Asteroid Hyalosis in an Autopsy Population

The University of California at Los Angeles (UCLA) Experience

Amani A. Fawzi, MD; Baotran Vo, BS; Ryan Kriwanek; Hema L. Ramkumar, BS; Chris Cha, BS; Amy Carts; John R. Heckenlively, MD; Robert Y. Foos, MD, DVM†; Ben J. Glasgow, MD

Objectives: To study the prevalence and associations of asteroid hyalosis (AH) in a series of autopsy eyes.

Methods: Retrospective review of the University of California at Los Angeles (UCLA) autopsy eye database from 1965 to 2000 yielded 10801 patients. The patients’ medical histories were reviewed for evidence of diabetes mellitus, hypertension, hyperlipidemia, alcohol abuse, hypercalcemia, hypothyroidism, and chronic renal failure. Autopsy records were searched for evidence of optic atrophy, macular degeneration, posterior vitreous detachment, atherosclerosis, and chronic renal failure. Asteroid hyalosis was diagnosed by examination of the autopsy eyes. Univariate and multivariate statistical methods were used to analyze our data.

Results: The prevalence of AH was 1.96% in this autopsy population. By χ² analysis, AH was significantly correlated with age (P<.001), male sex (P=.006), age-related macular degeneration (P=.02), hypertension (P=.03), atherosclerosis (P<.001), and posterior vitreous attachment (P<.001). After adjusting for age in a multivariate logistic regression analysis, statistical significance was found only for posterior vitreous attachment (P=.002) and male sex (P=.046). No statistically significant association was found with diabetes mellitus or alcohol abuse by univariate or multivariate analysis. Analysis of the odds ratio showed a strong age effect that increased from 5.0 (95% confidence interval, 2.2-11.3) in age group 41 to 50 years, compared with 25.4 (95% Wald confidence interval, 8.2-77.9) in the age group of patients older than 90 years.

Conclusions: A unique epidemiological autopsy cohort study of AH and its systemic associations yielded a higher prevalence of AH than previous studies. Asteroid hyalosis was strongly correlated with age and inversely correlated with posterior vitreous detachment. Unlike some previous reports, we found no statistically significant correlation between AH and diabetes mellitus.


Author Affiliations: Department of Ophthalmology, Jules Stein Eye Institute (Drs Fawzi, Heckenlively, and Glasgow); Messrs Kriwanek and Cha; and Mss Vo, Ramkumar, and Carts), Department of Pathology and Laboratory Medicine (Drs Foos and Glasgow), The David Geffen School of Medicine at University of California at Los Angeles.

However, that report surveyed a population from Beaver Dam, Wis, that was predominantly restricted to a white northern European background (99.4%). In addition, AH was diagnosed retrospectively by inspection of fundus photographs. The photographs were not interpretable in 3.6% of patients, most of whom were older (mean age, 71 years) and more likely to have a history of DM and cardiovascular disease. The authors indicated that AH was likely to be underestimated because photographs did not include the periphery and the camera focused on the posterior retina rather than on the vitreous.3

The limitations of the previous studies prompted us to study the prevalence of several systemic diseases in association with AH. Our study population was large enough to permit multivariant analyses, included a wide cross-sectional population reflective of the United States in general, and, to our knowledge, is the only cohort study of the prevalence of AH in human autopsy eyes.

METHODS

Retrospective review of the University of California at Los Angeles (UCLA) autopsy eye database from 1965 to 2000 included 10,801 patients (Figure 1). The patients' medical records were reviewed for evidence of DM, hypertension, hyperlipidemia, alcohol abuse, hypercalcemia, hypothyroidism, and chronic renal failure, in addition to autopsy evidence of optic atrophy, glaucoma, age-related macular degeneration, posterior vitreous detachment (PVD), atherosclerosis, and renal diseases. Racial backgrounds were categorized according to the classification provided in the report of the US census for 2000.

EXAMINATION OF AUTOPTSY EYES

Autopsy eyes were processed and examined using previously described methods.19 Posterior vitreous detachment was diagnosed by suspension of the eyes in air as reported previ-

<table>
<thead>
<tr>
<th>Source</th>
<th>Population</th>
<th>Selection</th>
<th>Prevalence, % (Sample Size)</th>
<th>Bilateral Cases, %</th>
<th>Male-Female Ratio</th>
<th>Patients With Diabetes Mellitus, %</th>
</tr>
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<tr>
<td>Bergren et al2</td>
<td>Eye clinic</td>
<td>Cross-sectional study with case-control subgroup</td>
<td>0.83 (12,205)</td>
<td>19</td>
<td>0.94:1</td>
<td>29</td>
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<tr>
<td>Moss et al3</td>
<td>Population Beaver Dam, Wis</td>
<td>Cross-sectional; population based</td>
<td>1.2 (4,926)</td>
<td>9</td>
<td>2.3:1</td>
<td>8.6</td>
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<td>Smith4</td>
<td>Eye clinic</td>
<td>Case series</td>
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<td>11</td>
<td>1.4:1</td>
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<td>Case-control study</td>
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<td>Eye clinic</td>
<td>Case-control study</td>
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<td>NS</td>
<td>3:1</td>
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<td>Case-control study</td>
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<td>Yazar et al14</td>
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<td>Case-control study</td>
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<td>Case-control study</td>
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<td>1.3:1</td>
<td>28</td>
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<td>Potter and Newcomb13</td>
<td>Eye clinic</td>
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<td>13.1</td>
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<td>19</td>
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<tr>
<td>Present study</td>
<td>Autopsy population</td>
<td>Cross-sectional; population based</td>
<td>1.96 (10,801)</td>
<td>19.8</td>
<td>2.5:1</td>
<td>7.2</td>
</tr>
</tbody>
</table>

Abbreviations: NA, not available; NS, not stated.

RESULTS

Review of our autopsy database yielded 212 cases (1.96%) of AH, of whom 42 cases (0.4%; 42 of 212 patients [19.8%]) were bilateral. In addition to the bilateral cases,
there were 97 cases with only the right eye affected and 73 with only the left eye affected.

AGE

In the autopsy population, the ages ranged from 0 (stillbirth) to 109 years, with a mean and median of 48 and 55 years, respectively. There were a total of 4274 patients (39.59%) older than 60 years, of whom 619 (5.73%) were 81 years or older, and 74 patients (0.69%) were 90 years or older. The age of patients with AH ranged from 9 to 97 years, with a mean and median of 67 years. By chi-square analysis, age was highly associated with AH whether unilateral \((P < .001)\) or bilateral \((P = .001)\), an effect that persisted after adjusting for sex in a multivariate model \((P < .001)\). Age-specific prevalence increased from 0.27% in patients younger than 40 years to 6.76% in patients older than 90 years (Figure 2).

SEX

There were 6725 males (62%) in the autopsy population. Of the patients with AH, 151 (71.2%) were male, which was statistically significant on chi-square analysis \((P = .006)\) and was less significant after adjusting for age in a multivariate model \((P = .046)\).

RACE

The racial backgrounds of patients in the autopsy reports revealed that 8081 patients were white (75%); 1368, African American (13%); 216, Asian (2%); and 1119 were categorized as other racial backgrounds (10%). Of the patients with AH, 156 were white (73.6%); 29, African American (13.7%); 4, Asian (1.9%); and 22 other (10.4%). There was no statistical significance for an association between AH and race whether in univariate or multivariate models.

DIABETES MELLITUS

Diabetes mellitus was reported in 780 patients (7.22%). Of those patients, only 20 had AH; this was not a statistically significant association by either chi-square or multivariate analysis. Diabetes mellitus was statistically associated with bilateral AH on chi-square analysis but not after adjusting for age and sex. On subgroup analysis for the different age groups, we found specific age subgroups (51-60 years, \(P = .006\); 41-60 years, \(P = .004\)) that showed a statistically significant association between AH and DM. The age groups with the lowest association were age groups younger than 40 years, 81 to 90 years, and 91 years and older; \(P = .50, .53, .73\), respectively.

POSTERIOR VITREOUS DETACHMENT

Of the 20227 eyes studied for PVD, 243 were found to have AH. The prevalence of AH in eyes with PVD was only 1.39%. No association was found for AH and PVD in our population. However, AH was associated with the absence of PVD, after adjusting for age and sex (Table 2). There was no association of partial PVD with AH after adjustment for age \((P = .89)\).

OTHER CONDITIONS

Age-related macular degeneration, hypertension, and atherosclerosis showed apparent statistically significant associations with AH by chi-square analysis but not after adjusting for age and sex in the multivariate model (Table 2). No other conditions, including hypercalcemia, hyperlipidemia, alcohol abuse, hypothyroidism, chronic renal failure, and optic atrophy, showed statistically significant association with AH, whether by chi-square or multivariate analysis (Table 2).

The population surveyed in this study of AH represents a large cross-sectional population of Los Angeles. The racial backgrounds surveyed match the demographic characteristics of the US population based on the 2000 cen-
The conclusions of Jervey and Anderson,9 noting particularly, Rodman et al17 found a predominance of white racial distribution of their surveyed population. Similarly, patients; however, no details are provided regarding the over-2-fold higher prevalence of AH among their white pa-
tients with AH.13

The majority of nonparticipants were older men, which although the results were not adjusted for age.3,7,10,12,13,15,16 An association of AH with male sex has been reported previously, statistical significance after adjusting for age. The associa-
tion of AH with any racial category, in either multivariate or uni-

We found a statistically significant higher prevalence for AH among males, which became of borderline sta-
tistical significance after adjusting for age. The associa-
tion of AH with male sex has been reported previously, although the results were not adjusted for age.3,7,10,12,13,15,16 One of the studies included a large population base3 but only 83.1% of the population participated in the survey. The majority of nonparticipants were older men, which may have led to underestimation of AH and its sex asso-
ciation. Of the other reports, little is known about the baseline characteristics of the population surveyed. Any survey of the ra-
cial characteristics of a population is subject to error be-
cause racial heterogeneity in the United States is often underreported.21 In any case, we found no association of AH with any racial category, in either multivariate or uni-
varyate models.

An association of AH with DM was found in studies derived from eye clinic populations. The eye clinic popu-
lation is biased toward patients with DM and with vi-
sion problems.24 Yazar et al14 surveyed an eye clinic popu-
lation ranging in age from 50 to 89 years. In all of these reports, excluding patients who are younger than 40 years could bias results toward finding an association, especially if patients are clustered in the 40- to 60-year age group. In the age group of 40 to 60 years, we had the highest prevalence of DM in our population and found a sta-
tistical association with asteroid hyalosis.

One obvious limitation to an autopsy study is the in-
ability to confirm the diagnosis of associated diseases by prospective clinical blood tests or studies. However, gen-
eral autopsy findings were available to confirm the his-
tory and clinical findings. It is also likely that our meth-
ods overlooked cases of early or undiagnosed DM, which represent a large proportion of individuals with DM. The prevalence of DM in our study was slightly lower (7.2%) than others (8.9% in the Beaver Dam Eye Study). A re-
cent report found the proportion of undiagnosed DM to range from 35% to 44% of total persons with diabetes aged 40 to 74 years between 1988 and 1994, depending on the diagnostic methods used.23 However, the reports by Ber-
gren et al,2 Wasano et al,12 and Potter and Newcomb13 used history of prior diagnosis or treatment as their criteria for diagnosis of DM. The diagnostic criteria for DM are continually updated. For our study and several clinical studies, the diagnosis of DM reflects the changing criteria used by health care professionals during the period in which the patients lived.

Unlike previous studies, we did not find an association of AH with partial PVD. We limited the scope of this investigation to include cases that had been carefully examined for PVD as part of another study.26 Wasano et al12 compared 59 consecutive cases of AH with 46 age-matched, healthy controls in an eye clinic setting. The authors found a lower prevalence of complete PVD in the AH population compared with controls and a significantly higher incidence of partial PVD in the AH population. They used slitlamp biomicroscopy to diagnose PVD, which can be limited in patients with cataract, media opacity, poor cooperation, narrow pupils, or intravitreal liquid lacunae (syneresis). Our study confirms that there is a lower prevalence of PVD in patients with AH. However, unlike Wasano et al, our data show a lower prevalence of partial PVD in patients with AH after correcting for age.

The most statistically significant association with AH is advancing age (P<.001). Only 1 previous report2 studied age-specific prevalence of AH. The population surveyed ranged from 43 to 86 years, and they found a progressively increasing prevalence with advancing age (P<.001). Our study covered a wider age range of a more broadly distributed population, which would explain the higher age-specific prevalence found in our study (Figure 1).

The definite association of AH with age invites speculation as to the mechanism of AH. The asteroid bodies feature a multilamellar structure comprising a mineral compound containing calcium, phosphorus, and oxygen, presumably a calcium apatite–like material.27 There is chondroitin-6-sulfate at the periphery and hyaluronic acid in the inner matrix.22 The stacks of parallel crystaline lamellae of asteroid bodies are closely associated with irregular collagen fibrils. It has been suggested that the aggregation of collagen fibers into parallel fibrils with aging26 in combination with an anionic field produced by N-acetylglucosamine found in hyaluronic acid may serve as a matrix on which calcium-apatite crystals could form.22 The reason for the lower prevalence of AH in patients with PVD is not readily apparent. Perhaps AH is less likely to form in the presence of vitreous detachment. Alternatively, the composition of the fibrils and vitreous in patients with AH may somehow prevent PVD. This raises fundamental questions about the composition of the vitreous fibrils and biochemical changes associated with aging. The biomolecular composition of the vitreous and asteroid bodies has only recently been explored, and many questions remain unanswered.

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Correspondence: Ben J. Glasgow, MD, Department of Pathology and Laboratory Medicine, The David Geffen School of Medicine at UCLA, 100 Stein Plaza, B-279, Los Angeles, CA 90095 (bglasgow@mednet.ucla.edu).

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REFERENCES