Uveitis in Granulomatosis with Polyangiitis (GPA)

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Introduction

Granulomatosis with polyangiitis (GPA) (previously Wegener's granulomatosis) is part of the spectrum of systemic necrotizing vasculiites. It is a rare systemic inflammatory disease with necrotizing granulomatous vasculitis of the small-to-medium sized vessels. The disease usually manifests in adults but rare cases have been reported in the pediatric population [1]. GPA can affect any organ, but most commonly affects the sinuses and lungs (respiratory tract), kidneys, and the eye [2]. The granulomatosis is characterized by necrosis and thrombosis of the vessels.

Ocular Manifestations

Ophthalmologic disease is the manifesting feature of GPA in 8–16 % of patients but develops in an estimated 50–60 % of patients [4]. Orbital disease (30 %), episcleritis, scleritis, and conjunctivitis are the most common ophthalmological manifestations of GPA. Uveal involvement and granulomatous sclerouveitis are less common presentations. Uveitis (including anterior and posterior involvement) accounts for less than 10 %, and retinal involvement accounts for less than 5 % of ocular manifestations of GPA [5].

Anterior, posterior, and panuveitis have all been described in isolation or is associated with scleritis in GPA. The majority of uveitis in GPA is an anterior uveitis (70 % of uveitis cases) and more commonly occurs synchronously with anterior scleritis [6]. Anterior uveitis can be acute, granulomatous, or chronic with relapsing phases and may induce cystoid macular edema [7]. Clinical examination may range from mild ocular injection to significant inflammation with mutton fat keratic precipitates and substantial synechiae.

Posterior uveitis, including retinal vasculitis is a rare manifestation of GPA, accounting for less than 5 % of uveitis cases [6]. It can occur in conjunction with posterior scleritis and clinical presentation can range from cotton wool spots to severe vaso-occlusive disease with vasculitis, thrombosis, exudates and hemorrhages, and optic neuropathy, all with potentially significant visual morbidity [5].

Isolated choroiditis has also been reported in GPA patients that can clinically manifest as uveitis, choroidal folds, RPE changes, and occlusion of choroidal vessels. On

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histopathology, there is infiltration of the choroidal vessels with granulomatous inflammation [8].

Laboratory Testing

Laboratory tests that suggest GPA can be nonspecific but more indicative of inflammation such as anemia, leukocytosis, thrombocytosis, and elevated ESR and CRP. ANCA (Anti-neutrophil cytoplasmic antibody) is present in 80–90 % of patients with GPA, although positive ANCA can also be seen with other small-to-medium vessel disease such as MPA (microscopic polyangiitis) [2]. It is the clinical manifestations of end organ disease that separates these disease entities. The c-ANCA measures antibody to neutrophil serine proteinase; p-ANCA corresponds to antibody directed against lysosomal enzymes, lactoferrin, or myeloperoxidase. The ANCA titers do not necessarily correlate with disease severity and should not be used for clinical response monitoring to therapeutic interventions [3].

Treatment

Treatment of GPA requires a multidisciplinary effort as disease activity may involve multiple organ systems. Ocular GPA requires in-depth evaluation of other potential organ involvement as the eye disease may be a harbinger of more widespread systemic disease even if the patient has minimal symptoms. Treatment of ocular disease must involve control of systemic inflammation in addition to periocular or topical agents. First line therapy usually includes the use of systemic corticosteroids and cytotoxic medications. Combination of steroids and cytotoxic agents are the usual mainstay of ocular GPA, especially with use of cyclophosphamide for induction. Rituximab has similarly been shown to induce remission effectively. After initial control, many patients are able to be kept in remission with use of low dose corticosteroids with either Methotrexate, mycophenolate mofetil, or azathioprine. With aggressive management, GPA has a mean survival rates of >95 % with the current immunomodulatory therapies available [3].

Conclusion

Granulomatosis with polyangiitis (previously Wegener's granulomatosis) is a rare systemic inflammatory disease that can affect any organ but more commonly the sinuses, lungs, kidneys, and eyes. Ophthalmological disease is the manifesting feature of GPA in 8–16 % of patients but develops in an estimated 50–60 % of patients [4]. Orbital disease, episcleritis, scleritis, and conjunctivitis are the most common ophthalmological manifestations of GPA but uveitis has also been reported (less than 10 % of GPA cases). The diagnosis is established by serologic testing for ANCA (Anti-neutrophil cytoplasmic antibody) which is present in 80–90 % of patients with GPA. The mainstay of treatment is high dose corticosteroids along with cytotoxic agents (cyclophosphamide, methotrexate) and more recently biologic therapies (Rituximab).

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