Current Landscape of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis

Classification, Diagnosis, and Treatment

Lindsay Lally, MD*, Robert Spiera, MD

KEYWORDS

- ANCA-associated vasculitis • Granulomatosis with polyangiitis (Wegener)
- Microscopic polyangiitis
- Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)

KEY POINTS

- Antineutrophil cytoplasmic antibody (ANCA) positivity by immunofluorescence should be confirmed with ELISA for proteinase-3 (PR3) or myeloperoxidase (MPO) in the diagnosis of ANCA-associated vasculitides (AAVs). Tissue biopsy for histologic confirmation should be obtained whenever possible.
- ANCA specificity may be associated with different prognostic and phenotypic features in granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA). Additionally, in eosinophilic granulomatosis with polyangiitis (EGPA), different clinical manifestations may be observed in those with ANCA positivity compared with those who are ANCA negative.
- Treatment of AAVs, which is divided into an induction phase followed by remission maintenance, should be tailored to disease activity and severity. Optimal duration of maintenance therapy is unknown.

INTRODUCTION

The AAVs include GPA, formerly Wegener's granulomatosis; MPA; and EGPA, formerly Churg-Strauss syndrome. These 3 primary systemic vasculitides are multisystem diseases characterized by pauci-immune necrotizing vasculitis of small- to

Disclosure Statement: The authors have nothing to disclose.
Division of Rheumatology, Hospital for Special Surgery, 535 East 70th Street, New York, NY 10021, USA
* Corresponding author.
E-mail address: lallyl@hss.edu

Rheum Dis Clin N Am 41 (2015) 1–19
http://dx.doi.org/10.1016/j.rdc.2014.09.003 **rheumatic.theclinics.com**
0889-857X/15/$ – see front matter

medium-sized blood vessels and an association with serologically detectable ANCAs in a majority of cases. Change has transformed the field of AAVs in recent years with the introduction of new nomenclature for these diseases, novel insights into the genetic underpinnings of AAVs, and advances in therapeutic approach, including the use of biologics.[1–4] This article focuses on the current understanding of AAV diagnosis and management and highlights existing controversies and unmet needs in the care of patients with AAVs. Because of differences in clinical phenotype, disease course, and serologic positivity, EGPA is discussed separately at the end of this article.

CLASSIFICATION AND NOMENCLATURE

The 1990 American College of Rheumatology (ACR) classification criteria for the systemic vasculitides proposed a series of criteria meant to enable discrimination between the various forms of systemic vasculitis.[5,6] At the time the ACR criteria were created, MPA was not recognized as a distinct entity; thus, classification criteria for MPA were not created. As such, the ACR criteria for GPA are of limited value in differentiating between GPA and MPA. These classification criteria were created before ANCA testing was widely available, so ANCAs, which have an undisputed role in the diagnosis of AAVs, were excluded from classification criteria.

Despite high sensitivity and specificity, ACR criteria are of limited value in AAVs, especially in distinguishing between GPA and MPA, which have certain clinical and histologic differences. GPA is characterized by necrotizing small vessel vasculitis with extravascular granulomatous inflammation, which is not present in MPA. Although pulmonary and renal involvement is common in both GPA and MPA, granulomatous involvement of the upper and lower airway occurs exclusively in GPA. Otolaryngologic manifestations, including rhinosinusitis, serous otitis media, and subglottic inflammation, are present in an estimated 90% of patients with GPA, making this the most commonly involved organ system in GPA,[7] whereas glomerulonephritis is the most frequent manifestation in MPA. These phenotypic distinctions may confer important prognostic and therapeutic differences, discussed later.

In 2012, the International Chapel Hill Consensus Conference on the Nomenclature of Systemic Vasculitides (CHCC) was convened with a goal of redefining the vasculitic syndromes with nomenclature reflective of the underlying pathogenesis, pathology, and clinical characteristics.[1] The 2012 CHCC nosology eliminated eponyms from the AAV nomenclature and cemented presence of granulomatous inflammation in the respiratory tract as the key difference between GPA and MPA. This nomenclature fails to account for ANCA antigen specificity, which some experts think should be included with clinicopathologic phenotype in classification of AAVs.[8,9] Efforts to create more comprehensive classification and diagnostic criteria for AAV are under way with an international observational study designed to develop and validate classification and diagnostic criteria for primary systemic vasculitis, including the AAVs.[10]

ANTINEUTROPHIL CYTOPLASMIC ANTIBODY

Antineutrophil Cytoplasmic Antibody Detection

Circulating ANCAs with different immunofluorescence patterns and antigen specificities characterize GPA and MPA. ANCAs, which have demonstrated pathogenicity in animal, in vitro, and ex vivo models,[11,12] are also an important diagnostic tool. In making a diagnosis of AAVs, the utility of ANCAs depends on the clinical setting and on the assay used. A perinuclear (p-ANCA) or cytoplasmic (c-ANCA) pattern may be seen by indirect immunofluorescence; however, this technique is hampered by potential for interference by antinuclear antibodies and subjective interpretation. Positive