MOLECULAR MECHANISMS OF DYSFUNCTION IN HEMORRHAGIC VASCULITIS

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Abstract

Various pathogenic mechanisms have been implicated in the induction of vasculitis, including cell-mediated inflammation, immune complex-mediated inflammation and autoantibody-mediated inflammation.

Keywords: Biomarkers, classification, management, vasculitis.

Despite the lack of vasculitis in animal models of chronic serum sickness, current evidence implicates immune complex deposition as the primary pathogenic mechanism in vasculitis associated with chronic infections such as hepatitis B and hepatitis C-associated mixed cryoglobulinaemia, which primarily affect small. Pathophysiology of Vasculitis

A description of vessel wall damage (eg, type and location of inflammatory infiltrate, extent and type of damage, presence or absence of fibrinoid necrosis) A description of healing responses (eg, intimal hypertrophy, fibrosis).

Pathophysiology of Vasculitis

Histologic description of an affected vessel should include the following:

A description of vessel wall damage (eg, type and location of inflammatory infiltrate, extent and type of damage, presence or absence of fibrinoid necrosis)

A description of healing responses (eg, intimal hypertrophy, fibrosis)

Certain features (eg, predominant inflammatory cell type, location of inflammation) suggest particular vasculitic processes and may aid in the diagnosis. For example, in many acute lesions, the predominant inflammatory cells are polymorphonuclear leukocytes; in chronic lesions, lymphocytes predominate.

Inflammation may be segmental or involve the entire vessel. At sites of inflammation, varying degrees of cellular inflammation and necrosis or scarring occur in one or more layers of the vessel wall. Inflammation in the media of a muscular artery tends to destroy the internal elastic lamina. Some forms of vasculitis are characterized by giant cells in the vessel wall. In some vasculitic disorders, such as granulomatosis with polyangiitis or Kawasaki disease, the vessel inflammation (true vasculitis) is only part of the pathophysiology and there is predominant parenchymal inflammation in a characteristic pattern that involves specific organs.

Leukocytoclastic vasculitis is a histopathologic term used to describe findings in small-vessel vasculitis. It refers to breakdown of inflammatory cells that leaves small nuclear fragments (nuclear debris) in and around the vessels. Inflammation is transmural and nongranulomatous. Polymorphonuclear leukocytes predominate early; later, lymphocytes predominate. Resolution of the inflammation tends to result in fibrosis and intimal hypertrophy. Intimal hypertrophy or secondary clot formation can narrow the vessel lumen and cause tissue ischemia or necrosis.

The term 'systemic vasculitis' describes a heterogeneous group of rare diseases, the systemic vasculitides, characterized by inflammation and fibrinoid necrosis of blood vessel walls. Vasculitis may be primary in origin (with no identifiable cause) or it may be secondary to infection, malignancy, or autoimmune disease. Although rare, there is evidence to suggest that vasculitis accelerating atherosclerosis is a complicating feature of most, possibly all, autoimmune diseases. This includes connective tissue diseases (CTDs) such as rheumatoid arthritis (RA), scleroderma, sarcoidosis and systemic lupus erythematosus (SLE).

In this review, which focuses on vasculitis associated with CTDs, we look at the progress that has been made in classifying the systemic vasculitides and discuss the pathogenesis of systemic vasculitides in CTDs and their adverse clinical sequelae, giving particular attention to RA and SLE. The standardized treatment for vasculitis is effective in the majority of patients, but some relapse and need other therapeutic approaches. In evaluating new treatment strategies for the management of systemic vasculitis, we explore the role of endothelin (ET)-1 in systemic vasculitides and discuss the therapeutic potential of endothelin receptor blockade in these entities.

Classification of the systemic vasculitides

Early attempts to classify systemic vasculitis into discrete categories were based primarily on blood vessel size, and indeed that approach still underpins more recent classification schemes.

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