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Overlap Syndromes: Coexistence of ANCA-associated Vasculitis and Hematologic Cancers

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Introduction

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) represents a group of autoimmune diseases characterized by the inflammation of small to medium-sized blood vessels, leading to organ damage. The primary forms of AAV include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) andeosinophilic granulomatosis with polyangiitis (EGPA). These syndromes are hallmarked by the presence of circulating ANCAs, directed against specific components of neutrophil granules, most notably proteinase 3 (PR3) and myeloperoxidase (MPO). While AAV is primarily known for its impact on organs such as the kidneys, lungs andskin, increasing evidence points to its intersection with hematologic malignancies, leading to complex clinical presentations that challenge diagnosis, treatment andprognosis. The coexistence of AAV and hematologic cancers is referred to as an "overlap syndrome," denoting the simultaneous or sequential development of both conditions in a single patient. This intersection is more than a coincidence; it may reflect shared pathogenic pathways, immune dysregulation, or therapy-related effects andit carries important implications for both research and clinical practice [1].

Description

The incidence of hematologic malignancies, such as lymphomas, leukemias andmyelodysplastic syndromes, appears to be increased in patients with autoimmune diseases, including AAV. Multiple epidemiological studies have indicated a bidirectional relationship wherein AAV may predispose patients to certain hematologic cancers and, conversely, hematologic malignancies may trigger or mimic AAV-like vasculitic syndromes. This complex interplay necessitates a nuanced understanding of their overlapping clinical, immunological andpathological features. Clinically, patients may present with constitutional symptoms such as fever, weight loss andfatigue, which are common to both AAV and hematologic cancers, leading to diagnostic confusion. Laboratory findings such as anemia, elevated inflammatory markers andabnormal leukocyte counts further complicate the clinical picture, especially when ANCAs are detected in malignancy-associated settings. Therefore, distinguishing true AAV from paraneoplastic vasculitis or ANCA positivity secondary to malignancy becomes imperative to guide appropriate treatment strategies [2].

The pathogenesis of the overlap between AAV and hematologic malignancies is multifactorial. Immune dysregulation is a central theme in both conditions. In AAV, the breakdown of tolerance leads to the production of pathogenic ANCAs, which activate neutrophils and cause vascular injury. In hematologic cancers, particularly lymphomas and leukemias, malignant transformation often arises from defects in immune surveillance or antigen-driven proliferation. It is plausible that chronic immune activation in AAV contributes to an environment conducive to oncogenesis. Persistent inflammation, repeated cycles of tissue damage and repair andlong-term immunosuppressive therapy, particularly with agents such as cyclophosphamide, have all been implicated in increasing the risk of malignancy in these patients. Conversely, hematologic malignancies themselves may induce autoimmune phenomena, including vasculitis, through the production of autoantibodies, cytokine dysregulation, or direct infiltration of vascular tissues by malignant cells [3].

Diagnosis of overlap syndromes involving AAV and hematologic malignancies is inherently challenging and necessitates a multidisciplinary approach. A thorough clinical evaluation, coupled with detailed laboratory work-up and imaging, is essential to delineate the nature of the disease process. Renal biopsy, skin biopsy, or bone marrow examination may be necessary to confirm vasculitic involvement and to detect malignancy. Immunohistochemistry and molecular studies can provide critical insights into clonality and immune phenotypes. The presence of ANCAs should be interpreted cautiously in the context of malignancy, as low-titer ANCA positivity can be seen in a range of neoplastic and infectious conditions without true vasculitic pathology. In contrast, high-titer, disease-specific ANCAs, such as PR3-ANCA or MPO-ANCA, in conjunction with compatible clinical and histologic features, support the diagnosis of true AAV [4].

Treatment of patients with overlapping AAV and hematologic malignancies presents significant therapeutic dilemmas. Standard therapy for AAV typically includes high-dose corticosteroids and immunosuppressive agents such as cyclophosphamide, rituximab, azathioprine, or methotrexate. However, many of these agents are also used in the treatment of hematologic cancers, raising concerns about cumulative toxicity, immunosuppression andtreatment-related complications. For example, rituximab, a monoclonal antibody targeting CD20, is effective in both AAV and B-cell lymphomas and may serve as a unifying therapeutic agent in overlap syndromes. In addition to biological mechanisms, psychosocial and quality-of-life aspects must be considered in patients with overlap syndromes. The burden of dual diagnoses, uncertainty regarding prognosis andthe complexity of treatment regimens contribute to significant psychological stress, fatigue anddiminished quality of life. Supportive care, including psychosocial counseling, nutritional support andsymptom management, should be integrated into the overall care plan. Coordination among rheumatologists, hematologists, nephrologists, pathologists andprimary care providers is essential to ensure holistic, patient-centered management [5].

Conclusion

In conclusion, the coexistence of ANCA-associated vasculitis and hematologic malignancies represents a challenging yet fascinating overlap syndrome that underscores the deep interconnection between autoimmunity and cancer. While the precise mechanisms remain incompletely understood, growing evidence supports a multifaceted relationship involving immune dysregulation, chronic inflammation, therapeutic exposures andshared genetic susceptibilities. Accurate diagnosis requires high clinical suspicion, judicious use of diagnostic tools andawareness of the diverse presentations of both

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diseases. Treatment must be tailored to the individual, balancing the need for immunosuppression with the control of malignancy and minimizing harm. As our understanding of the immune system deepens, new opportunities will arise to better diagnose, treat andultimately prevent these complex and intersecting disorders, paving the way for improved outcomes and enhanced quality of life for affected patients.

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Conflict of Interest

None.

References

1. Mejia-Vilet, Juan M., Ana Malvar, Arnon Arazi and Brad H. Rovin. "The lupus nephritis management renaissance." *Kidney Int* 101 (2022): 242-255.
2. Kitching, A. Richard, Hans-Joachim Anders, Neil Basu and Elisabeth Brouwer, et al. "ANCA-associated vasculitis." *Nat Rev Dis Primers* 6 (2020): 71.
3. Jennette, J. Charles and Ronald J. Falk. "Pathogenesis of antineutrophil cytoplasmic autoantibody-mediated disease." *Nat Rev Rheumatol* 10 (2014): 463-473.
4. Jennette, J. Charles, Ronald J. Falk and Marco A. Alba. "Nomenclature of Vasculitides: 2012 Revised International Chapel Hill Consensus Conference: Nomenclature of Vasculitides and Beyond." *Arthritis Rheum* 65 (2016): 15-28.
5. Ayoub, Isabelle and Patrick H. Nachman. "Advances in ANCA-associated vasculitis and lupus nephritis." *Nat Rev Nephrol* 17 (2021): 89-90.

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