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4

Vasculitis related to viral and other microbial agents

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A B S T R A C T

Vasculitis due to infection may occur as a consequence of the inflammation of vessel walls due to direct or contiguous infection, type II or immune complex-mediated reaction, cell-mediated hypersensitivity, or inflammation due to immune dysregulation triggered by bacterial toxin and/or superantigen production. As immunosuppressive therapy administered in the absence of antimicrobial therapy may increase morbidity and fail to effect the resolution of infection-associated vascular inflammation, it is important to consider infectious entities as potential inciting factors in vasculitis syndromes. The causality between infection and vasculitis has been established in hepatitis B-associated polyarteritis nodosa (HBV-PAN) and hepatitis C-associated (cryoglobulinemic) vasculitis (HCV-CV). The review summarizes the recent literature on the pathophysiological mechanisms and the approaches to the management of HBV-PAN and HCV-CV. Roles of other viral and microbial infections, which either manifest as vasculitic syndromes or are implicated in the pathogenesis of primary vasculitides, are also discussed.

Abbreviations: MC, mixed cryoglobulinemia; CV, cryoglobulinemic vasculitis; RF, rheumatoid factor; Ig, immunoglobulin; GCA, giant cell arteritis; PAN, polyarteritis nodosa; HSP, Henoch–Schonlein purpura; KD, Kawasaki's disease; GPA, granulomatosis with polyangiitis; HIV, human immunodeficiency virus; AIDS, acquired immune deficiency syndrome; PCR, polymerase chain reaction; IVIG, intravenous immunoglobulin.

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Practice points

- Viral and microbial etiologies should be considered in any vasculitic syndrome.
- Testing for HBV and HCV should be performed in the evaluation of small-to medium-sized vessel vasculitis, in particular PAN and CV.
- Treatment of infection-related vasculitis requires eradicating the infective agent as well as using immunosuppressive drugs as needed to control vascular inflammation/damage.

Research points

- Clinical trials are needed to assess the efficacy and safety of steroids and other immunosuppressive agents, for example, biologics, to improve the treatment of severe HBV-PAN and HCV-CV.

Introduction

Infection is a well-recognized trigger of vasculitis. The mechanisms may involve the direct infection of vascular wall or via indirect immunological effects such as type II, III, or IV hypersensitivity reactions [1,2]. Many infectious agents including viral, bacterial, or fungal agents, or microbial antigens have been reported in the literature to be associated with vasculitis (Table 1). However, a causal relationship has only been firmly established in a few instances of vasculitis, such as chronic hepatitis B virus (HBV)-associated polyarteritis nodosa (PAN) and hepatitis C virus (HCV) with cryoglobulinemic vasculitis. These two entities are included as "vasculitis associated with probable etiology" in the 2012 Chapel Hill Consensus Conference on the Nomenclature of Vasculitides [3]. It is crucial to evaluate for infective etiologies in any workup of vasculitis so that appropriate antimicrobial/viral therapies can be given as the etiology-based treatment, as immunosuppressants alone may not be sufficient and may even be detrimental.

While a vasculitic syndrome may be readily identified in a patient with an established diagnosis of HBV or HCV, vasculitis may present as an uncommon feature of a ubiquitous infection. Therefore, a heightened suspicion for temporal and epidemiological clues is necessary. This review article primarily addresses HBV- and HCV-related vasculitis, and, briefly, it covers vasculitis associated with other microorganisms.

HBV-associated PAN

Clinical manifestations

Characterized by arteritis of medium/small arteries without small-vessel involvement, glomerulonephritis, or antineutrophil cytoplasmic antibodies (ANCAs), PAN is classified as an idiopathic

Table 1
Vasculitis syndromes and associated infectious agents.

Giant cell arteritis; aortitis	*Coxiella burnetii*, Parvovirus B19, Cytomegalovirus, Varicella zoster
Central nervous system vasculitis	*Mycoplasma pneumoniae*, Varicella zoster
Polyarteritis nodosa	Hepatitis B Virus, Hepatitis C Virus, Epstein–Barr virus, Cytomegalovirus, Parvovirus B19, Ehrlichiae
Kawasaki's disease	*Mycoplasma pneumoniae*, Epstein–Barr virus, Parvovirus B19
Granulomatosis with polyangiitis	*Staphylococcus*, Epstein–Barr virus, Parvovirus B19
Henoch–Schonlein purpura	*Mycoplasma pneumonia*, Parvovirus B19, Cytomegalovirus
Behcet's disease	Parvovirus B19