PRIMEVIEW

ANCA-ASSOCIATED VASCULITIS

nature reviews disease primers

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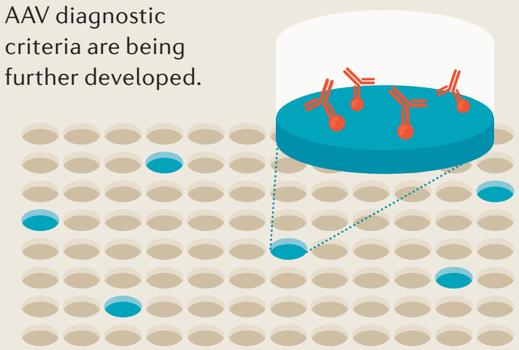
Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) comprises three autoimmune disorders, granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic GPA (EGPA), which all involve inflammation and damage in small blood vessels.

DIAGNOSIS

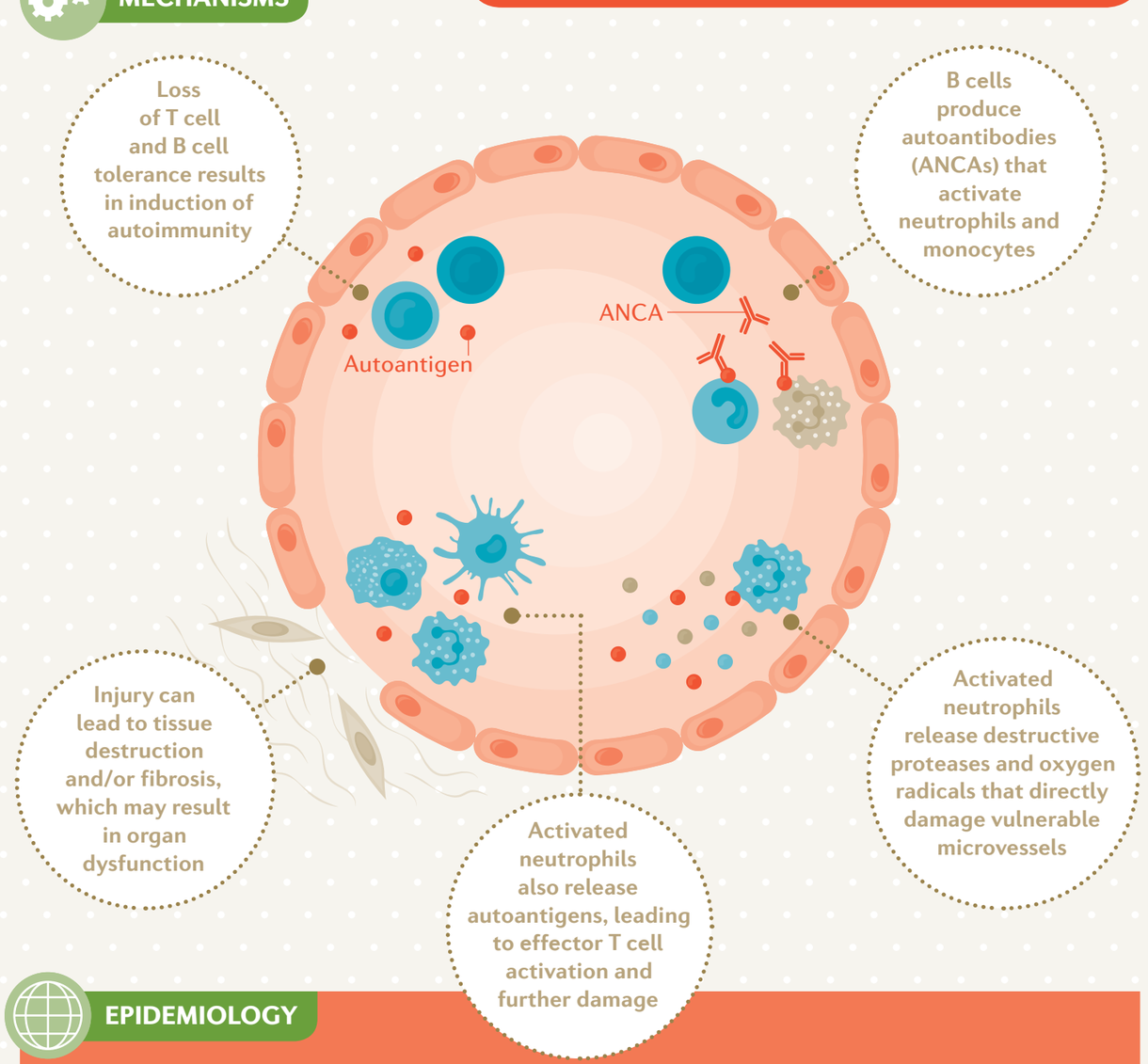
Patients with AAV usually present with non-specific symptoms of systemic inflammation, such as weight loss, fatigue, and joint and muscle pain, and are, therefore, often misdiagnosed. Various tissues and organs are affected in AAV, with frequent involvement of the respiratory tract (for example, asthma in EGPA) and the kidneys (glomerulonephritis). The Chapel Hill Classification defines the AAV subtypes based on vessels affected, manifestations and inflammatory features. Diagnosis of AAV relies on ANCA testing and assessment of clinical, imaging and histopathological evidence. However, detection of ANCAs (either leukocyte proteinase 3 (PR3)-ANCAs or myeloperoxidase (MPO)-ANCAs) is not in itself diagnostic of AAV, as they occur in other conditions. The AAV subtypes show histopathological differences; whereas all AAVs show necrotizing small-vessel vasculitis on biopsy, granulomas occur in GPA and eosinophilic infiltrates in EGPA.

AAV diagnostic criteria are being further developed.



MECHANISMS

GPA and MPA are associated with a loss of immunological tolerance to PR3 or MPO, whereas EGPA can be ANCA-positive (usually MPO-ANCA) or ANCA-negative



EPIDEMIOLOGY

AAVs are rare disorders, with GPA and MPA being more common than EGPA. AAV incidence varies by ethnicity: GPA is more common in white populations, whereas MPA is more common in Asian populations. Risk factors for AAV include both genetic and environmental factors, including infection and silica exposure. The use of some drugs, such as propylthiouracil and cocaine–levamisole, is also associated with ANCA-positive vasculitis with some AAV features. Epidemiological studies of specific AAV subtypes are needed to identify potentially distinct triggers for each subtype.

MANAGEMENT

Initial treatment to induce disease remission involves reducing inflammation with immunosuppressive drugs, typically glucocorticoids and either cyclophosphamide or rituximab. Thereafter, therapy to maintain remission involves minimizing the glucocorticoid dose and ongoing rituximab, or replacing cyclophosphamide with less-toxic immunosuppressive drugs, such as azathioprine or methotrexate. Organ damage in patients with AAV requires specialist assessment and management.

OUTLOOK

The understanding of AAV pathogenesis is increasing, leading to improvements in diagnosis and management of these diseases; however, challenges remain. Treatments are fairly non-specific and often have adverse effects, and the optimal duration and intensity of maintenance therapy is unclear. Further advances in knowledge of disease processes, improved diagnostic criteria and the identification of validated biomarkers to assess treatment response and predict relapse should aid in the development of more precise, personalized treatment. Potential treatments, such as immunomodulatory small-molecule inhibitors and monoclonal antibodies, as well as novel biomarkers to predict flares, such as markers of T cell activity or B cell abundance, are in various stages of development.

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