Choroidal Neovascular Membranes in the United Kingdom

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Epidemiology of Angioid Streaks-Associated Choroidal Neovascular Membranes in the United Kingdom

Abstract

Background: The purpose of this study is to determine the incidence of angioid streak-associated choroidal neovascular membranes (CNV) in the UK and provide other epidemiological data, clinical characteristics, therapies used, and short-term outcomes following treatment of this condition.

Procedure: This is a prospective multicenter cohort study. Patients newly diagnosed of angioid streaks-associated CNV were identified prospectively over a 14-month period (January 2009-March 2010) by active surveillance through the British Ophthalmic Surveillance Unit (BOSU). Questionnaire-based data was obtained from reporting ophthalmologists at baseline and 12 months. The main outcome measure was incidence of angioid-streak-associated CNV. Secondary outcomes included clinical characteristics, treatments used, and visual outcomes.

Results: Forty-four cases of angioid streak-associated CNV were reported to BOSU, giving an annual incidence of 0.057 (95% CI: 0.040-0.074) per 100,000 population. Affected patients had a mean age of 47 years (range: 14-62 years), presented with a mean (SD) LogMAR visual acuity (VA) of 0.53 (0.51) (Snellen equivalent 6/18), and had most often subfoveal CNV. At one year, the mean LogMAR visual acuity had declined to 0.73 (0.59) (Snellen equivalent 6/56). Visual acuity improved > two Snellen lines in six cases (21%) and deteriorated > two lines in 13 cases (41%). Treatments used included anti-VEGF in 25 eyes (83%), photodynamic therapy (PDT) in two (7%), and observation in three (11%).

Conclusions: This study represents the first population-based prospective study evaluating the incidence of angioid streak-associated CNV in the UK. Despite new treatments for CNV, the visual outcome of patients with this disorder remains guarded.

Introduction

Angioid streaks (AS) are irregular, radiating, orange-red jagged lines that extend from around the optic nerve head into the mid-peripheral retina, including the macula. Early in the course of the disease, AS appear as well-defined orange lines; as the disease progresses, they become less well-defined and more pigmented. They represent crackline dehiscences in Bruch’s membrane [1]. AS can be associated to systemic diseases, most commonly pseudoxanthoma elasticum, Ehlers-Danlos, Paget disease, sickle cell disease, or they may be idiopathic [2]. Rarely, they may be associated with abetalipoproteinemia [2-5].

Choroidal neovascular membranes (CNVs) may develop in up to 86% of patients with AS; when left untreated, they undergo progressive scarring leading to visual loss, often to levels of < 20/200 [1,4-7]. The age at presentation of patients with AS-associated CNVs varies between 11 to 85 years with a mean age of 44 to 59 years [1,8-14]. Due to the brittle nature of Bruch’s membrane in these patients, acute visual loss can occur also following minor trauma as a result of choroidal rupture and sub-macular haemorrhage [15-16]. Bilateral visual loss is not uncommon, and it has been reported to occur in 42 to 71% of patients [6,17]; legal blindness has been reported in about 50% of patients due to the occurrence of bilateral CNV [1].

The management of patients with AS-associated CNV is challenging. Several treatment modalities have been used, including laser photocoagulation [18-19], photodynamic therapy (PDT) [20-21], transpupillary thermotherapy [8,23], feeder vessel occlusion [11], and surgical removal of the CNV or macular translocation [25-26]. Poor visual outcomes are often obtained with these treatments, and a high recurrence rate is observed. Intravitreal injection of anti-VEGF (vascular endothelial growth factor) has been recently used with promising results [13,25-29]. However, due to the rarity of this condition, no prospective randomised clinical trial (RCT) is available to evaluate the outcomes and complications of these treatments.

The purpose of this study was to prospectively estimate the incidence of AS-associated CNV in the general population in the UK and to gain knowledge in the aetiology, clinical characteristics, management, and response to treatment of this group of patients.

Abbreviations

CNV- choroidal neovascular membrane
UK- United Kingdom
BOSU- British Ophthalmology Surveillance Unit
SD- Standard Deviation, PDT- Photodynamic Therapy
AS- angioid streaks
RCT- Randomised Controlled Trial
VA- Visual Acuity

Categories: Ophthalmology
Keywords: epidemiological data, laser, ranibizumab, anti-vegf, bevacizumab, cnv, photodynamic therapy, pseudoxanthoma elasticum, angioid streaks, choroidal neovascular membrane
Materials And Methods

Patients with newly diagnosed AS-associated CNV were identified prospectively through active surveillance by the British Ophthalmological Surveillance Unit (BOSU) during a 14-month period from January 2009 to March 2010. BOSU operates a monthly active surveillance scheme throughout the United Kingdom (UK) [30]; it was developed to assist in the investigation of uncommon ocular conditions that are of public health or scientific importance. The surveillance scheme involves all permanently employed ophthalmologists in the UK with clinical autonomy (consultants and associate specialists) who form the reporting base. Before the initiation of a study, BOSU informs all ophthalmologists about the new ocular condition under investigation, including the specific case definition. At the end of each month, a report card is sent to each ophthalmologist, who then returns it specifying whether a new case had been seen that month or whether no cases were seen. After case notification, incident and follow-up questionnaires are sent by the investigators to reporting ophthalmologists.

The baseline incident questionnaire collected data on demographics (age, gender, and ethnicity), ocular history, visual acuity (VA), systemic associations, family history of AS, CNV location, and investigations used for diagnosis. The 12-month follow-up questionnaire collected data on VA, treatment(s) performed, complications of treatment, status of the CNV (active/inactive), whether new CNVs developed during the 12 month follow-up period in the affected and fellow eye, investigations used to assess CNV activity, and whether the case was discharged or continued to followed. Paired t-tests were used to compare visual acuity at baseline and at follow-up.

This study was conducted in accordance with the tenets of the Declaration of Helsinki. Approval was granted by the North East of Scotland Multi-centre Research Ethics and Research and Development committees.

Results

During the study period, the response rate to BOSU was 77%. The investigators received 56 case reports, 12 were duplicates, leaving 44 cases of AS-associated CNV. Based on the 2009 population of UK (Available at: United Kingdom Office for National Statistics http://www.statistics.gov.uk/cgi/nugget.asp?id=6), these 44 cases gave an annual incidence of 0.057 cases (95% CI: 0.040-0.074) per 100,000 population. For 35 (79.5%) of these 44 cases, baseline questionnaires were completed by reporting ophthalmologists and received by the investigators; 12 month data questionnaires were completed for 30 of these 35 patients.

There were 20 males and 13 females (gender not available in two) with a mean age of 47 years (range: 24-62 years). Thirty-three patients were of British white origin; two were Caribbean. The right eye was affected in 18 patients. AS were associated with pseudoxanthoma elasticum in 22 patients (63%) and sickle cell in one; in 12 patients (24%), AS seemed to be idiopathic. A family history of AS was present in five patients. The AS-associated CNV was subfoveal in 18 eyes, juxtafoveal in 10, and extrafoveal in seven.

Fundus fluorescein angiography (FFA) was used to diagnose AS-associated CNV in all cases. Other imaging techniques were used to evaluate these patients, including optical coherence tomography (OCT) in 32/35 cases (91%), autofluorescence (AF) in 4/35 cases (11%), and indocyanine green angiography (ICG) in 1/35 cases (3%).

At baseline, the mean LogMAR VA (SD) was 0.53 (0.51) (Snellen equivalent 6/18) (n=35). At one-year follow-up (FU), the mean LogMAR VA was 0.73 (0.59) (Snellen equivalent 6/36) (n=30). Figure 1 illustrates the change of VA from baseline to last follow-up. No statistically significant difference in VA between baseline and one-year follow up was detected (p=0.053, 95% confidence interval of -0.66 to -0.9, paired t-test). VA improved by 0.2 LogMAR (+2 Snellen lines) in six eyes (21%) and deteriorated by 0.2 LogMAR (+2 Snellen lines) in 13 cases (41%). At the end of the follow-up period, 21 patients (70%) maintained driving vision (>6/12) in their affected eye(s).

![FIGURE 1: Visual acuity (LogMAR) at presentation and at one year follow-up](image)

Visual acuity (LogMAR) at presentation and at one year follow-up in patients with angioid-streak associated choroidal neovascular membranes. Diamonds = eyes treated with anti-vascular endothelial growth factor therapy; squares = eyes observed; triangles = eyes treated with PDT.

New CNV developed in the affected eye at a different location in five eyes (17%) and in the fellow eye in two
observed visual acuity, stable = stable or improved VA, > 2 = VA improvement by > 2 Snellen lines, > 2 = VA reduction by > 2 Snellen lines, Ret = neovascular membranes.

Myung et al [40]
Wiegand et al
Bhatnagar et al [37]
Neri et al [36]
Sawa et al et al
Mimoun et al
Vadala et al
Finger et al
Finger et al[42]
Amouko & Shah & Authors [38][34][45][44]

1: Summary of the studies (with n > 5 cases) reporting the results of anti-VEGF therapy for angioid streaks-associated choroidal neovascular membranes.

Authors  Year  # of Eyes  # of Patients  FU (Months)  Design  Drug  Average # of injections  Mean / Baseline VA  Mean / FU VA  Sig  Stable (%)  > 2 Lines Improve
Shah & Amouko [42]  2012  12  9  21.7  Pet  Ran  5.7  6/15  6/12  No (p=0.6)  92  75
Finger et al [35]  2011  7  7  12  Pro  Ran  12  20/63  20/32  Yes (p=0.012)  N/A  N/A
Finger et al [43]  2011  18  14  28  Ret  Bev  6.5  20/80  20/40  Yes (p=0.04)  94  50
Ladas et al [44]  2010  15  14  12  Pro  Ran  7  20/100  20/50  Yes (p=0.006)  93.3  N/A
Vadala et al [45]  2010  9  9  14  Pro  Ran  5  20/80  20/40  Yes (p=0.01)  100  78%
El Mani et al [34]  2010  18  17  13  Ret  Bev  4.8  20/80  20/44  Yes (p=0.01)  100  66
Mimoun et al [35]  2010  35  27  24  Ret  Ran  5.7  20/43  20/46  No (p=0.73)  85.7  14.3
Sawa et al [36]  2009  15  13  19  Ret  Bev  4.5  6/15  6/18  No (p=0.35)  87  33
Neri et al [37]  2009  11  11  23.8  Pro  Bev  3.5  6/24  6/12  Yes (p=0.018)  100  N/A
Bhatnagar et al [27]  2007  9  9  6  Ret  Bev  1.8  20/368  20/289  No (p=0.056)  100  22
Wiegand et al [50]  2009  9  6  19  Ret  Bev  4.4  20/50  20/50  No (p N/A)  78  55.5
Noda et al [40]  2010  5  4  12  N/A  Bev  N/A  N/A  N/A  N/A  No (p N/A)  60  20
Myung et al [38]  2010  9  9  28.8  Ret  Bev  8.4  20/368  20/281  No (p=0.14)  100  30

TABLE 1: Summary of the studies (with n > 5 cases) reporting the results of anti-VEGF therapy for angioid streaks-associated choroidal neovascular membranes.

In: number, FU: follow up, VA: visual acuity, FU VA: visual acuity at last follow up, Sig: statistically significant difference between baseline and last observed visual acuity, stable: stable or improved VA, > 2 = VA improvement by > 2 Snellen lines, > 2 = VA reduction by > 2 Snellen lines, Ret = retrospective case series, Pro= prospective case series, Bev = bevacizumab, Ran = ranibizumab, * = treatment naïve, N/A= not available.

In the current study, stabilisation or improvement of VA was achieved in 56% of eyes treated with anti-VEGF (n=25) with only 20% experiencing a > two Snellen lines of visual acuity improvement. This is in keeping with findings by Noda, et al. [40] and Bhatnagar, et al. [27] in their small case series, and slightly more favourable that outcomes reported by Mimoun, et al. [35], the largest series, although retrospective, published prior to the current study.

Although this study has several limitations, including the small number of patients included, missing data (in 35/44 cases data available at baseline and in 30/44 cases data was available at 12 months), the short follow-up period, and the inherent limitation of any surveillance study, namely incomplete ascertainment, it provides important epidemiological data and useful information for the management and counselling of patients with
this rare retinal disease.

Conclusions

Patients with AS-associated CNV have now a more favourable visual prognosis with the use of anti-VEGF therapies. Early diagnosis and treatment are essential to restore and maintain vision. Despite of anti-VEGF treatment, in a proportion of patients visual deterioration still occurs and, hence, new therapeutic options are much needed.

Additional Information

Disclosures

Human subjects: The North of Scotland Research Ethics Committees on 27/05/2008 issued approval #: 08/S0802/66. This study was conducted in accordance with the tenets of the Declaration of Helsinki. The ethics committee waived the need for informed consent for this study. Animal subjects: This study did not involve animal subjects or tissue.

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