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Episcleritis as the Primary Clinical Manifestation in a Patient With Polyarteritis Nodosa

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Purpose: To alert ophthalmologists to ocular manifestations that could indicate polyarteritis nodosa.

Case: A 71-year-old man exhibited unilateral episcleritis as the primary clinical manifestation of polyarteritis nodosa.

Observations: The patient's ocular symptoms did not respond well to either topical betamethasone eye drops or low-dose oral prednisone. Five months after the onset of ocular symptoms, the patient progressively developed fever, pneumonia, and renal dysfunction. Positive antineutrophil cytoplasmic antibody indicated polyarteritis nodosa as the underlying systemic disease. Intravenous methylprednisolone (1 g/day) was started; however, the patient succumbed 10 days later after intracranial hemorrhage.

Conclusions: Ophthalmologists should be aware that such a common ocular manifestation as episcleritis can be the initial manifestation of polyarteritis nodosa and that its early diagnosis can reduce mortality from this disease. **Jpn J Ophthalmol 2000;44:151–153**

Key Words: Antineutrophil cytoplasmic antibody, episcleritis, iritis, polyarteritis nodosa.

Introduction

Polyarteritis nodosa (PAN) is a rare systemic disease with vasculitis. Polyarteritis nodosa is potentially fatal and its diagnosis may be difficult owing to its varied clinical manifestations.[1,2] Although this disease affects small- and medium-sized arterioles in various organs, ocular involvement is rarely a presenting manifestation symptom.[3–8] We describe a patient who initially developed unilateral episcleritis and then fatal vasculitis in multiple organs.

Case Report

A 71-year-old man complained of pain and hyperemia in his left eye and visited an ophthalmologist on July 1, 1997. He had a history of mild hypertension. There was no remarkable family history. His visual acuity was 1.0 OU. The left eye showed diffuse episcleritis. The cornea and anterior chamber appeared clear bilaterally. Ophthalmoscopy revealed no abnormality in either eye. The patient was treated with topical betamethasone; however, he developed iritis in the left eye and episcleritis with severe pain in both eyes 3 weeks later. These symptoms initially responded well to oral prednisone (30 mg/day), but then recurred when the prednisone was tapered 4 weeks later. Five months after his initial visit, the patient developed a severe headache. Laboratory examination disclosed a slightly elevated erythrocyte sedimentation rate of 15 mm/h and elevated leukocyte count (11,300 cells/mm^3). The results of other systemic and laboratory tests were negative or within normal range, including rheumatoid factor, *Treponema pallidum* hemoagglutination, blood pressure, serum cholesterol levels, serum triglycerides, plasma glucose level, and chest x-ray. The patient showed no signs of fever or lymphoadenopathy.

When the patient was referred to our hospital for examination on December 1, 1997, his visual acuity

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was 0.9 OD and 1.2 OS. Intraocular pressure was 36 mm Hg in the right eye and 21 mm Hg in the left. Exophthalmometry showed mild protrusion of his right eye; right eye, 23 mm compared with the left, 19 mm. Slit-lamp examination revealed bilateral diffuse episcleritis with dilated conjunctival and episcleral vessels showing a bright red color, more prominent in the right eye, which also had a shallower anterior chamber. The cornea and anterior chamber appeared clear bilaterally. Mildly dilated retinal vessels without retinal hemorrhage were observed by ophthalmoscopy. Computed tomography (CT) of the brain and orbit revealed no pathological findings. Magnetic resonance imaging showed multiple lacunae infarction in the brain, but otherwise demonstrated normal findings both in the orbit and in the brain.

The patient was admitted to our hospital 10 days later, complaining of increasing bilateral ocular pain, headache, and fever. He also had weakness in both lower extremities, and dysesthesia in a glove-stocking type of distribution, which was diagnosed neurologically as polyneuropathy. The patient had lost more than 10 kg of body weight within 2 months. Results of laboratory studies showed elevated C-reactive protein (15.1 mg/dL) and elevated leukocyte count (11,500 cells/mm^3). A chest x-ray showed abnormal shadows in both lower lobes, suggesting pneumonia. Systemic treatment with intravenous antibiotics was not successful; C-reactive protein further elevated to 28.4 mg/dL, and the leukocyte count increased to 14,300 cells/mm^3.

One month after admission, the patient developed renal dysfunction. Laboratory examination showed elevated blood urea nitrogen (104 mg/dL) and elevated creatinine (5.8 mg/dL), and hemodialysis was begun. Immunological study of the patient's serum revealed that the perinuclear type of antineutrophil cytoplasmic antibody (p-ANCA) titer was 839 (normal < 10), and the cytoplasmic type of antineutrophil cytoplasmic antibody (c-ANCA) titer was 12 (normal < 10), suggesting that the patient had had PAN. Methylprednisolone (1 g/day) was instituted intravenously. The patient died 10 days later after hemorrhagic infarction of the right middle cerebral artery. Autopsy was not permitted by the patient's family.

Discussion

The patient initially had unilateral then bilateral episcleritis, with severe ocular pain, which did not respond well to topical betamethasone and low-dose oral prednisone. Such refractory episcleritis could be associated with collagen vascular diseases (eg, rheumatoid arthritis, systemic lupus erythematosus, PAN, or Wegener's granulomatosis). The patient complained of headache when referred to our hospital, and the laboratory examination revealed mildly elevated erythrocyte sedimentation rate and leukocyte count. Other findings indicating general inflammatory diseases were absent, so that we initially failed to focus on the systemic vascular diseases. Five months after the onset of ocular symptoms, multisystemic inflammation progressively developed, resulting in death after unsuccessful treatment with pulsed corticosteroid. Laboratory study revealed positive p-ANCA and borderline c-ANCA. These clinical findings can be differentiated from Wegener's granulomatosis, in which respiratory tract inflammation, renal disease, oral ulcer or discharge, granulomatous vasculitis, and a positive c-ANCA test are found; rheumatoid arthritis, in which a distinct form of polyarticular and symmetric arthritis are found; temporal arteritis, in which headache, jaw claudication, and sudden visual loss resulting from ischemic optic neuropathy are found. Although histologic evidence of necrotizing arteritis could not be obtained in our patient, his clinical findings satisfied the American College of Rheumatology 1990 criteria for the classification of polyarteritis nodosa.[9]

Ten to 20% of patients with PAN reportedly have ocular involvement, such as scleritis, peripheral ulcerative keratitis, nongranulomatous uveitis, choroidal and retinal vasculitis, and orbital pseudotumor.[3–8] Akova et al[7] reported 5 cases of PAN with ocular involvement, of whom initially sought the attention of an ophthalmologist. PAN was diagnosed after the ophthalmologic manifestation had appeared in all cases.

The combination of corticosteroid and cyclophosphamide reportedly increases the 5-year survival rate to 80%. The rate has been 12% without treatment.[10] The severity of the disease has justified intensive treatment with high-dose corticosteroids and pulsed cyclophosphamide.[11,12] Azathioprine has been found to be effective in maintaining remission in this disease.[13] Plasma exchanges are also indicated in patients with renal failure or those dependent on hemodialysis.[14] To decrease its mortality, we believe ophthalmologists should be aware that common ocular inflammations can be the initial manifestation of such a fatal vascular disease as polyarteritis nodosa.

References

1. Fauci AS, Haynne BS, Katz P. The spectrum of vasculitis: clinical, pathologic, immunologic, and therapeutic consideration. Ann Intern Med 1978;89:660–76.

2. Cohen RD, Conn DL, Ilstrup DM. Clinical features, prognosis and response to treatment in polyarteritis. Mayo Clin Proc 1980;55:146–55.
3. Stillerman ML. Ocular manifestations of diffuse collagen disease. Arch Ophthalmol 1951;45:239–50.
4. Wise GN. Ocular periarteritis nodosa. Report of two cases. Arch Ophthalmol 1952;48:1–11.
5. Sheehan B, Harriman DGF, Bradshaw JPP. Polyarteritis nodosa with ophthalmic and neurological complications. Arch Ophthalmol 1958;60:537–47.
6. Koike R, Yamada M, Matsunaga T, Yoshida S, Tsukagoshi H. Polyarteritis nodosa (PN) complicated with unilateral exophthalmos. Intern Med 1993;32:232–6.
7. Akova YA, Jabbur NS, Foster CS. Ocular presentation of polyarteritis nodosa. Clinical course and management with steroid and cytotoxic therapy. Ophthalmology 1993;100:1775–81.
8. Ferreira FP, Faria A, Ganhão F. Polyarteritis nodosa with primary ocular involvement. J Fr Ophthalmol 1995;48:788–93.
9. Lightfoot RW Jr, Michel BA, Bloch DA, et al. The American College of Rheumatology 1990 criteria for the classification of polyarteritis nodosa. Arthritis Rheum 1990;33:1088–93.
10. Leib ES, Restivo C, Paulus HE. Immunosuppressive and corticosteroid therapy of polyarteritis nodosa. Am J Med 1979;67:941–7.
11. Langford CA, Sneller MC. New developments in the treatment of Wegener's granulomatosis, polyarteritis nodosa, microscopic polyangiitis, and Churg-Strauss syndrome. Curr Opin Rheumatol 1997;9:26–30.
12. Guillevin L, Lhote F. Treatment of polyarteritis nodosa and microscopic polyangiitis. Arthritis Rheum 1998;41:2100–5.
13. Savage C, Harper L, Adu D. Primary systemic vasculitis. Lancet 1997;349:553–8.
14. Guillevin L, Cevallos R, Durand-Gasselin B, Lhote F, Jarrousse B, Callard P. Treatment of glomerulonephritis in microscopic polyangiitis and Churg-Strauss syndrome. Ann Med Interne (Paris) 1997;148:198–204.