Identical Twins With Subretinal Neovascularization Complicating Senile Macular Degeneration

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ABSTRACT
This is the first report, to our knowledge, of proliferative macular degeneration developing in the same eye of identical twins. The concept of a familial predisposition in age related macular degeneration is consistent with other known risk factors including race, iris pigmentation, hyperopia and macular drusen which are known to be genetically determined. Monozygotic twins provide ophthalmology with an excellent opportunity to study the hereditary aspects of ocular disease.

Senile Macular Degeneration (SMD) is the leading cause of severe visual loss among the elderly in the United States and England. The clinical and pathologic features of this disease have more recently been described in increasing detail by Gass and others. These include: drusen, atrophy of the retinal pigment epithelium, serous detachment of the retinal pigment epithelium, subretinal neovascularization, and disciform scars. These latter two features, subretinal neovascularization and disciform scars, account for the majority of severe visual loss in patients with SMD.

Patient complaints commonly include decreased visual acuity, metamorphopsia, distortion of color, and central scotomas, especially when the disease process involves the fovea. Despite our better understanding of the clinicopathology, the etiology of SMD remains obscure. Increased age, light skin and iris pigmentation, hypertension, hyperopia, cigarette smoking and family history have all been implicated as possible risk factors for SMD.

Identical twins provide a unique opportunity for the study of genetic and environmental components in disease. We would like to present the first reported case of subretinal neovascularization in SMD in monozygotic twin sisters who had remarkably similar medical histories and "identical" physical, mental and social characteristics.

CASE REPORTS
CASE 1: A 72-year-old white female was referred to the Retina Service (A.L.) at the Wills Eye Hospital on June 9, 1982, with a chief complaint of distorted vision in her right eye for one month. Her past ocular history was unremarkable. Her past medical and surgical histories included mastoid surgery for a cholesteatoma at age 20 and meningitis at age 21. Her visual acuity at presentation was 20/70 RE and 20/30 LE. Slit lamp examination showed dark pigmentation of the irides.
FIGURE 1: Case 1. (A) Initial pre-treatment intravenous fluorescein angiogram demonstrating a subretinal neovascular membrane with hemorrhage temporal to the fovea of the right eye. (B) Post-treatment angiogram showing persistent neovascularization and hemorrhage. (C) Fluorescein angiogram 16 months following unsuccessful retreatment showing persistent neovascularization and large cicatricial macular scar.

Fundusoscopic examination showed a mottling of the retinal pigment epithelium and subretinal hemorrhages temporal to the foveal avascular zone of the right eye. The left eye showed minimal drusen. Fluorescein angiography was performed revealing a normal choroidal and retinal filling pattern with an area of hyperfluorescence representing a subretinal neovascular membrane temporal to the foveal avascular zone of the right eye (Figure 1). The left eye had transmission defects consistent with drusen. The neovascular membrane was treated with krypton red laser photocoagulation (200 spot size, 0.2 seconds, 200 milliwatts, 150 applications) on June 18, 1982. A follow-up fluorescein angiogram on July 2, 1982, showed subretinal hemorrhage with persistence of the subretinal neovascular membrane. Visual acuity was count fingers RE. Krypton laser photocoagulation was again performed using similar treatment settings. The patient's latest follow-up examination on June 7, 1984, showed a visual acuity of 20/400 RE and 20/40 LE. A

FIGURE 2: Case 2. (A) Initial pre-treatment intravenous fluorescein angiogram demonstrating a subretinal neovascular membrane with hemorrhage extending into the foveal avascular zone of the right eye. The visual acuity was 20/200. (B) Post-treatment angiogram showing successful eradication of the neovascularization with absorption of the foveal hemorrhage. The patient's visual acuity improved to 20/50 and has remained stable over an 8-month follow-up. Cases 1 and 2 are identical twins.
persistent subretinal neovascular membrane accompanying a macular disciform scar remained in the right eye. The drones were unchanged in the left eye.

CASE 2: A 73-year-old white female, the identical twin sister of the first patient, was referred to the Retina Vascular Service (LEM) at the Wills Eye Hospital on September 30, 1983, with a chief complaint of progressive "blurred and distorted vision" in her right eye for a few months prior to presentation. The patient stated that she could not read with her right eye. Her past ocular history was unremarkable. Her past medical and surgical history included mastoid surgery for cholesteatoma and a tonsillectomy at age 20 and 21 respectively. She also had hepatitis in 1960. Her family history was significant in that her identical twin sister was treated for SMD with subretinal neovascularization in June 1982. Her initial visual acuity was 20/200 RE and 20/20 LE. Slit lamp examination showed brown pigmentation of the irides, and early cataractous changes in both eyes. Funduscopic examination revealed normal optic discs. There were areas of confluent drusen bilaterally and a subretinal neovascular membrane with accompanying subretinal hemorrhage in the right eye. Fluorescein angiography was performed on her initial visit and confirmed the presence of a subretinal neovascular membrane nasal to the fovea in the papillomacular bundle (Figure 2). Krypton red laser photocoagulation was performed on the same day. The following treatment parameters were used — spot size 200μ, 0.5-1.0 second exposure time, 450 milliwatts and 141 laser applications to achieve a grey white coagulation reaction of the entire SRNVM.

Follow-up examination on October 24, 1983, showed a visual acuity of 20/50 RE and 20/40 LE. No scotoma was noted with Amsler grid testing. Follow-up fluorescein angiography revealed resolution of the subretinal neovascular membrane following krypton red laser treatment. Her visual acuity and Amsler grid testing were stable on the last examination on June 7, 1984, eight months following krypton laser treatment.

DISCUSSION

As SMD continues to be the leading cause of blindness in patients over age 65 in the United States, further elucidation of its pathogenic mechanisms are necessary if successful means of prevention and treatment are to be discovered. The etiologic factors involved in subretinal neovascularization complicating SMD merit special attention as this proliferative stage of SMD accounts for approximately 90% of the severe visual loss from the disease. Presently, a number of personal and environmental risk factors have been associated with SMD, especially increased age.

The genetic identity of monozygotic twins makes them ideal for studies evaluating the interaction of heredity and environment in human life. This case of identical twin sisters with subretinal neovascularization complicating SMD is unique. Both twins presented with similar symptoms approximately 16 months apart. Both twins had neovascular membranes in their right eye. Although specific genetic mechanisms are not now known, certainly this case report affirms clinical impressions and epidemiologic studies which suggest a family history of SMD as an associated risk factor for developing the disease. This increased risk of the same disease in the co-twin of an affected twin reflects the concept of familial predisposition to a disease. Other risk factors identified with SMD such as race, light iris color, hypertension, light skin pigmentation, and hyperopia are suggested to be independently predisposed among family members.

Given that monozygotic twins are genetically identical, similar environmental conditions and life experiences should also contribute equally to disease processes. This case report also supports this concept as these twins shared a common background until early in their third decade. Some investigators have suggested that light toxicity and Vitamin A or E deficiency in animals and hyperlipidemia in humans are exogenous factors which may contribute to the genesis of SMD.

Neovascularization has been found to be associated with inflammation, tumors, and ischemia. Angiogenic substances have been isolated from tumors, and inflammatory cells which have been shown to experimentally induce neovascularization. Fluid from eyes with neovascularization has also been shown to induce neovascularization. We recently reported a case of subretinal neovascularization with associated choroidal nonperfusion and retinal ischemia. The interrelationships among these three conditions and subretinal neovascularization are yet to be determined.

Until the genetic and environmental risk factors associated with the pathogenesis of subretinal neovascularization and SMD can be elucidated, treatment may be directed at stopping the progression of the disease process. Argon laser photocoagulation has been proven beneficial in treating SRNVM 200μ from the foveal avascular zone (FAZ). Krypton laser treatment may be advantageous in treating SRNVM's located within the FAZ. Further efforts should be made to educate physicians and patients as to the early identification and progression of SMD, utilizing the Amsler grid and fluorescein angiography when indicated. This will certainly facilitate early detection and treatment of proliferative macular disease and provide the patient with an opportunity to maintain visual function.

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