Further Insight Into West African Crystalline Maculopathy

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Objective: To describe new features and ocular coherence tomographic scans of individuals with West African crystalline maculopathy (WACM).

Design: Prospective observational case series.

Participants: All 14 patients with WACM identified in the medical retina clinic during a 6-month period.

Methods: Full ophthalmic examination and high-resolution ocular coherence tomographic imaging and fluorescein angiography where indicated.

Main Outcome Measures: Ethnicity and dietary history of individuals, location of crystals, and associated retinal comorbidity.

Results: Patients originated from several West African countries. Two patients had unilateral WACM. The crystals were yellow-green in color, birefringent, and located in the layer of Henle of the fovea. Coexistent retinal pathology was present in all patients.

Conclusions: Several new features of the condition are described. Breakdown of the blood retinal barrier may play a role in the formation of the crystals.


WEST AFRICAN CRYSTALLINE MACULOPATHY (WACM) is the formation of asymptomatic yellow-green colored crystals in the maculae of patients of West African ancestry. This condition was first described by Sarraf et al in 2003,1 based on observations in 6 individuals from the Igbo tribe in Southeast Nigeria. He hypothesized that WACM is caused by the ingestion of Kola nuts. A subsequent report of 3 cases by Browning2 suggested that diabetes was implicated in the pathogenesis.

We present a series of 14 individuals with WACM and demonstrate the first ocular coherence tomographic (OCT) scans of these crystals within the macula. We also show that these patients may have several other associated retinal vascular diseases and can have unilateral crystal formation.

RESULTS

During the 6-month period, 14 patients with WACM were identified. Four individual case studies are presented below to highlight novel features of this condition, and the findings of all of the patients are summarized in the Table. For completeness, we have included partial data on 4 patients in this table.

Ocular coherence tomographic scanning was often hindered by the presence of macular edema, but where clear images of the crystals were obtained, it shows that they are deposited in the layer of Henle of the fovea. In several cases the macula was examined through a rotating polarizing filter and confirmed the crystals to be birefringent.
CASE 1

An 80-year-old man was originally referred to the ophthalmology clinic by an optometrist 6 years ago for bilateral cataracts. On examination in the clinic, he was noted to have retinal hemorrhages in the left temporal periphery and bilateral WACM. A blood test detected the presence of sickle cell–hemoglobin disease. He had a left vitreous hemorrhage 2 years previously that resolved without intervention. The crystals are demonstrated in the color photo of the left fundus (Figure 1).

CASE 2

A 57-year-old man was diagnosed with type 2 diabetes 15 years ago, and had received insulin treatment for the past 5 years. He had renal failure secondary to diabetic nephropathy and underwent a cadaveric renal trans-
plant; he now has diabetic peripheral neuropathy. He had good glycemic control, with a hemoglobin A1C level of 5.8%, and no recorded history of clinically significant macular edema or retinal treatment. On examination in the ophthalmology clinic, he was diagnosed with minimal nonproliferative diabetic retinopathy and the presence of bilateral WACM was noted. The WACM is shown with color fundus photography (Figure 2, A and B). The lack of diabetic maculopathy allowed the crystals to be well visualized with OCT in the layer of Henle of the fovea (Figure 2, C and D).

**CASE 3**

A 39-year-old woman lost the vision in her right eye more than 20 years previously and underwent evisceration with an orbital prosthesis and cosmetic shell while living in Nigeria. The cause of visual loss or indication for the surgery performed remains unknown. She had sickle-cell hemoglobin disease and had a brother with unilateral visual loss that occurred in the first decade of life. His diagnosis is also uncertain. Examination of the left eye showed a dragged disc, a long-standing fibrotic tractional retinal detachment in the temporal periphery, and WACM (Figure 3).

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**Table. Relevant Histories of 14 Consecutive Patients With West African Crystalline Maculopathy (continued)**

<table>
<thead>
<tr>
<th>Case No./Sex/Age, y</th>
<th>Country/Tribe, Emigration, y</th>
<th>BCVA</th>
<th>Crystals</th>
<th>Ophthalmic Comorbidity</th>
<th>Medical History</th>
<th>Diabetes</th>
<th>Smoker</th>
<th>Medications</th>
<th>Kola Nut Ingestion</th>
<th>Other Frequently Eaten Local Produce</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/M/58</td>
<td></td>
<td>6/12</td>
<td>Bi</td>
<td>NIDDM</td>
<td>None</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>11/M/50</td>
<td>Ghana/Ewe/1984</td>
<td>6/12</td>
<td>Bi</td>
<td>IDDM</td>
<td>Hypertension</td>
<td>Yes</td>
<td>Never</td>
<td>Insulin, amlodipine, losartan, furosemide</td>
<td>Very rarely</td>
<td>Cassava, palm oil greens, plantains</td>
</tr>
<tr>
<td>12/F/69</td>
<td>Ghana</td>
<td>6/9</td>
<td>Bi</td>
<td>NIDDM, Left CSMO</td>
<td>Hypertension</td>
<td>Yes</td>
<td>Never</td>
<td>Amlodipine, candesartan, simvastatin frusemid, pioglitazone, doxazosin, atenolol, metformin, glibenclamide</td>
<td>Very rarely</td>
<td>Cassava, plantains, palm oil greens</td>
</tr>
<tr>
<td>13/M/53</td>
<td>Ghana/Ashanti/1982</td>
<td>6/12</td>
<td>Uni (right)</td>
<td>IDDM</td>
<td>Hypertension</td>
<td>Yes</td>
<td>Never</td>
<td>Insulin, metformin, trandopril, atenolol, furosemide, moxonidine, simvastatin</td>
<td>Very rarely</td>
<td>Cassava, plantains, palm oil greens</td>
</tr>
<tr>
<td>14/M/68</td>
<td>Nigeria/Delta/1977</td>
<td>6/9</td>
<td>Bi</td>
<td>IDDM, bi treated CSMO</td>
<td>Hypertension</td>
<td>Yes</td>
<td>Never</td>
<td>Insulin, metformin, gliclazide, ramipril, bendroflazide, amiodipine, aspirin</td>
<td>Occasional</td>
<td>Cassava, plantains, palm oil greens</td>
</tr>
</tbody>
</table>

Abbreviations: BCVA, best-corrected visual acuity; Bi, bilateral; CSMO, clinically significant macular edema; FEVR, familial exudative vitreoretinopathy; (N)IDDM, (non)–insulin-dependent diabetes mellitus; NPL, no perception of light; NSAIDs, nonsteroidal anti-inflammatory drugs; Uni, unilateral.

*a* Other eye eviscerated.

*b* Novartis Pharmaceuticals, East Hanover, New Jersey.

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**Figure 1.** Left color fundus photo of case 1, showing West African crystalline maculopathy.
CASE 4

A 75-year-old woman was originally referred by the optometrist with bilateral cataracts. Fundus examination was normal at this stage. Right phacoemulsification cataract surgery was performed, but her initial postoperative visual acuity was 6/60. Fundus examination showed the presence of a recent left branch retinal vein occlusion and unilateral WACM (Figure 4, A and B). Fundus fluorescein angiography confirmed the branch retinal vein occlusion and macular edema (Figure 4C). Six months later, visual acuity in her right eye had spontaneously improved to 6/9, although the crystals were still present on examination.

COMMENT

Several new findings of this condition are presented. They include the presence of unilateral crystals, variation in country and tribe of origin, and other associated retinal vascular diseases.

All patients in the initial case series of 6 patients with WACM were from the Igbo tribe of Southeast Nigeria.1 In the second case series of 3 patients with WACM, 1 was from the Igbo tribe, while the other 2 were from a different tribe in Nigeria (Ibibio) and the Bassa tribe of Liberia.2 Two further patients have since been described, including 1 from Cameroon.3 Our case series contains patients originating from Nigeria, Sierra Leone, and Ghana. This is not an entirely unexpected finding, as a close genetic relationship between these West African populations is clearly recognized at a molecular genetic level.4 It is possible that WACM represents a metabolic abnormality, predisposing the patient to the formation of the crystals when present with other retinal disease. This may reflect an ancestral mutation in this population for which haplotype analysis may provide further clues. However, an environmental cause is equally probable.

In both previous series, all of the patients were older than 50 years. Two patients in our series were aged between 40 and 50 years at the time of diagnosis, although it is likely that the formation of crystals depends primarily on the nature and duration of the associated retinal vascular disease rather than the age of the patient, as these patients had either diabetes or familial exudative retinopathy and sickle cell disease for many years. One patient (patient 4) developed WACM while in our care, showing that the crystals can form in a matter of months in some circumstances.

Sarraf et al1 hypothesizes that kola nut ingestion may play a role in the formation of the crystals. Five of our patients denied kola nut ingestion at any point in their life. Additionally, kola nuts are widely used throughout West Africa, yet it is clear from our clinic, which contains a large number of patients of West African origin, that WACM is not common. It therefore is unlikely that this is the cause of the condition, although it should be
noted that some patients may not be happy to admit to kola nut use.

An alternative dietary cause cannot be excluded. There are many foods that are eaten exclusively in West Africa, many of which do not have English names. However, most of the patients in this case series have lived in the United Kingdom for several decades and only developed the associated retinopathies since emigration. Therefore, if an ingested substance is responsible, the metabolic load persisted until precipitation in the macula many years later.

Browning suggests that diabetes mellitus is important in the pathophysiology of the condition. While 11 of our patients had diabetes mellitus, 3 did not, though all of the patients who we observed with macular crystals did have coexistent retinal pathologies. These were diabetic maculopathy, sickle cell retinopathy, branch macular vein occlusion, and familial exudative vitreoretinopathy. Each of these conditions results in certain degrees of retinal ischemia. We propose that macular crystal formation occurs after a breakdown of the blood retinal barrier in predisposed patients. This is further supported by the unilateral presence of macular crystals in the eye with the branch macular vein occlusion of patient 2.

The use of the high-speed spectral OCT machine showed that the crystals are deposited in the layer of Henle of the retina. This layer is the foveal portion of the outer plexiform layer of the retina, made up of elongated inner processes of the foveal photoreceptors. It is absent in the peripheral retina. It is unclear whether the crystals are ingested and pass through a faulty blood retinal barrier because of the retinal pathology or are precipitated out in the layer of Henle, perhaps owing to slow flow in the axons induced by the ischemia. It also remains unknown whether they are intracellular or extracellular.

It is not currently known what the crystals are composed of. Until pathological studies of retinæ with...
Submitted for Publication: September 8, 2008; final revision received November 25, 2008; accepted December 8, 2008.

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Financial Disclosure: None reported.

Additional Contributions: The authors acknowledge John Marshall, BSc, PhD, for providing expert advice.

REFERENCES


In 1795, Dr Isaac Thompson concocted an eye water of zinc sulfate, saffron, camphor, and rose water. It was sold as late as 1939. This is 1 of a series of 32 medical trade cards advertising the product from 1875 through 1895.


