Crystalline Retinopathy Associated With Chronic Retinal Detachment

Irma Ahmed, MD; H. Richard McDonald, MD; Howard Schatz, MD; Robert N. Johnson, MD; Everett Ai, MD; Alan F. Cruess, MD, FRCSC; Joe Robertson, MD; Richard S. Munsen, MD; Craig G. Wells, MD

Objective: To describe the presence of crystalline opacities located at the level of the inner retina in patients with chronic retinal detachment.

Methods: We reviewed the clinical records, fundus photographs, and fluorescein angiograms of patients with superficial retinal crystals in the presence of a chronic retinal detachment.

Results: Eleven eyes in 11 patients with chronic retinal detachment were found to have these peculiar crystalline opacities on the inner retinal surface. In 5 patients, the crystalline opacities were noted on initial assessment prior to surgery and persisted without change in appearance or number after surgical repair. In 6 eyes, the crystals were not appreciated until after surgical repair of the retinal detachment. The crystals appeared similar in all 11 eyes, were highly refractile, and were located in the posterior pole. Eight of the eyes had retinal detachment associated with retinal dialysis and 6 of these had a history of trauma. There was a definite history of vitreous hemorrhage in 2 eyes. The crystals did not seem to be associated with any visual deficit.

Conclusions: Chronic retinal detachment can be associated with crystals on the inner retinal surface. The cause and composition of these crystals are unknown. They seem to be visually inconsequential and unchanging.


CRYSTALLINE retinopathy may be associated with a variety of toxicological or inherited disorders; various chemicals, drugs, and metabolic by-products may also result in highly refractile deposits in various layers of the retina.1-48 Genetically determined metabolic conditions can also result in crystal deposition in the retina and be associated with significant visual deficit.3,11,19,20,31,33,37,39,45-47 Calcium oxalate and calcium phosphate crystals associated with chronic total retinal detachments have been reported in the past; however, these crystals are located in the outer retinal layers and were noted only on histopathological examination with no clinical correlates.49-51 Herein we describe superficial crystalline deposits on the inner retinal surface in a series of patients with chronic retinal detachment.

The patients ranged in age from 20 to 64 years (median age, 32 years) (Table 1). All were white. Four patients were female and 7 were male. Six patients had a definite history of trauma. Two patients were suspected of having a history of drug abuse. No patient had a positive family history of systemic or inherited illnesses and findings from all such investigations were normal.

The initial visual acuity in the affected eyes of these patients ranged from 20/20 to 20/200. All patients who underwent surgical repair of retinal detachment demonstrated improved visual acuity postoperatively. Those who did not require surgical intervention maintained stable visual acuity on follow-up. The crystalline opacities were noted at the time of initial assessment in 5 patients and postoperatively in 6 patients. Eight patients had retinal dialysis associated with retinal detachment. Six had a definite history of blunt trauma; 5 cases did not. The length of follow-up in our series ranged from 5 months to 11 years, with a mean length of follow-up of 43.8 months.

All patients except case 1 underwent some form of surgical intervention. The nonoperated patient had a stable chronic retinal detachment with a broad demarcation line. Eight patients underwent a scleral buckling procedure with cryotherapy. The patient in case 2 (Figure 2) had a large retinal dialysis from the 5-o’clock to the 8-o’clock position with a chronic retinal detachment and a demarcation line up to the inferior retinal arcade. This patient refused a scleral buckling procedure and opted for barrier laser and cryotherapy.
PATIENTS AND METHODS

We reviewed the family history, medical history, and ophthalmic findings of 11 patients with chronic retinal detachments who had small, highly refractile, crystalline opacities on the inner retinal surface. Their histories and examination records were reviewed for age, race, sex, extent of systemic disease, drug use, preoperative visual acuity, final postoperative visual acuity, time when the retinal crystalline opacities were first observed, retinal detachment anatomy, retinal break location and size, operative procedure, length of follow-up, and final anatomical status.

REPORT OF CASES

Case 1

A 38-year-old woman was referred for assessment of iridescent particles on the surface of the left retina. Her medical history was positive for iron-deficiency anemia, acne, and mild gastritis. There was no history of oxalosis or exposure to tamoxifen, canthaxanthin, or methoxyflurane. There was no history of substance abuse.

Visual acuity was 20/20 OD and 20/25 OS. Examination results from the right eye were entirely normal. Numerous highly refractile crystalline opacities were located at the inner retina–posterior hyaloid interface (Figure 1). A rhegmatogenous retinal detachment was seen inferotemporally. There were 2 retinal breaks at the 5-o’clock position. Surrounding this chronic-appearing detachment was a broad, heavily pigmented demarcation line. Results of fluorescein angiography were normal. The patient was lost to follow-up for 3 years, at which time she was seen again with no change in her vision, in the status of the localized chronic retinal detachment, or in the appearance of the retinal crystals.

Case 2

A 31-year-old man had a large inferotemporal dialysis and chronic rhegmatogenous retinal detachment in his left eye. He had no definite history of direct trauma to his eye but had been involved in a previous motor vehicle crash. He had a history of cocaine and alcohol abuse. There was no history of oxalosis or exposure to canthaxanthin or methoxyflurane.

On examination, visual acuity was 20/25 OD and 20/25 OS. Fundus examination results from the right eye were unremarkable. In the left eye, a retinal dialysis extended from the 5-o’clock to the 8-o’clock position with a chronic-appearing retinal detachment extending down to the inferior vascular arcade. A demarcation line was present at the posterior extent of the detachment. A macrocyst was present within the detached retina. In the macula, refractile crystals appeared to be on the inner retinal surface (Figure 2). Results of fluorescein angiography were normal, without evidence of any vasculocclusive disease that might be seen with talc retinopathy. The patient declined scleral buckling surgery. Barrier laser and cryotherapy were applied to wall off the retinal detachment. The patient was followed up for 5 months without change in the anatomical status of the detachment or in the appearance of the crystalline retinopathy. He was subsequently lost to follow-up.

Two cases had documented vitreous hemorrhage. Case 5 had a unilateral vitreous hemorrhage and a superotemporal horseshoe tear, which was treated with cryotherapy. Two months later, this patient was seen with an inferotemporal retinal detachment. A vitrectomy, gas-fluid exchange, and a scleral buckling procedure with cryotherapy were performed. Case 8 was found to have old blood present at the vitreous base intraoperatively.

The retinas of all 9 eyes undergoing surgical repair were attached. The eye treated with barrier laser (case 2) remained stable throughout the follow-up period. Although no treatment was applied, the retinal detachment in case 1 also remained stable on all subsequent assessments.

COMMENT

In all our patients, small refractile deposits were located on the superficial retina, no deeper than the inner limiting membrane. They were present only in the eye with the chronic retinal detachment and were noted at the time of initial examination in 5 eyes and at postoperative examination in 6 eyes. They did not change in size or number once observed and were scattered randomly in the macula and not associated with retinal blood vessels in the posterior pole (Figure 3 and Figure 4). In case 2, they appeared to be most concentrated in a circular pattern in the parafoveal zone. This pattern of distribution is suggestive of canthaxanthin toxicity; however, the patient denied a history of canthaxanthin use and his other eye was completely normal.

Calcium oxalate and calcium phosphate crystals have been documented histologically in the outer retina of eyes with retinal detachment by Cogan et al. It has been suggested these crystals represent some relationship to de-
generating rod and cone elements, as some crystals were located within the retina at the former site of the rod and cone nuclei and anterior to the outer limiting membrane. The biochemical and metabolic significance of these crystals is obscure. Because we have no histological specimens to assess the definitive composition or etiology of these crystalline opacities, we must speculate as to their origin. It is possible that as the vitreous separates from the retina, there may be particularly firm, pinpoint adhesions to the lamellae (basement membrane of Müller cells) of the internal limiting membrane to which vitreous remains adherent. These small, raised areas may give the appearance of shiny opacities at the level of the internal limiting membrane. These, however, are unlike Gunn dots, which are glistening white dots at the level of the internal limiting membrane and represent Müller cell footplates.

Resolution of retinal hemorrhage in patients with sickle cell retinopathy has been linked to the development of an “iridescent spot” that shows refractile copper-colored gran-

<table>
<thead>
<tr>
<th>Patient No./Age, y/Sex</th>
<th>Medical History</th>
<th>Preoperative Visual Acuity</th>
<th>Postoperative Visual Acuity</th>
<th>Crystals Observed</th>
<th>Chronic RD</th>
<th>Retinal Dialysis</th>
<th>Surgery</th>
<th>Length of Follow-up</th>
<th>Final Anatomical Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/38/F</td>
<td>Iron-deficiency anemia</td>
<td>20/25</td>
<td>No surgery</td>
<td>Preoperatively</td>
<td>Yes</td>
<td>No</td>
<td>None</td>
<td>3 y</td>
<td>No change in RD</td>
</tr>
<tr>
<td>2/31/M</td>
<td>Cocaine and alcohol abuse</td>
<td>20/25</td>
<td>20/25</td>
<td>Preoperatively</td>
<td>Yes</td>
<td>Yes</td>
<td>Barrier laser and cryotherapy</td>
<td>5 mo</td>
<td>No change in RD</td>
</tr>
<tr>
<td>3/36/M</td>
<td>Unremarkable</td>
<td>20/32</td>
<td>20/32</td>
<td>Preoperatively</td>
<td>Yes</td>
<td>Yes</td>
<td>SB/cryotherapy</td>
<td>8 mo</td>
<td>Attached</td>
</tr>
<tr>
<td>4/20/F</td>
<td>Unremarkable</td>
<td>20/20</td>
<td>20/20</td>
<td>Preoperatively</td>
<td>Yes</td>
<td>Yes</td>
<td>First procedure, cryotherapy; second procedure, vitrectomy/air-fluid exchange</td>
<td>21 mo</td>
<td>Attached</td>
</tr>
<tr>
<td>5/64/F</td>
<td>Unremarkable</td>
<td>20/25</td>
<td>20/25</td>
<td>Postoperatively</td>
<td>Yes</td>
<td>Yes</td>
<td>SB/cryotherapy</td>
<td>10 y</td>
<td>Attached</td>
</tr>
<tr>
<td>6/28/F</td>
<td>Suspected substance abuse</td>
<td>20/40</td>
<td>Lost to follow-up</td>
<td>Postoperatively</td>
<td>Yes</td>
<td>No</td>
<td>SB/cryotherapy</td>
<td>6 mo</td>
<td>Attached</td>
</tr>
<tr>
<td>7/27/M</td>
<td>Trauma</td>
<td>20/200</td>
<td>20/20</td>
<td>Postoperatively</td>
<td>Yes</td>
<td>Yes</td>
<td>SB/cryotherapy</td>
<td>12 mo</td>
<td>Attached</td>
</tr>
<tr>
<td>8/26/M</td>
<td>Trauma</td>
<td>20/200</td>
<td>20/20</td>
<td>Postoperatively</td>
<td>Yes</td>
<td>Yes</td>
<td>SB/cryotherapy</td>
<td>11 y</td>
<td>Attached</td>
</tr>
<tr>
<td>9/28/M</td>
<td>Blunt trauma</td>
<td>20/20</td>
<td>20/20</td>
<td>Postoperatively</td>
<td>Yes</td>
<td>Yes</td>
<td>SB/cryotherapy</td>
<td>2 y</td>
<td>Attached</td>
</tr>
<tr>
<td>10/32/M</td>
<td>Blunt trauma (hockey fight)</td>
<td>20/20</td>
<td>20/20</td>
<td>Postoperatively</td>
<td>Yes</td>
<td>Yes</td>
<td>SB/cryotherapy</td>
<td>11 y</td>
<td>Attached</td>
</tr>
<tr>
<td>11/27/M</td>
<td>Trauma (concussion as a child)</td>
<td>20/100</td>
<td>20/32</td>
<td>Preoperatively</td>
<td>Yes</td>
<td>Yes</td>
<td>SB/cryotherapy</td>
<td>8 mo</td>
<td>Attached</td>
</tr>
</tbody>
</table>

*All patients were white. SB indicates scleral buckle surgery.
ules representing hemosiderin-laden macrophages subjacent to the internal limiting membrane. Although in our series no retinal hemorrages were observed, it is possible that the crystalline retinopathy in our series represents blood breakdown products secondary to vitreous hemorrhage which, for unknown reasons, have become attached to the internal limiting membrane of the retina. However, only in cases 5 and 8 was there a clear history of vitreous hemorrhage, though the frequent finding of retinal dialysis in our series raises the question of trauma. We noted these crystalline opacities in 5 of these 11 patients on initial assessment. In 2 cases, no buckling procedure was performed. In 6 patients, these opacities were first observed after surgery. These crystalline opacities may have been present but undetected at the time of initial examination. However, it is certainly conceivable that they appeared following surgery.

Yellow-white vitreous opacities have been described in patients with idiopathic dialyses. These opacities were located in shallowly detached peripheral vitreous slightly posterior to the elevated rim of the retinal dialysis and were felt to represent spontaneously avulsed peripheral neurosensory retina and possibly nonpigmented ciliary epithelium. Of note was the fact that these opacities were also seen in the normal eye of 2 patients with a unilateral retinal dialysis. These yellow-white opacities were different from the brown pigmented opacities seen in traumatic retinal dialyses that probably represent pigment or blood breakdown products. We observed intraretinal opacities in the posterior pole, not only in areas of previously attached retina.

Table 2. Causes of Retinal Crystals

<table>
<thead>
<tr>
<th>Cause</th>
<th>Vision Changes</th>
<th>Description and Location of Crystals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canthaxanthin</td>
<td>Normal</td>
<td>Inner retinal yellow refractile crystals in an oval configuration surrounding the central macula.4,5</td>
</tr>
<tr>
<td>Talc/cornstarch emboli</td>
<td>Often good vision</td>
<td>White glistening crystals located in the perifoveal arterioles, nerve fiber layers, and inner nuclear layers.12,26</td>
</tr>
<tr>
<td>Primary hyperoxaluria</td>
<td>Mild visual impairment</td>
<td>Calcium oxalate crystals are seen at the level of retinal pigment epithelium, inner retina, and choroid and are largely confined to the posterior pole.32,43-47</td>
</tr>
<tr>
<td>Methoxyflurane</td>
<td>Mild visual impairment</td>
<td>Calcium oxalate crystals at the level of the retinal pigment epithelium, sensory retina, and along retinal arteries.27</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>Significant visual impairment with high doses; reversible with termination of low doses</td>
<td>Fine intraretinal superficial refractile lesions are located in the temporal paramacular area and represent products of irreversible axonal degeneration induced by high doses.23,48</td>
</tr>
<tr>
<td>Bietti crystalline dystrophy</td>
<td>Progressive loss of visual acuity and night vision</td>
<td>Yellowish-white crystalline deposits located in all layers of the retina, particularly in the posterior pole. Crystals and lipid inclusions have been seen histopathologically in choroidal fibroblasts.2,3,34</td>
</tr>
<tr>
<td>Cystinosis</td>
<td>Progressive decrease in vision and field loss</td>
<td>Deposits of cysteine lie in the choroid and the retinal pigment epithelium in patients with infantile cystinosis.17,28</td>
</tr>
<tr>
<td>Bilateral acquired parafoveal telangiectasis</td>
<td>Reduced vision due to associated choroidal neovascularization or macular edema</td>
<td>Yellow opacities near the inner retinal surface postulated to be cholesterol or calcium.11,21</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>Slight decrease in vision following long-term use</td>
<td>Superficial and deep intraretinal glistening deposits distributed in a circinate pattern throughout the posterior pole sparing the periphery.15</td>
</tr>
<tr>
<td>Sjögren-Larsson syndrome</td>
<td>Assessment of visual function difficult due to the presence of severe mental retardation</td>
<td>Glistening irregular bodies located in the superficial layers of the retina.29</td>
</tr>
<tr>
<td>Gyrate atrophy</td>
<td>Decreased</td>
<td>Areas of pigmented change are associated with numerous elongated glittering crystals in the late stages of this condition.33</td>
</tr>
</tbody>
</table>
but also in detached retina. We did not observe crystals in uninvolved eyes.

Recently, a clinical finding named the white dot fovea has been described.34,44 Yokotsuka et al44 described it in 58 eyes of 30 Japanese patients with a mean age of 64 years and it was found to be bilateral in 93% of these cases. It was found to be without subjective symptoms or visual disturbance and clinically innocuous. Another report described this condition in an African American patient.43 The clinical appearance of white dot fovea in both of these reports is identical and is characterized by the presence of numerous white dots on the foveal surface distributed diffusely or along the foveal margin, forming a gray ring and often simulating a macular hole. Scanning electron microscopy demonstrated that these granules have multiple protrusions with cililike structures resembling glial cells and are located on the retinal surface.34 It is believed that white dot fovea represents an age-related change of the fovea.35,44 The crystalline retinopathy we observed is unlike the white dot fovea. In our series, crystalline deposits were found not only in the macula but also in the extramacular area and had a yellowish refractile quality. The patients in our series were generally young and had a history of retinal detachment, unlike those cases described with the white dot fovea. Similarities include the innocuous nature of both conditions and the fact that both occur on the superficial retina.

There are many known causes of retinal crystals (Table 2), however, in our series of 11 patients, these conditions were not elicited on history or examination. In case 6, there was a suspected history of substance abuse; however, superficial crystals were observed throughout the macula and not only in the small perifoveal arterioles as would be expected with talc emboli. In conclusion, retinal detachments, particularly when chronic and secondary to dialyses, can be associated with small, superficial, highly refractile deposits, the histochimical origin of which is unknown. These deposits may remain unchanged for many years and are not associated with visual deficit.

Accepted for publication July 2, 1998.

This research was funded in part by the Retina Research Fund at St Mary’s Medical Center, San Francisco, Calif, and by a grant from the Wayne and Gladys Valley Foundation, Oakland, Calif.

Reprints: H. Richard McDonald, MD, 1 Daniel Burnham Court, Suite 210C, San Francisco, CA 94109.

REFERENCES