and histological evaluation, timely diagnosis, and tailored immunosuppressive therapy in patients presenting with complex vasculitic syndromes.

**Case Presentation**

A 39yearoldwoman with uncontrolled diabetes mellitus for 16 years presented to the physician withthree non-healing ulcers on the lateral aspect of left foot.She also complained of persistent, intense dull aching pain in the anterior chest region lasting one month. There was no associated palpitatios,breathlessness,orthopnea, PND, cough or fever.

She gave a history of recurrent painful oral ulcers for the past 3 years .However, there was no evidence of vaginal ulceration, ocular involvement, arthralgia, photosensitivity, or Raynaud's phenomenon. There was no family history of autoimmune or connective tissue disorders.

**Clinical Examination**

**On** examination, the patient was afebrile, conscious , and hemodynamically stable. Three well-defined indurated ulcers 2 x 2 cms with punched out margins with healthy granulation tissue was seen onthe left lower one third lateral aspect of left foot. There was nodischarge, erythema, or tenderness in the area. Other areas were normal.

Table 1 shows a summary of the baseline investigations. The patient's inflammatory markers were very high, with an ESR of 118 mm/hr and a CRP of 19.8 mg/dL (CRP< 6 mg/dL)urine routine showed proteinuria and glucosuria. The tests for both viral markers (HBsAg, Anti-HCV, HIV) and Quantiferon-TB Gold were negative.

The serological analysis revealed c-ANCA positivity (1:10 dilution) via indirect immunofluorescence and a robustly positive PR3-ANCA by ELISA (39.66 U/mL, subsequently 153 U/mL). p-ANCA, ANA by IF and Line Immunoassay - LIA-17 and anti-dsDNA by ELISA were negative. Complement C3 and C4 ((116&33 mg/dL)were normal. The HLA-B51 by PCR and Pathergy test were positive.The antiphospholipid antibody panel, which included anticardiolipin antibody, beta-2 glycoprotein, and lupus anticoagulant was reportedas negative.

**Radiological findings:** CT thorax showed multiple cavitary and subpleural pulmonary nodules and changes suggestive of chronic sternal osteomyelitis. Cardiac evaluation was normal.

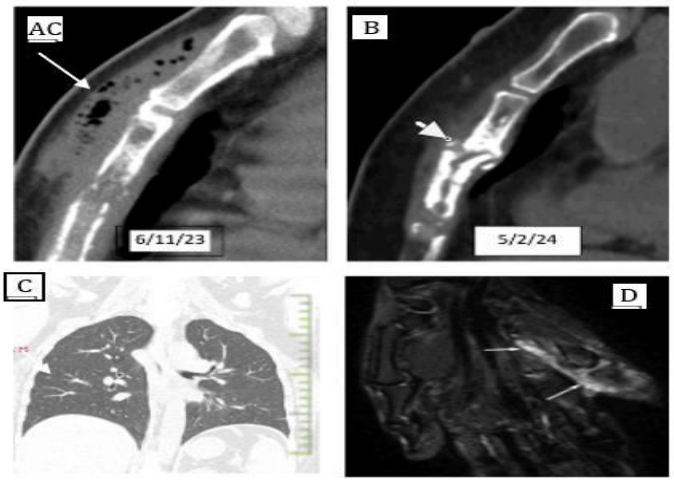


**Fig 1. A and B. Sternal osteomyelitis, C. CT thorax, D. Hand osteomyelitis**

**Histopathology:**

- A skin biopsy showed leukocytoclastic vasculitis, which is a sign of inflammation in small blood vessels.
- The renal biopsy showed characteristics IgA nephropathy, including mesangial hypercellularity and IgA deposition seen using immunofluorescence.
- A sternal biopsy revealed non-granulomatous small-vessel vasculitis.

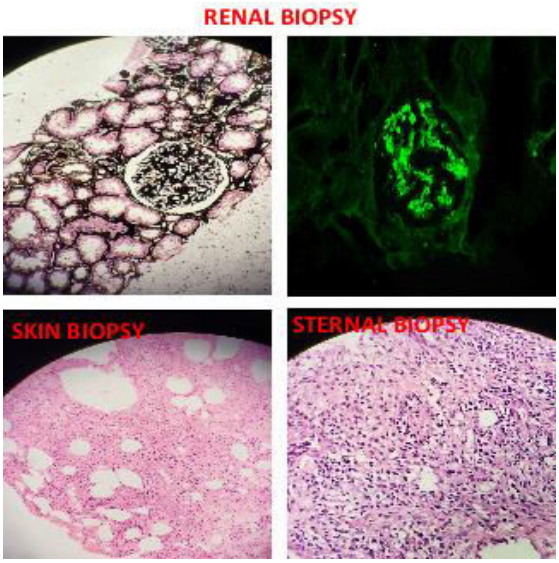


**Fig 2. Renal, Skin and sternal biopsy**

**Treatment and Follow-up**

The patient was given intravenous pulse methylprednisolone (500 mg/day for 5 days)followed by oral corticosteroids. Azathioprine (started as 50 mg/day and titrated to 2mg/kg/day dose) and colchicine (0.5 mg twice a day) werestarted as immunosuppressants. Glycemic control was done andlocal wound care was given.

She improved in four weeks with healing of skin and mouth ulcers. The chest pain reduced and the inflammatory markers returned to normal. At six-month follow-up, she remained asymptomatic, with resolution of pulmonary nodules on repeat CT thorax and significant improvement in renal parameters. She continues on low-dose azathioprine and colchicine, with no relapse to date.

**Table 1. Baseline Investigations**

| Parameters | Result |
|---|---|
| ESR | 118 mm/hr |
| CRP | 19.8 mg/dL (↑) |
| Urine Routine | 3+ proteins<br>3+ glucose |
| Urinary PCR | 3.7 |
| 24 hour urine proteins | 1450mg/dl |
| Viral markers | Non-reactive |
| Quantiferon-TB Gold (QTB) | Negative |
| Antiphospholipid profile | Negative |
| c-ANCA (IF) | Positive (1:10 dilution) |
| PR3-ANCA (ELISA) | 39.66 → 153 U/mL |
| p-ANCA | Negative |
| ANA (LIA-17) | Negative |
| Anti-dsDNA (ELISA) | Negative |
| HLA-B51 (PCR) | Positive |

## DISCUSSION

Antineutrophil cytoplasmic antibody-associated vasculitis (AAV) comprises autoimmune small-vessel diseases characterized by necrotizing inflammation and the presence of PR3- or MPO-ANCAs, though ANCA-negative forms also occur. The major subtypes include granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis. AAV predominantly affects the kidneys, lungs, and upper respiratory tract, often causing severe organ damage. Despite established classifications, atypical and overlap syndromes with immune-mediated diseases such as IgA nephropathy or Behçet-like illness are increasingly recognized, presenting diagnostic and therapeutic challenges. Early recognition and

immunosuppressive therapy remain vital for improving patient outcomes

AAV is caused by pathogenic ANCAs targeting proteinase-3 (PR3) or myeloperoxidase (MPO), which activate neutrophils, resulting in endothelial damage, necrotizing inflammation, and fibrinoid necrosis (15). The process encompasses NETosis, cytokine secretion, and complement activation, resulting in glomerular and systemic small-vessel injury (16). In contrast, IgA nephropathy (IgAN) is characterized by mesangial accumulation of aberrantly glycosylated IgA1 immune complexes, which activate complement through the alternative and lectin pathways (17). The coexistence of both diseases in this case indicates an immunological continuum between immune-complex and ANCA-mediated vasculitis, possibly initiated by prolonged antigenic stimulation or a common genetic predisposition (18).

The renal biopsy of our patient demonstrated mesangial IgA with kappa and lambda deposits and small-vessel necrotizing inflammation in the skin, indicative of mixed immune-complex and pauci-immune processes. This overlap has been intermittently documented and may suggest that IgA-mediated immune activation prime neutrophils for ANCA-mediated injury (19). Moreover, the presence of HLA-B51 and recurring mucocutaneous ulcers in our case suggest the potential for Behçet-like vasculitis, characterized by hyper-reactive neutrophil and endothelial responses (20). While ANCA positive is rare in Behçet's illness, its presence has been associated with increased severity of vascular involvement (21).

Masiak et al. (2024) examined 284 AAV patients and found that 14.1% had concurrent autoimmune disorders, including as thyroiditis, rheumatoid arthritis, and psoriasis. These individuals exhibited an extended delay to diagnosis and a less severe renal progression. This highlights that polyautoimmunity might alter disease phenotype and hinder early detection, reflecting our patient's unusual cutaneous onset with postponed renal manifestations.

The management of AAV is with high-dose corticosteroids with B-cell-depleting therapy. Cyclophosphamide and rituximab continue to be mainstay induction treatments, exhibiting similar remission rates in severe illness (24, 25). In overlapping circumstances, particularly when immune-complex deposition is present, treatment must weigh efficacy against the risk of infection, especially in patients with diabetes mellitus.

The patient was treated with pulse methylprednisolone, followed by an oral steroids and azathioprine was selected for maintenance considering the risk of infection. Furthermore, colchicine was incorporated to address Behçet-like mucocutaneous ulcerations (26). This combination led to rapid ulcer healing, stabilization of inflammatory markers, and remission within six months.

Overlapping vasculitis disorders may result in diverse consequences. Studies indicates that renal prognosis in ANCA + IgA overlap is dependent upon the predominant lesion pattern, with histopathology showing crescentic necrotising glomerulonephritis demonstrating inferior renal survival compared to those with mesangial IgA predominance (28). Timely identification and immunosuppressive treatment has good prognosis inrenal disease.

The favorable outcome in our patient, marked by cutaneous remission, removal of pulmonary nodules, and stabilization of renal function, shows the advantages of timely identification, biopsy correlation, and tailored immunosuppression.

## CONCLUSION

This case broadens the clinical spectrum of overlap vasculitis by highlighting the coexistence of ANCA-associated vasculitis with Behçet-like features and IgA nephropathyin a diabetic patient. It reinforces the concept that autoimmune diseases may intersect along shared immunopathogenic pathways, necessitating comprehensive serologic and histologic evaluation. Awareness of such overlap is essential for early diagnosis, appropriate immunomodulation, and improved patient outcomes.

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