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BRIEF COMMUNICATION

Radiation Retinopathy Caused by Low Dose Irradiation and Antithyroid Drug-Induced Systemic Vasculitis

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Abstract

Background: We report on a patient with Graves' disease with radiation retinopathy caused by low-dose irradiation and antithyroid drug-induced antineutrophil cytoplasmic antibody (ANCA)-positive vasculitis.

Case: A 38-year-old woman with Graves' disease presented with bilateral blurred vision, microaneurysms, telangiectasia, and macular edema. The patient was examined by ophthalmoscopy and fluorescein angiography, and radiation retinopathy was diagnosed.

Observations: The patient had been treated with low-dose irradiation for her Graves' ophthalmopathy a few years earlier. She also had ANCA-positive vasculitis induced by the antithyroid drug (propylthiouracil, PTU) that had been prescribed for her at that time. Because of multiple avascular areas on both retinas, she was treated by intensive retinal photocoagulation to control progressive retinopathy.

Conclusions: The radiation doses used to treat Graves' disease ophthalmopathy are low. Nevertheless, there is still a risk of radiation retinopathy developing in patients with PTU-induced ANCA-positive vasculitis. **Jpn J Ophthalmol** 2005;49:261–263 © Japanese Ophthalmological Society 2005

Key Words: antineutrophil cytoplasmic antibody, Graves' disease, propylthiouracil, radiation retinopathy

Introduction

Radiation retinopathy is a slowly progressive retinal vascular disorder with characteristic fundus abnormalities.[1] The structure and permeability of the retinal and optic nerve vessels are affected by radiation exposure. Frequent opthalmoscopic findings include microaneurysms, retinal telangiectases, dot and blot retinal hemorrhages, cotton-wool spots, macular edema, and intraretinal microvascular abnormalities.[1] In general, radiation retinopathy is rare for total radiation doses of less than 45 Gy.[1]

Antineutrophil cytoplasmic antibody (ANCA)-positive vasculitis was first described by Davies et al.[2] and is useful for diagnosing cases of systemic vasculitis. The presence of antibodies to specific target antigens (proteinase 3 and myeloperoxidase) of antineutrophil cytoplasmic antibodies is highly specific for several types of systemic vasculitis, including Wegener's granulomatosis, microscopic polyangiitis, Churg-Strauss syndrome, and idiopathic necrotizing crescentic glomerulonephritis.[3]

Recently, ANCA-positive vasculitis has been observed in patients with Graves' disease who were treated with propylthiouracil (PTU).[4] We report a case of radiation retinopathy induced by low-dose radiation (25 Gy) and ANCA-positive vasculitis.

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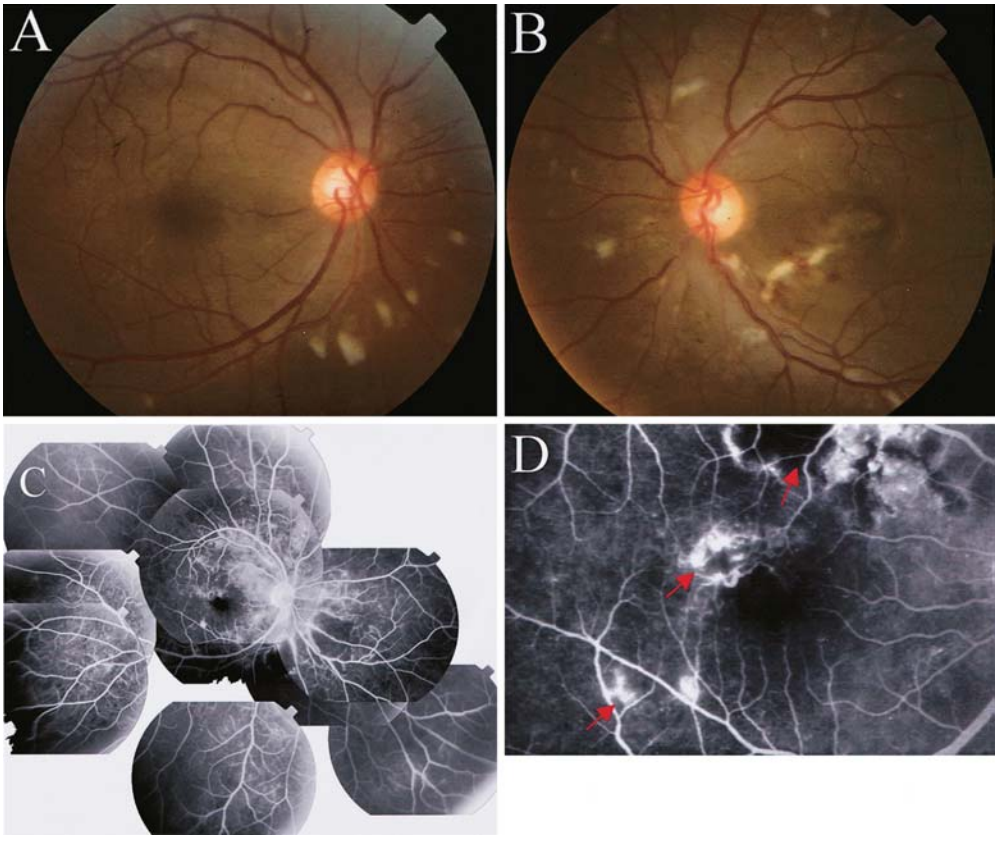

Figure 1A–D. Color fundus photographs (**A** right fundus, **B** left fundus) taken in May 2001 at the onset of retinopathy in a 38-year-old woman. Macular edema and numerous microaneurysms, cotton-wool spots, and hemorrhages were seen, particularly in the arcade of the posterior pole. Fluorescein angiograms of the right fundus taken in May 2001 (**C**) and June 2003 (**D**; Rodenstock scanning laser ophthalmoscope). Multiple avascular areas were found on both retinas in May 2001 (**C**). In spite of intensive photocoagulation, her retinopathy is still progressive, associated with microaneurysms and telangiectasia (*red arrows*) (**D**).

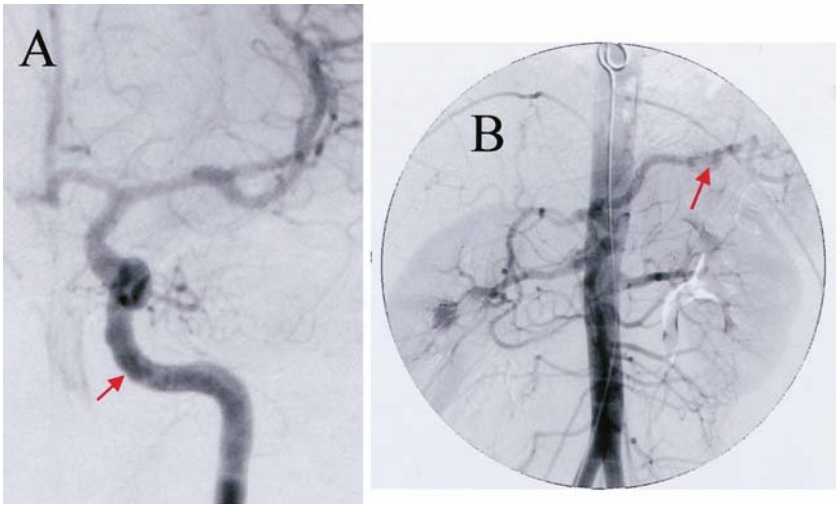

Figure 2A,B. Angiograms showing irregular patterns on the inner walls of the patient's right carotid artery (**A**) and aneurysm of splenic arteries (**B**; May 2001).

Case Report

A 38-year-old woman had bilateral blurred vision and was referred to our clinic in April 2001. On examination, her visual acuity was 25/20 (OD) and 20/50 (OS). Macular edema and numerous microaneurysms, cotton-wool spots, and hemorrhages were seen, particularly in the arcade of the posterior pole (Fig. 1A,B). Fluorescein angiograms were performed, and multiple avascular areas were found on both retinas (Fig. 1C). She was therefore treated with intensive photocoagulation of the avascular areas.

The patient had no history of diabetes, hypertension, or kidney disease. She had been diagnosed with Graves' disease in August 1997 and treated with PTU until November 1999. For her Graves' ophthalmopathy (exophthalmoses and ocular immobility), she was treated with

low-dose radiation (25 Gy) in October 1998. Subsequently, her PR-3 ANCA titer was found to be elevated to 8.4 U/ml (normal range, <3.5 U/ml). Because patients with ANCA-positive vasculitis frequently *have* aortic disorders, angiography was performed in May 2001. Irregular patterns were observed on the inner walls of the bilateral carotid arteries (Fig. 2A). In addition, a typical aneurysm was observed on the splenic artery (Fig. 2B). Therefore, ANCA-positive vasculitis induced by PTU was diagnosed in this patient.

Fortunately, since 2001 the patient has maintained good visual acuity; her most recent examination, in June 2004, showed a visual acuity of 25/20 (OD) and 20/50 (OS). However, in spite of intensive photocoagulation, her retinopathy is still progressive, with associated microaneurysms, telangiectasia (red arrows, Fig. 1D), and macular edema. We are carefully following her condition.

Discussion

Although this patient had a history of ANCA-positive vasculitis, when she developed retinopathy in April 2001, she had not taken PTU for 5 months, and she was generally well. We found no elevation of her white blood cell count, c-reactive protein, or erythrocyte sedimentation rate in May 2001. We also found no evidence of the typical ocular manifestations of ANCA-positive vasculitis, that is, scleritis, keratitis, or iriditis.[5] Therefore, her progressive retinal disease is unlikely to be caused by her ANCA-positive vasculitis alone.

Because of her typical ophthalmoscopic findings (progressive microaneurysms, cotton-wool spots, hemorrhages, and macular edema),[1] we believe that her retinal lesions were mainly caused by radiation retinopathy. It is likely that her baseline systemic vasculitis increased her risk for radiation retinopathy even though only a low dose of radiation (25 Gy) was used for her Graves' ophthalmopathy treatment. In radiation retinopathy, the tight intercellular junctions of the vascular endothelial cells lose their integrity, causing an increase in vascular permeability.[6] ANCA-positive vasculitis also leads to damage of the systemic vascular endothelial cells by activated neutrophils. Thus ANCA-positive vasculitis and radiation retinopathy may have similar pathogeneses.[3]

The doses of radiation used to treat Graves' disease ophthalmopathy are low. Nevertheless, there is still a risk of radiation retinopathy in patients with PTU-induced ANCA-positive vasculitis.

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