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Editorial

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ANCA-associated vasculitis: a new therapeutic area for precision medicine

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The antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAVs) are categorized into three distinct and heterogeneous clinical conditions: granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA)[1].

They are rare autoimmune diseases of unknown aetiology, characterised by inflammation that can cause necrosis of blood vessels. AAVs are considered small vessel vasculitides but vessels of larger size may be involved. The discovery of perinuclear and cytoplasmic patterns on indirect immunofluorescence (P-ANCA and C-ANCA) and the main specificities myeloperoxidase and proteinase 3 (PR3) were recognised in the 1980s[2]. The Chapel Hill Consensus Conference described AAVs in 1994 and the classification was revised in 2012[1]. This classification, based on clinical phenotype, has been challenged as ethnic studies and genome-wide association studies clearly support the view of a genetic role in the aetiology of AAV and the associations with HLA (DQ in MPA), SERPINA1 (in GPA), and PRTN3 (in GPA) were primarily aligned with ANCA specificity rather than with clinical definition of GPA or MPA[3].

Although AAV is a rare disease, recent studies focusing on the healthcare burden of AAV reveal a high level of source consumption[4].

The clinical presentation can be quite varied, ranging from skin vasculitis to fulminant multisystem disease. Typical features of GPA include nasal crusting, epistaxis, uveitis, orbital mass, upper respiratory tract involvement with bronchial or tracheal stenosis, and often renal involvement. Patients with MPA present with more severe renal disease than GPA, together with polyneuropathy. EGPA typically presents with a multisystem disease (involving in particular the kidneys, heart, and peripheral nerves) on a background of asthma of adult onset, nasal polyposis, and peripheral blood or tissue eosinophilia[5].

In the large majority of patients, an induction of remission using cyclophosphamide or rituximab should be considered at the onset of AAV. Other induction regimens with methotrexate or mycophenolate mofetil should only be considered for patients with limited disease, without major organ involvement or life-threatening disease[6]

Pathogenesis of AAV involves B and T lymphocytes, endothelial cells, monocytes, ANCAs, and the alternative complement pathway[7].

Rituximab was approved by the Food and Drug Administration (FDA) in the 2011 in the induction treatment of patients with GPA and MPA, after two randomized trials demonstrated non-inferiority of rituximab to cyclophosphamide in inducing remission in both new and relapsed patients with GPA and MPA[5]. Rituximab is also recommended in maintaining remission in patients with GPA and MPA[5].

The optimal duration in terms of both efficacy and safety of rituximab maintenance remains still unknown, and optimizing B cell-depleting therapy as well as minimizing glucocorticoid regimens are main topics in the research agenda of AAV[8].

Very recently (October 8, 2021), avacopan, an orally administered selective complement 5a receptor inhibitor, has been approved by FDA as an adjunctive treatment of adult patients with severe active AAV, in combination with standard therapy[9]. It may represent a new step towards steroid-free regimens in AAV.

A better clinical and molecular characterization of AAV should drive this new drug discovery era in AAV in order to reach the ambitious goal of precision medicine in AAV[10].

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