Ocular Manifestations of ANCA-associated Vasculitis

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KEYWORDS

• Wegener's granulomatosis • Churg-Strauss syndrome
• Microscopic polyangiitis • Antineutrophil cytoplasmic antibody

Vasculitis is characterized by blood vessel inflammation and necrosis of vascular endothelium. End-organ damage is the result of the destruction and occlusion of blood vessels. The antineutrophil cytoplasmic antibody (ANCA) associated vasculitides—Wegener's granulomatosis (WG), microscopic polyangiitis (MPA), and Churg-Strauss syndrome (CSS)—are diseases in which small to medium-sized blood vessels are affected. ANCAs not only serve as a marker for disease but are also thought to play a major role in disease pathogenesis. Proteinase-3 and myeloperoxidase, the two antigens that are the targets of ANCAs observed in these diseases, are found within the neutrophil, and degranulation of these leukocytes is thought to initiate the cascade of destruction.[1–3]

Of the three ANCA-associated vasculitides, WG is the most common. In a population-based study from Norfolk, England, the incidence of WG was 8.5 cases per million. The reported incidences of MPA and CSS were 3.6 cases and 2.4 cases per million, respectively.[4] Ophthalmologic findings, with ocular blood vessels as the target of disease, can be common, particularly in WG. They can sometimes be the presenting finding. Ocular or orbital involvement has been reported to occur in 29% to 52% of patients with WG.[5–7] In one cohort of 158 patients, 15% presented with ocular manifestations at diagnosis.[8] Ocular or orbital disease occurs less frequently in MPA and CSS. In a cohort of 85 patients with MPA, confirmed in most on biopsy, only one had ocular manifestations.[9] However, ocular findings can still be the initial presenting sign in these diseases.[2]

Therefore, the ability to recognize the ocular manifestations of vasculitis and associate them with the underlying systemic disease is important so that treatment can be

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initiated promptly to prevent morbidity and mortality. The systemic findings of WG, MPA, and CSS are described in other articles within this issue (see the articles by Chung and Seo; Baldini and colleagues; Holle and colleagues elsewhere in this issue for futher exploration of this topic). This article describes ocular and orbital findings (**Table 1**). However, one must be aware that many of the findings described and illustrated here are not pathognomic for ANCA-associated vasculitis and may be seen in other vasculitic, inflammatory, or infectious processes.

CONJUNCTIVAL, EPISCLERAL, AND SCLERAL DISEASE

These manifestations can sometimes be difficult to distinguish from each other because they all can present with ocular redness and discomfort. The key to distinguishing them is recognizing the depth of tissue involvement associated with the blood vessel plexus (**Fig. 1**). For example, in episcleritis, the superficial episcleral plexus is thought to be affected by the vasculitis process (see **Fig. 1**B), in contrast to scleritis, in which the deep episcleral plexus is affected (see **Fig. 1**C).

Conjunctival disease has been reported to occur in 4% to 16% of patients with WG.[10–12] Early disease presents with conjunctival hyperemia. Granulomas can also be present and disease is often bilateral. Progressive disease is characterized by cicatrizing conjunctivitis, which may result in symblepharon, or bands of fibrovascular tissue stretching across the ocular surface to the eyelids; entropion with an inturning eyelid; and trichiasis with eyelashes directed against the globe (**Fig. 2**). The palpebral surface of the upper eyelid is most commonly involved. Ocular exposure may occur, increasing the risk of secondary infectious keratitis. Exposure is often exacerbated by a tear deficiency caused by loss of the mucin-producing conjunctival goblet cells and destruction of lacrimal glands. Symptoms of conjunctival disease often include ocular redness, foreign body sensation, blurred vision from tear dysfunction, and possibly bloody tears.

The first reported case of MPA involving the conjunctiva and eyelid was in a 23-year-old black woman with renal failure and ulcerative skin and conjunctival nodules.

Table 1
Prevalence of ophthalmic findings in the ANCA-associated vasculitides

	Wegener's Granulomatosis	Microscopic Polyangiitis	Churg-Strauss Syndrome
Conjunctivitis	4%–16%	+	+
Episcleritis	+	+	+
Scleritis	16%–38%	+	–
Peripheral ulcerative keratitis	+	+	+
Retinal vasculitis	+	+	+
Orbital disease Mass/myositis/ dacryoadenitis	+	–	+
Nasolacrimal obstruction	7%–10%	–	–
Neuroophthalmic manifestations	+	–	+

Numerical values listed are obtained from the references listed in the text. Plus signs indicate manifestations that have been documented in case reports. Minus signs indicate manifestations that have not yet been reported for the respective disease entity.