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Review Article

# Pauciimmune vasculitis

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ABSTRACT

Pauciimmune vasculitis encompasses a group of systemic necrotizing vasculitis with paucity of immune complex deposition on microscopic examination. All these diseases have anti-neutrophil cytoplasmic antibody (ANCA) positivity, hence, also termed as ANCA associated vasculitides. It encompasses a spectrum of small vessel vasculitis; granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). Activated neutrophils (and eosinophils in EGPA) resulting from known and unknown environmental influences on a susceptible genetic background cause vascular injury in various organ systems. The spectrum of disease extends from involvement of upper and lower respiratory tracts to life threatening renal and nervous system involvement. High index of suspicion and early diagnosis and initiation of immunosuppression therapy is crucial for minimizing the risk of morbidity and mortality.


## 1. Introduction

The systemic necrotizing vasculitides are a group of multisystem disorders characterized by involvement of small and medium-sized vessels. Pauci-immune vasculitis is characterized by absent or minimal immune complex deposits in the vessel wall on histopathological examination of affected tissues. These diseases have anti-neutrophil cytoplasmic antibody (ANCA) (either to proteinase-3-PR3-ANCA or to myeloperoxidase – MPO-ANCA) positivity and are also known as – ANCA associated vasculitis (AAV). AAV comprise three distinct entities – Granulomatosis with polyangiitis (GPA), Microscopic polyangiitis (MPA) and Eosinophilic Granulomatosis with Polyangiitis (EGPA).

## 2. Classification criteria and nomenclature

Classification of AAV is a work in evolution. The American College of Rheumatology (ACR) in 1990[1] proposed classification criteria for seven vasculitides, including GPA (then called Wegener's granulomatosis)[2] and EGPA (then called Allergic granulomatosis with polyangiitis – AGPA)[3] but did not define MPA (Table 1). The Chapel Hill Consensus Conference (CHCC)

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**Table 1 – ACR 1990 classification criteria for GPA and EGPA.**

| Disease | Criteria | Number required to be positive | Sensitivity | Specificity |
|---|---|---|---|---|
| GPA (Wegener's granulomatosis)[2] | 1. Abnormal urinary sediment (red cell casts or greater than five red blood cells per high-power field)<br>2. Abnormal findings on chest radiograph (nodules, cavities, or fixed infiltrates)<br>3. Oral ulcers or nasal discharge<br>4. Granulomatous inflammation on biopsy | 2/4 | 88.2% | 92% |
| EGPA (AGPA/Churg-Strauss syndrome)[3] | 1. Asthma<br>2. Eosinophilia greater than 10% on differential blood cell count<br>3. Mononeuropathy (including multiplex) or polyneuropathy<br>4. Non-fixed pulmonary infiltrates on chest radiograph<br>5. Paranasal sinus abnormality<br>6. Biopsy containing a blood vessel with extravascular eosinophils. | 4/6 | 85% | 99.7% |

GPA; granulomatosis with polyangiitis, EGPA; eosinophilic granulomatosis with polyangiitis.

in 1994[4] defined GPA, MPA and EGPA amongst the 10 types of vasculitis; these were later modified in the 2012 Chapel Hill Consensus Conference[5] (Table 2). The current nomenclature, and hence forth in the review, recognizes three forms of AAV, viz. GPA, MPA and EGPA. A major international effort is currently underway, under the aegis of both the ACR and the EULAR (European League against Rheumatism) called as the Diagnosis and Classification of Vasculitis (DCVAS)[6] which aims to establish new criteria for vasculitis and validate them internationally.

## 3. Epidemiology and environmental factors

Varying rates of incidence and prevalence have been reported for AAV depending on the population studied and the definitions used. AAV are rare in childhood - GPA has been reported to have a low childhood annual incidence of 0.3/million. In adults, peak onset is in the seventh and eighth decades. For GPA, varying incidence rates of 0.7/million to 21/million have been reported, with a prevalence ranging from 23.7 to 160/million. MPA is reported to be more common in Asians than GPA; however it is more common in Caucasians than in Asians. Worldwide incidence rates vary from 0.5 to 24/million with prevalence varying from 39 to 104.7/million. Incidence rates for EGPA vary from 0.14 to 4/million, with prevalence from 14 to 45.7/million.[7] Data from India is scarce[8]; The diagnosis is often delayed due to high endemicity of pulmonary tuberculosis which may mimic GPA.[9] A declining North-South gradient has been described for GPA in the Northern hemisphere[10]; such a gradient is yet to be established in the Southern hemisphere[11] or for any of the other AAV. This suggests significant contribution of environmental factors to development of AAV. A case-control study from the UK described farming, silica exposure and history of allergy to be significant risk factors for AAV[12] (Table 3). Hydrocarbon exposure has been linked to ANCA vasculitis, with a propensity for pulmonary hemorrhage.[13] The association of drugs and ANCA-positivity as well as ANCA vasculitis is well described.[14] Usually MPO-ANCA results from drug exposure.

**Table 2 – 2012 Chapel Hill consensus definitions (quoted with permission from reference 5).**

| Disease | Definition |
|---|---|
| AAV | Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (i.e., capillaries, venules, arterioles, and small arteries), associated with myeloperoxidase (MPO) ANCA or proteinase 3 (PR3) ANCA. Not all patients have ANCA. Add a prefix indicating ANCA reactivity, e.g., MPO-ANCA, PR3-ANCA, ANCA- negative. |
| GPA | Necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small to medium vessels (e.g., capillaries, venules, arterioles, arteries and veins). Necrotizing glomerulonephritis is common. |
| MPA | Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (i.e., capillaries, venules, or arterioles). Necrotizing arteritis involving small and medium arteries may be present. Necrotizing glomerulonephritis is very common. Pulmonary capillaritis often occurs. Granulomatous inflammation is absent. |
| EGPA | Eosinophil-rich and necrotizing granulomatous inflammation often involving the respiratory tract, and necrotizing vasculitis predominantly affecting small to medium vessels, and associated with asthma and eosinophilia. ANCA is more frequent when glomerulonephritis is present. |

ANCA; anti neutrophil cytoplasmic antibody, AAV; ANCA associated vasculitis, GPA; granulomatosis with polyangiitis, EGPA; eosinophilic granulomatosis with polyangiitis, MPA; Microscopic polyangiitis, MPO; myeloperoxidase, PR3; proteinase 3.