Neoplastic and Paraneoplastic Vasculitis, Vasculopathy, and Hypercoagulability

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KEYWORDS

• Neoplastic • Paraneoplastic • Vasculitis • Vasculopathy
• Hypercoagulability

Rheumatologists are often consulted regarding both typical and atypical vasculitides, vasculopathies, and hypercoagulability. It is important to keep in mind that all of these can come from neoplastic or paraneoplastic causes. In these cases, the treatment must focus on treating the underlying malignancy rather than aggressive immunosuppression. This article focuses on reported cases, pathophysiologic mechanisms, and lessons that can learned from the literature regarding neoplastic and paraneoplastic vasculitides, vasculopathies, and hypercoagulability.

Currently, the literature regarding malignancy-related vasculitides, vasculopathies, and hypercoagulability mostly comprises case reports. Some reports are on cases in which the paraneoplastic phenomenon precedes the diagnosis of malignancies by years.[1,2] However, there are many case-series and registry data suggesting that certain vasculitides, vasculopathies, and hypercoagulability states (eg, antiphospholipid syndrome) may increase the risk of malignancy.[3,4] Medications commonly used in treating these vascular syndromes have also been reported to increase the risk of malignancy.[5,6] There are also reports of specific chemotherapy drugs causing cutaneous vasculitis.[7,8] Hence, outside of cases clearly illustrated to be paraneoplastic, this article only includes cases in which the malignancy and the paraneoplastic manifestations are diagnosed within 12 months of each other.

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Another complicating factor is that most vasculitides, vasculopathies, and hypercoagulable states are thought to be triggered by a particular event, which may include malignancy, in a genetically susceptible host. This may account for the various types of vascular syndromes associated with various malignancies rather than one type of syndrome being associated with a particular neoplasm. Malignancy could serve as a trigger and, once triggered, vasculitis could run a course independent of the malignancy.[9] In this article, only case reports of concordant disease courses will be included (**Box 1**).

PATHOPHYSIOLOGY

The exact pathophysiology of paraneoplastic vascular syndromes is unknown. This article describes pathophysiologic mechanisms as they pertain to each vascular syndrome. In general, proposed mechanisms involve an increased cellular turnover leading to generation of autoantibodies that cannot be appropriately cleared. Whereas this accounts for the increased incidence of autoantibodies found in patients with malignancies, it fails to explain the lack of immune complexes in many paraneoplastic vasculitides.[10] Release of tumor angiogenic factors and/or cytokines, which in turn cause endothelial damage and increased vascular permeability, inflammation, and fibrosis, has been postulated as another potential mechanism.[9,11,12]

Box 1
Neoplastic and paraneoplastic vascular syndromes

Vasculitis

Immune complex–mediated

- Leukocytoclastic vasculitis (Palpable purpura, UV, EED)
- Henoch-Schönlein purpura
- Cryoglobulinemia

ANCA-associated

- Granulomatosis with polyangiitis
- Microscopic polyangiitis
- Churg-Strauss

Other

- Primary angiitis of central nervous system
- Giant cell arteritis
- Polyarteritis nodosa

Vasculopathy

Cutaneous lymphocytic vasculopathy

Raynaud's phenomenon

Erythromelalgia

Hypercoagulability

Thromboembolism

Antiphospholipid antibodies

Abbreviations: ANCA, antineutrophil cytoplasmic antibody; EED, erythema elevatum diutinum; UV, urticarial vasculitis.