exceptional cases seem to indicate that something in addition to a mechanical, tractional relationship participates in macular hole formation, at least in some instances. The OCT images in the case reported here depict this apparently tractionless sequence more clearly than previously described.

An alternative explanation is that the traction component is below the resolution of OCT. A possible mediator might be the outer wall of vitreoschisis as has been proposed by Sebag, and this may be depicted on the left side of Figure 2A and B as focal areas of minimal separation of what might alternatively be interpreted as the internal limiting membrane. Degenerative factors such as subtle defects or breaks in the internal limiting membrane (tractionally or senescently induced) may allow hydration of the fovea and distort tissue enough to form a full-thickness macular hole. This may explain why surgical removal of vitreofoveal traction does not uniformly prevent macular hole formation.

The mechanisms of macular hole formation are still incompletely understood but may involve degenerative and tractional factors. A full understanding of pathogenetic mechanisms would likely optimize treatment and prevention of full-thickness macular holes.

William E. Smiddy, MD

Correspondence: Dr Smiddy, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, 900 NW 17th St, Miami, FL 33136 (wsmiddy@med.miami.edu).

Financial Disclosure: None reported.


Interdigitating Dendritic Cell Sarcoma of the Eyelid With a Rapidly Fatal Course

Interdigitating dendritic cells participate in the immune system as antigen-presenting cells, stimulating T lymphocytes. Interdigitating dendritic cells normally are localized in the T-cell–rich areas of lymph nodes and are believed to be derived from hematopoietic precursors and to belong to the mononuclear phagocytic system. Interdigitating dendritic cells sarcoma is an extremely rare malignancy derived from these antigen-presenting cells normally localized in lymphoid organs. Only 45 cases have been reported in the literature to date. We are unaware of previous reports of this sarcoma in the eyelid and could not find any reference to it in a MEDLINE search.

Report of a Case. A 72-year-old man who had an unknown recurrent lesion in his lower right eyelid for 8 months was referred to our department. Two prior biopsies revealed a nevoid lesion and dermatofibroma. The patient was referred to our clinic when the tumor recurred. His best-corrected visual acuity was 0.8 OD. A 20-mm × 6-mm multinodular, ulcerated tumor was present on his right lower eyelid (Figure 1). The anterior chamber and the vitreous were free of inflammation and the lens revealed a mild senile cataract. The patient underwent sufficient surgical resection with a 4-mm–wide tumor-free margin and reconstruction using a tarsoconjunctival flap combined with a skin graft. Microscopically, the tumor consisted of medium to large spindle-shaped cells with hyperchromatic nuclei. The cells were arranged in fascicles and formed whorls. The mitotic count was high (Figure 2). The final diagnosis was interdigitating dendritic cell sarcoma. The tumor cells...
strongly expressed S-100 protein, and many tumor cells showed reactivity with antibodies to lysozyme and CD68 as well as CD45 (Figure 3). Numerous small, reactive CD3-positive T lymphocytes were mixed. Some tumor cells were positive for CD83 and fascin. No reactivity was seen with antibodies to cytokeratins, HMB-45, Melan-A, or CD1a or as markers for follicular dendritic cells, such as CD21, CD23, and CD35. The tumor staging revealed no metastatic disease. After careful deliberation of treatment options with his oncologist, the patient declined chemotherapy and local radiation therapy. Two years later, the patient had a local recurrence and metastatic lung and liver disease. A biopsy of a presumed metastasis in the lung confirmed the diagnosis. His clinical condition deteriorated and he died rapidly.

Comment. Interdigitating dendritic cell sarcoma is an extremely rare malignancy derived from antigen-presenting cells. Monocytes and related cells can be divided into 2 major categories: phagocytes and dendritic cells. The dendritic cells include (1) the follicular dendritic cell, (2) the Langerhans cell, (3) the intestinal dendritic cell, (4) the indeterminate cell, and (5) the interdigitating dendritic cell. Special immunohistochemical markers help to classify these dendritic cell neoplasms. The immunohistochemical diagnosis in this case was based on the World Health Organization classification for hematopoietic and lymphoid tissues. Patients with interdigitating dendritic cell sarcoma usually have lymph-node enlargement at initial examination, though they rarely have extranodal disease. A solitary skin tumor similar to our patient’s was reported by Miracco et al. This sarcoma has a high potential of local recurrence and systemic disease. Of only 45 cases that have been reported in the world literature, the median overall survival (Kaplan-Meier method) from the time of diagnosis is reported to be 15 months. There is no consensus on a standard chemotherapy or radiation therapy regimen for interdigitating dendritic cell sarcoma. Chemotherapy regimens used in malignant lymphoma showed variable degrees of remission; field radiation seems to be the best treatment of localized disease.

To our knowledge, interdigitating dendritic cell sarcoma has not involved the eyelid. Although optimal therapy for this tumor is yet to be determined, adjuvant chemotherapy or radiation therapy may be reasonable given its highly malignant course.

Ingrid Boldin, MD
Gudrun Brix-Gru¨nwald, MD
Michael M. Scarpatetti, MD
Christine Beham-Schmid, MD, PhD
Angelika Klein, MD

Correspondence: Dr Boldin, Department of Ophthalmology, Medical University Graz, Auenbruggerplatz 4, A-8036 Graz, Austria (ingrid.boldin@yahoo.de).

Financial Disclosure: None reported.
Flawed Study Design in Report on IntereXpert Agreement of Plus Disease Diagnosis in Retinopathy of Prematurity

We are concerned that the article by Chiang and colleagues1 and accompanying editorial by Phelps2 could lead to mismanagement and inappropriate care for infants with retinopathy of prematurity (ROP). Based on their study, Chiang and colleagues concluded: "IntereXpert agreement of plus disease diagnosis is imperfect. This may have important implications for clinical ROP management, continued refinement of the international ROP classification system, development of computer-based diagnostic algorithms, and implementation of ROP telemedicine systems."1(p875) These comments imply more than the words stipulate. We believe that many readers will interpret this conclusion to mean that the diagnosis of plus disease is so faulty that it is useless in the management of ROP.

The conclusions drawn by Chiang et al are inappropriate for the design of their study. Selected wide-angle photographs were sent to experts for their review. Noticing considerable disagreement in the diagnosis of plus disease among these experts, Chiang and colleagues made far-reaching conclusions about the inability of experts to agree on the proper diagnosis of plus disease. Such a conclusion would require masked paired examinations of the same infant rather than a review of wide-angle photographs.

Additional flaws in the study design are apparent. The camera used in the experiment offers a minified view compared with the standard reference photograph of plus disease.3 The camera itself places weight on the eye and can change the appearance of plus disease or stage 3 ROP. Experts were shown photos that were devoid of any other anatomical information (eg, presence or absence of stage 3 disease). These additional factors are helpful during indirect ophthalmoscopy in real life. Pictures shown to experts were very ambiguous. Thus, Chiang et al probed intereXpert agreement in a gray area, exactly where disagreement is expected.

Given the design of the study, the only appropriate conclusion is that the use of wide-angle photographs leads to considerable variability in the assessment of plus disease. This study calls into question the use of the wide-angle photographs for the diagnosis of plus disease, rather than the diagnosis of plus disease per se.

If readers interpret these articles to indicate that plus disease is an unreliable feature of ROP diagnosis, then their clinical practice behavior may change in a dangerous way. Indeed, it is hard to imagine any resulting change in practice that would benefit the collective group of infants who have advanced ROP. Plus disease is difficult to diagnose clinically in borderline cases; however, when the full spectrum of plus disease is considered, there are few characteristics of ROP that have demonstrated such a strong association with the clinical sequelae of ROP. A change in practice that leaves out plus disease or causes physicians to underestimate its importance, based on this study, could place many children at increased risk of blindness.

We urge clinicians to continue to emphasize the importance of plus disease in clinical decision making. Plus disease has been extensively and clinically tested as one of the most important and alarming findings in ROP. Meanwhile, Chiang and colleagues have shown us that wide-angle photography is not useful for the diagnosis of plus disease. For this observation, we can be grateful.

William V. Good, MD
Earl A. Palmer, MD
Robert J. Hardy, PhD

Correspondence: Dr Good, Smith-Kettlewell Eye Research Institute, 2318 Fillmore St, San Francisco, CA 94115 (good@ski.org).

Financial Disclosure: None reported.

In reply

We appreciate the opportunity to respond to the thoughtful comments by Drs Good, Palmer, and Hardy. With regard to study design issues: (1) We agree that a contact retinal camera can alter the appearance of retinal vessels but note that many of these same changes may occur during indirect ophthalmoscopy with scleral depression. (2) It is true that our study images were presented to graders without peripheral views or demographic data. However, the standard photographic definition of plus disease also displays only the posterior retina.1 Future research to determine whether this additional information would influence diagnostic reliability may be warranted. (3) We agree that our study did not directly measure whether multiple experts performing serial ophthalmoscopy on the same infants would diagnose plus disease consistently. The strengths and limitations of our study design were discussed in the original article.2 We also note that the Cryotherapy for ROP study found that 12% of eyes diagnosed as having threshold disease after ophthalmoscopy by one certified examiner were diagnosed as having less-than-threshold disease during confirmatory examination by a second certified examiner,3 and we suspect that a fully masked study design might show even higher levels of disagreement.

Based on results from the Early Treatment for ROP study, plus disease has become the critical factor determining whether an infant requires treatment for ROP.3 By definition, plus disease is either present or absent. It was...