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Ocular Involvement in Systemic Vasculitis Associated With Perinuclear Antineutrophil Cytoplasmic Antibodies

Antineutrophil cytoplasmic antibody (ANCA) formation to myeloperoxidase or perinuclear (p-ANCA) is infrequent in ocular disease and is reported in approximately 10% of patients with Wegener granulomatosis. As opposed to cytoplasmic (c-ANCA) positivity (antibodies to proteinase 3), which is well recognized, higher levels of p-ANCA are also identified in microscopic polyangiitis, Churg-Strauss syndrome, inflammatory bowel disease, and crescentic glomerulonephritis. The sensitivity and specificity of both tests are high for a vasculitic process frequently associated with a systemic disease that requires prompt immunosuppressive therapy. 1,2

We report 4 cases of p-ANCA positivity showing a spectrum of severe ocular involvement. Two patients had been systemically unwell previously, but it was the ocular disease that prompted ANCA measurement.

Report of Cases. Case 1. A 76-year-old man had a 12-month history of red smarting eyes. Examination revealed bilateral peripheral ulcerative keratitis with normal visual acuity and no proptosis. Investigations revealed chronic renal failure and elevated lesions at the level of the retinal pigment epithelium at the posterior pole in case 4.

Figure 1. Photograph showing right convergent squint, periorbital edema, and eyelid erythema but no proptosis in case 2.

Figure 2. Fundus photograph of the right eye showing a swollen optic disc and creamy white, elevated lesions at the level of the retinal pigment epithelium at the posterior pole in case 4.

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fluorescence and late hyperfluorescence at fluorescein angiography. Magnetic resonance imaging showed marked, diffuse enhancement of the pachymeninges, results of a lumbar puncture indicated central nervous system inflammation, and p-ANCA findings were positive (anti-myeloperoxidase 54%).

Treatment with immunosuppressants resulted in a reduction in p-ANCA titre with dramatic improvement of symptoms. Despite 1 recurrence of headache associated with an increase in p-ANCA levels, 5 years later the patient’s disease remained well controlled with oral steroids.

Comment. These 4 cases demonstrate the diversity and aggressiveness of eye disease associated with systemic vasculitis characterized by increased p-ANCA levels. Two patients probably have Wegener granulomatosis, 1 with chronic renal failure, keratomalacia, and vasculitic anterior ischemic optic neuropathy and the other with necrotizing glomerulonephritis, enlarged orbital muscles, and peri orbital inflammation. The presence of p-ANCA in conjunction with the clinical signs and chronic renal failure led to the diagnosis of systemic vasculitis and probably Wegener granulomatosis. In the latter case, both c-ANCA and p-ANCA findings were positive. Interestingly, neither patient showed evidence of proptosis, and the latter had no scleritis or pain.

In case 3, the patient had ulcerative colitis, one of the rarer associations of p-ANCA, and developed posterior scleritis progressing to serous retinal detachments. In a study of patients with anterior uveitis, p-ANCA was a susceptibility marker for immune-mediated diseases, including ulcerative colitis.3

In case 4, the patient had diffuse inflammatory pachymeningitis with multiple cranial neuropathies and choroiditis similar to acute multifocal pigmented epiphieliopathy. As far as we are aware, no case of increased p-ANCA levels and acute multifocal placoid pigment epitheliopathy has previously been reported.

Other reports of p-ANCA in association with central nervous system and ocular disease include a case of Wegener granulomatosis with pachymeningitis, multiple cranial neuropathies, and central retinal artery occlusion.4 and 1 of pseudo-Foster Kennedy syndrome with pachymeningitis.5 Prompt systemic treatment in both cases resulted in a favorable systemic response, although vision did not improve.

In all cases, p-ANCA testing was repeated to confirm positivity, and serial measurements showed a reduction in titre with treatment in 2 cases. Results of other studies have also shown correlation with disease activity.2

This series highlights the importance of p-ANCA in addition to c-ANCA in the diagnosis of often aggressive ocular disease that involves the sclera, orbit, and posterior ciliary circulation associated with systemic vasculitis and that all require immunosuppressive treatment.1

In 2 cases, no other systemic involvement was evident until after the eye manifestation, and in the third case, if p-ANCA levels had been tested previously, with appropriate therapy the patient may have avoided relapse. Positive p-ANCA findings highlight the need for referral for a systemic workup and prompt administration of immunosuppressive agents to reduce the risk of visual morbidity, organ damage, and even death.

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