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Photodynamic Therapy for Exudative Hamartoma in Tuberous Sclerosis

Tuberous sclerosis is a systemic disorder characterized by hamartomas in multiple organs, commonly including the skin and brain, as well as additional cardiac, renal, pulmonary, and ocular findings. Approximately 50% of cases with tuberous sclerosis have ocular involvement with unilateral or bilateral retinal astrocytic hamartomas. Although most retinal astrocytic hamartomas remain asymptomatic or gradually regress during life, some exceptional cases may develop symptomatic alterations by an enlarged tumor with leakage, macular edema, accumulating lipid exudates, serous retinal detachment, or vitreous hemorrhage. Persisting macular edema and lipid accumulation may cause persistent visual impairment. This article highlights the novel approach with photodynamic therapy.

Figure. A, Sagittal T1-weighted magnetic resonance image (MRI) without contrast shows a pineal cyst (arrow) of 1.2 cm in diameter in a child with retinoblastoma, which is isointense relative to cerebrospinal fluid (CSF) with a rim slightly hyperintense relative to CSF. B, Axial T2-weighted FLAIR (fluid-attenuated inversion recovery) image shows contents of cyst (arrow) hyperintense relative to CSF. C, Sagittal T1-weighted postgadolinium MRI shows no internal cyst enhancement (arrow).

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Report of a Case. A young boy developed multiple petal mal seizures at age 2 years and was diagnosed with tuberous sclerosis based on typical cerebral lesions including subependymal, paraventricular astrocytomas as seen with computed tomography. He later experienced additional symptoms of the disease, including multiple slightly elevated, yellow-red, butterfly-shaped papules distributed on his face (sebaceous adenoma), multiple small nodules in the right kidney, and 2 discrete cardiac calcifications, all of which are tumors typical for tuberous sclerosis.

Annual ophthalmic examinations were initiated when the patient was aged 17 years. By then, his best-corrected visual acuity was 20/25 OD and 20/32 OS. Extensive fundus examination in the right eye disclosed a retinal type 3 hamartoma at the superotemporal arcade and type 1 lesions. The type 3 hamartoma had a typical mulberry appearance and a peripheral semitranslucent rim of approximately 1 disc diameter. Three other astrocytic type 1 hamartomas were present at the inferior arcade of the fundus in the left eye.

At age 22 years, the patient had progressively blurred vision with metamorphopsia in his right eye; this was present for 2 weeks. On examination, his visual acuity was 20/80 OD, and it had remained 20/32 OS. Biomicroscopical analysis of his right eye displayed a normal optic disc with well-perfused retinal vessels. The previously described retinal type 3 hamartoma had remained unchanged. However, one of the type 1 hamartomas localized inferior to the type 3 hamartoma had changed its appearance. This lesion, still showing the characteristics of a retinal type 1 hamartoma, had increased in size and was surrounded by subretinal fluid accumulation with multiple small, whitish dots of lipid exudates extending close to the center of the macula.
As our patient described his symptoms as starting only 2 weeks previously, we decided to observe the natural course for at least another 5 weeks before considering any therapy. During this follow-up period, his visual acuity decreased to 20/200 OD. The size of the type 1 hamartoma increased, and the serous retinal detachment expanded beyond the center of the macula (Figure 1A). One set of fluorescein angiographic images (Heidelberg Retina Angiograph; Heidelberg Engineering GmbH, Heidelberg, Germany) was acquired 5 weeks before photodynamic therapy (PDT), and the other set was taken 1 day before PDT. Comparing these 2 sets, it was obvious that the tumor’s vascularization was rapidly growing (Figure 2A and B). Based on positive treatment results with PDT in choroidal neovascularizations and choroidal hemangiomas, the patient and his parents decided to try this novel approach and signed an informed consent form.

Photodynamic therapy was performed using a modified doubled exposure time of 166 seconds.3 Two weeks after PDT, the patient reported no more metamorphopsia. Nine weeks later, the macula was without signs of a serous detachment, and the lipid exudates continued to decrease in number and size. One year after PDT, the patient’s visual acuity increased to 20/32 OD. On biomicroscopical analysis, the macula remained dry with only a few small lipid exudates inferior to the treated retinal hamartoma. At this time, the flattened, noncalcified tumor became extremely subtle and appeared only as an ill-defined, translucent thickening of the retinal nerve fiber layer resembling healthy chorioretinal tissue (Figure 1B and Figure 2C).

Comment. This is the first description of applying PDT to a symptomatic retinal hamartoma in the case of tuberous sclerosis. Although the natural course of the disease with increasing macular edema was documented for 7 weeks prior to PDT, no recurrence of tumor vascularization has been observed during the following 4 years. A close follow-up was also important so as not to miss the diagnosis if a malignant transformation into an astrocytoma were to occur, which has been described for these lesions and could not have been ruled out by histological analysis.3

Figure 1. Color fundus photography of the right eye. A, The color fundus photograph shows the eye immediately before photodynamic therapy. The extrafoveal type 1 hamartoma (white arrow) has enlarged significantly and shows retinal neovascularization on the surface. The macular edema has increased in all dimensions. The lipid exudates form a radial spike pattern (Henle layer) involving the center of the macula. Radial folds of the vitreous surface and the inner limiting membrane are visible between the border of edema and the optic disc. The contour and size of the type 3 retinal hamartoma (black arrow) at the superotemporal arcade has remained constant. B, The color fundus photograph shows the eye 1 year after photodynamic therapy. The extrafoveal type 1 hamartoma (arrow) has changed to a red-gray color and has become extremely subtle, resembling healthy retinal tissue. The tumorous tissue has reduced in size and appears only as an area of a mild, ill-defined, translucent thickening. There is no visible macular edema, and only some small lipid exudates inferior to the treated hamartoma can be seen. The retinal type 3 hamartoma has remained constant.

Figure 2. Fluorescein angiography of the right eye. A, Fluorescein angiography shows the early venous phase at first consultation 2 weeks after the onset of metamorphopsia and 5 weeks prior to photodynamic therapy. The tumor vascularization of the type 1 hamartoma (arrow) is barely visible as a focal hyperfluorescence at the center (1020 × 700 µm). The surrounding irregular hyperfluorescence is caused by tumor masses and fluid edema. There is a hypofluorescent area with a diameter of 1750 × 1750 µm at the superotemporal arcade, corresponding to the type 3 hamartoma. The vessels on the retinal surface are constricted and bended by the tumorous tissue. B, Fluorescein angiography shows the venous phase prior to photodynamic therapy. The type 1 hamartoma (black arrow) demonstrates an increased hyperfluorescence corresponding to the capillary network of the tumor vascularization. The vascular lesion shows a significantly increased size, with a diameter of 1520 × 1040 µm, and demonstrates the typical signs of active proliferation by a polynodular net of vessels. The hyperreflective patches demarcate the border of the macular edema and correspond to the lipid exudates on the fundus image. The white arrow indicates the avascular zone of the macula. C, Fluorescein angiography shows the venous phase 1 year following photodynamic therapy. The type 1 hamartoma (arrow) demonstrates a mild irregular hyperfluorescence in the center. The hypofluorescent patches corresponding to lipid exudates have resolved completely. The hypofluorescent area of the type 3 hamartoma has remained constant.
Systemic Sarcoïdosis Manifested as Unilateral Eyelid Retraction

Upper eyelid retraction is a common manifestation of thyroid-related orbitopathy with a limited differential diagnosis. We report an unusual case of isolated, unilateral eyelid retraction that was the first manifestation of systemic sarcoïdosis.

Report of a Case. A 45-year-old African American woman had unilateral, left upper eyelid retraction for 3 years. She denied any history of thyroid disease, trauma, or previous surgery to the eyelids. She was taking no medications, and her family history was noncontributory. Review of systems was unremarkable for a history of asthma, chronic cough, shortness of breath, photophobia, fever, or night sweats. The patient reported some weight gain and fatigue over the preceding few months.

Visual acuity was 20/20 OD and 20/25 OS, and intraocular pressure at applanation was 12 mm Hg OU. Pupillary reactions, ocular motility, and visual fields in response to confrontation were normal. Exophthalmometry was 20 mm OU with a base of 100 mm, with no increased resistance to retropulsion. There was left upper eyelid retraction with 2 mm of scleral show (Figure 1) and left upper eyelid lag on downgaze, with a higher upper eyelid crease on the right. There was no change in the position of the left upper eyelid with manual elevation of the right upper eyelid. In addition, instillation of 2.5% topical phenylephrine hydrochloride in the right eye did not result in change in the eyelid position of either eye. Eversion of both upper eyelids showed no lesions or papillary conjunctivitis. There were no palpable anterior orbital masses, and the lacrimal glands appeared normal. Slitlamp biomicroscopy showed normal anterior segments in both eyes. Fundus examination yielded unremarkable findings.

Results of investigations, including thyroid function tests (total triiodothyronine, free thyroxine, and thyroid-stimulating hormone) and complete blood cell count, were normal. Magnetic resonance images of the head and orbits showed no enlargement of the extraocular muscles or any abnormality in the area of the superior sulcus or levator–superior rectus muscle complex. The lacrimal glands were not enlarged. There were no intracranial abnormalities.

The patient was followed up for 3 months, and results of repeated thyroid function tests were normal. There was no change in the eyelid position. She underwent levator muscle recession with excision of Muller muscle of the left upper eyelid. The