Etiology of Choroidal Neovascularization in Young Patients

Salomon Y. Cohen, MD, Antoine Laroche, MD, Yann Leguen, MD, Gisèle Soubrane, MD, PhD, Gabriel J. Coscas, MD

Background: Choroidal neovascularization (CNV) is a common cause of legal blindness in developed countries. In patients younger than 50 years of age, CNV can be due to various causes, but to the authors' knowledge there has been no large epidemiologic study to compare the relative incidence of the various causes of CNV in this younger-aged group.

Methods: A retrospective study was performed of patients seen over a 30-month period to precisely define the relative incidence of the various etiologies of CNV in patients younger than 50 years of age who had been referred to a tertiary care ophthalmology department in western Europe.

Results: Clinical charts and angiograms of 363 patients were reviewed. The etiology of CNV was high myopia in 225 (62%) patients, pseudo-presumed ocular histoplasmosis syndrome in 42 (12%), angioid streaks in 17 (5%), and miscellaneous hereditary, or traumatic or inflammatory disorders in 16 (4%). Choroidal neovascularization could not be related to any etiology in 63 (17%) patients, and was considered to be idiopathic lesions. Choroidal neovascularization was subfoveal in 62% of the patients due to myopia versus 30% to 36% in patients due to other etiologies. Laser photocoagulation was applied in the majority of patients due to all etiologies except myopia.

Conclusion: These data provide the relative incidence of the various etiologies of CNV in young patients and emphasize the importance of myopia as an etiology of CNV in such patients. In addition, an apparent preferential localization of CNV to the subfoveal region in myopic eyes precludes its treatment with photocoagulation.

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Vision loss in young adults can be due to various causes, including choroidal neovascularization (CNV), which is important because of its generally poor prognosis and because some eyes may be amenable to laser treatment.[1] Numerous studies have been performed to analyze the course, the results of laser photocoagulation, and the visual prognosis of CNV due to various causes in young patients.[2–20] No study, however, has precisely defined the relative incidence of these etiologies. Accordingly, we performed a retrospective study of patients younger than 50 years of age referred because of CNV over a 30-month period.

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From the Department of Ophthalmology, University of Paris XII, Creteil.

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Reprint requests to Gabriel J. Coscas, MD, Clinique Ophtalmologique Universtaire, 40 Avenue de Verdun, F-94010 Créteil, France.

Patients and Methods

This study was performed at the Clinique Ophtalmologique Universtaire de Créteil, which is the main referral center in France for the diagnosis and treatment of CNV. The study consisted of a retrospective analysis of clinical charts and angiograms of patients younger than 50 years of age who were examined for the first time in our department between July 1, 1990, and December 31, 1992, and who were confirmed to have CNV. In all patients,

Table 1. Main Results

Etiology	No. of Patients (%)	Prevalence of Women	Mean Age (yrs)	Prevalence of Bilateral CNV	Prevalence of Subfoveal Localization	Photocoagulated Eyes
		No. (%)		*No. (%)*	*No. (%)*	*No. (%)*
High myopia	225 (62)	118 (52)	37.8	32 (14)	160 (62)	65 (38)
CNV considered to be idiopathic	63 (17)	42 (67)	36.7	6 (10)	21 (30)	48 (70)
Pseudo-presumed ocular histoplasmosis syndrome	42 (12)	35 (84)	35.3	5 (12)	17 (36)	30 (64)
Angioid streaks	17 (5)	10 (59)	44.4	8 (47)	9 (36)	16 (64)
Miscellaneous etiologies	16 (4)					
Total	363	212 (58)	38	51 (14)	215 (52)	199 (48)

CNV = choroidal neovascularization.

CNV was diagnosed by fluorescein angiography. The charts were analyzed regarding patient sex, age at the first examination, unilaterality or bilaterality of CNV, localization of CNV, amenability to laser photocoagulation, and etiology of CNV. Other information about the patients, such as smoking history, was not entered in all charts and thus was not analyzed.

Localization of CNV was defined by the distance between the outer limit of the neovascular net in the early frames of the fluorescein angiogram and the center of the foveal avacular zone and/or the center of the area of macular xanthophyllic pigment observed on the blue light picture.[21,22] In many patients, however, the foveal avascular zone and xanthophyllic pigment could not be seen clearly, particularly in myopic eyes, and localization of the fixation point was obtained by means of the 50-μm krypton laser-aiming beam test. This test consisted of the patient looking firmly at the aiming beam and following the beam as it was moved in different directions; the test was repeated until the patient's response was consistent and reproducible. During the study period, the standard in our department was to perform laser photocoagulation if the CNV were not subfoveal.

The etiology of CNV was diagnosed as follows: myopia was implicated when the refractive error was −6 diopters or worse and when there were fundus changes such as peripapillary chorioretinal atrophy, gyrate atrophy of the retinal pigment epithelium and choroid, lacquer cracks, or posterior staphyloma. Pseudo-presumed ocular histoplasmosis syndrome (pseudo-POHS) was implicated when the fundus contained multiple small yellow or whitish chorioretinal lesions, with or without inflammatory signs, vitreous cells, and anterior uveitis or papillitis, even if the eye was highly myopic. Angioid streaks, dominant drusen, and toxoplasmosis were identified by their well-defined clinical and angiographic features. Choroidal neovascularization was considered to be idiopathic when it could not be ascribed to any etiology.

Results

The charts of 363 patients were reviewed. These included those of 212 women (58%) and 151 men (42%), ranging in age from 10 to 49 years (mean, 38 years). Fifty-one patients had bilateral CNV; therefore, a total of 414 eyes were involved. In 215 eyes (52%), the CNV was subfoveal and thus not amenable to laser treatment.

The etiology of the CNV was myopia in 225 patients (62%), pseudo-POHS in 42 patients (12%), and angioid streaks in 17 patients (5%). Miscellaneous disorders accounted for 16 patients with CNV: traumatic rupture of Bruch membrane (8 patients), toxoplasmosis (4 patients), dominant drusen (2 patients), Best disease (1 patient), and trauma due to radiotherapy (1 patient). The CNV was considered to be idiopathic in 63 patients (17%) (Table 1).

Among the 225 patients in whom CNV was due to high myopia, there were 118 women (52%) and 107 men (48%), ranging in age from 17 to 49 years (mean, 37.8 years). Choroidal neovascularization was bilateral in 32 (14%) of these patients. Among these 257 eyes, 160 (62%) had subfoveal CNV that was not amenable to laser treatment; photocoagulation could be applied to only 97 (38%) of these eyes.

Of the 63 patients with idiopathic CNV, there were 42 women (67%) and 21 men (33%), ranging in age from 15 to 49 years (mean, 36.7 years). Choroidal neovascularization was bilateral in six patients (10%). Among these 69 eyes, 21 (30%) had subfoveal CNV; therefore, photocoagulation could be applied to 48 eyes (70%). Pseudo-POHS was diagnosed in 42 patients, 35 women (84%) and 7 men, ranging in age from 18 to 49 years (mean, 35.3 years). Of the 47 eyes, CNV was bilateral in 5 patients (12%) and subfoveal in 17 (36%); therefore, laser photocoagulation could be applied in 30 (64%) of these eyes. Angioid streaks were observed in 17 patients, 10 women (59%) and 7 men, ranging in age from 29 to 49 years

(mean, 44.4 years). Choroidal neovascularization was bilateral in 8 eyes (47%). Subfoveal localization of the CNV was observed in 9 (36%) of these 25 eyes; photocoagulation was applied to the 16 eyes (64%) deemed to be amenable to this treatment (Table 1).

Discussion

Choroidal neovascularization is a nonspecific phenomenon that is a complication of numerous inherited and acquired conditions. It is thought to be due to an imbalance between factors that inhibit and enhance angiogenesis.[23] Choroidal neovascularization is seen often in the presence of other anatomic conditions, including ruptures in Bruch membrane and in chronic chorioretinal disorders.[24] Choroidal neovascularization is seen most commonly in patients with age-related macular degeneration, which occurs after 50 years of age. However, numerous studies have described the clinical characteristics, the angiographic pattern, the course and outcome, and the response to treatment of CNV that occurs in younger patients due to myopia,[2-4] POHS[5,6] and pseudo-POHS, multifocal choroiditis,[8-12] angioid streaks,[13-16] and of CNV considered to be idiopathic.[17-20] However, to our knowledge, no study has compared the relative incidence of these etiologies in patients seen at a single, large referral center and the characteristics of the CNV in each of these etiologic categories. Our referral center is located in western Europe—we did not observe any patient with POHS because *Histoplasma capsulatum* is not endemic to Europe.[25]

In the current study, we showed that CNV in young patients, regardless of etiology, was more common in women than in men (women, 58%). This female preponderance was maximal for CNV due to pseudo-POHS (women, 84%). For patients with this syndrome, authors of all previous publications also have reported a female preponderance[8-10]; however, the reason for this apparent imbalance is not known.

Pseudo-POHS, or disorders that simulate the POHS,[26] corresponds to disorders that share many of the features of the POHS but that are not related to infection with histoplasmosis. These syndromes have been termed *multifocal choroiditis* and *panuveitis,*[8] *recurrent multifocal choroiditis,*[10] and *punctate inner choroidopathy,*[9] the latter being seen most commonly in young women with myopia. The causes of these diseases are unknown, and it is unclear whether these conditions are distinct entities or, rather, different manifestations of a single condition.[27] In the current retrospective study, we did not attempt to study the patient characteristics and symptoms in each of such patients to separate these entities; rather, these patients were pooled and their symptoms were termed *pseudo-POHS.*

Our results emphasize the importance of myopia among the causes of CNV, and also the preferential subfoveal localization of CNV in myopic eyes. High myopia was found to be the most common cause of CNV in younger patients, with a relative incidence of 62%. The incidence of myopia differs depending on the country in which the study is performed.[28] France's population is not known to have a high incidence of myopia[29]; therefore, the risk for overestimating the relative incidence of myopia among the various etiologies of CNV in our study appears low. Choroidal neovascularization is one of the more common and the more severe complications of pathologic myopia,[30] because the CNV associated with myopia has been found to be subfoveal in 62% of patients. Previous studies also have suggested a preferential subfoveal localization of myopic CNV, observed in 58% to 74% of such patients.[31] In the current study, subfoveal CNV was not photocoagulated, but even when juxtafoveal, the management of CNV is controversial.[4] However, a randomized study performed in our department did show that laser treatment of juxtafoveal CNV is beneficial for at least 2 years.[3] Accordingly, we usually treat juxtafoveal CNV in myopic eyes, but this is based on results of our limited study, because no multicentric randomized clinical trial has been conducted. In addition, the current study was not designed to define the management of juxtafoveal CNV; therefore, this management remains controversial.

Choroidal neovascularization was frequently considered to be idiopathic in many patients in our study. Little is known about the pathogenesis of this type of CNV that occurs in otherwise healthy adults with no underlying ocular disease, but an inflammatory pathogenesis was suggested recently, based on indocyanine green angiographic findings.[32] The optimal management of idiopathic CNV was defined by the Macular Photocoagulation Study group,[18,20] which recommended treatment for extrafoveal and juxtafoveal CNV. Pseudo-POHS appears to be a relatively common cause of CNV in western Europe. To date, there is no clear recommendation for treating this particular type of CNV. However, this form of CNV is similar to that which is secondary to the POHS,[8] and the Macular Photocoagulation Study did recommend photocoagulation for both extrafoveal and juxtafoveal CNV of POHS.[5,6] A prior retrospective study performed in France also suggested the usefulness of photocoagulation for juxtafoveal CNV in multifocal choroiditis.[12] The management of extrafoveal and juxtafoveal CNV in patients with angioid streaks is difficult because of the high rate of recurrences.[13-16] However, recent publications have suggested that laser photocoagulation may be beneficial.[13-16]

To our knowledge, this is the first report of the incidence of CNV based on etiology in young patients in western Europe. Generalization of our results to other populations is, of course, questionable. Despite a widespread use of laser surgery by French ophthalmologists to treat diabetic retinopathy, for example, macular photocoagulation remains a specialized surgery that is performed at only a few centers. We cannot estimate the percentage of patients with CNV who are referred to our center versus those who are treated elsewhere. It is possible that our center gets a disproportionate number of referrals of patients with more complicated findings (i.e., those in whom CNV is closer to the macula) because of its long-standing specialization in this field. This could account for an overestimation in the percentage of patients with

subfoveal CNV. However, there is no reason to suggest a bias regarding the relative incidences of the various etiologies of CNV, or of the comparison between the percentages of subfoveal CNV due to the different etiologies, which are the focus of the current report.

Choroidal neovascularization in young patients continues to have a poor visual prognosis, with marked societal and economic manifestations. Further studies are needed to elucidate the pathogenesis of CNV in young patients and to define the long-term prognosis of this condition based on the underlying cause.

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