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Chorioretinal architecture in Aicardi syndrome: An optical coherence tomography and fluorescein angiography study

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Abstract

Aicardi syndrome is a rare congenital disorder with a classic triad of infantile spasms, chorioretinal lacunae, and agenesis of the corpus callosum. We report the use of fluorescein angiography and spectral domain optical coherence tomography to examine the posterior segment structures in an 8-month-old girl with Aicardi syndrome. Most of the observed features correlated with previously published histopathological findings, but inner-nuclear layer cysts have not been previously described. To our knowledge, this is the first study of the tomographic and angiographic chorioretinal features in vivo

Case Report

An ophthalmic examination was requested for a 2-day-old girl who presented to the intensive care nursery at the University of California, San Francisco, for evaluation of infantile spasms, vertebral anomalies, and multiple brain malformations. Fetal imaging at 6 months gestation revealed an absent septum pellucidum, corpus callosum agenesis, abnormal configuration of the lateral ventricles, a prominent cisterna magna, schizencephaly, right frontal polymicrogyria, and subcortical heterotopias. She was born at full term by an uncomplicated vaginal delivery. There were no known in utero exposures to infections, tobacco, alcohol, or drugs. There was no maternal history of recurrent miscarriages and no family history of consanguinity.

On examination, the patient was light averse but did not fixate. Portable slit-lamp examination of the anterior segment was normal. Funduscopy examination revealed multiple chorioretinal lacunae and coloboma-like optic disks in both eyes. This patient

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Study conducted at the University of California, San Francisco, California.

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demonstrated the cardinal features of Aicardi syndrome, with the triad of agenesis of the corpus callosum, infantile spasms, and chorioretinal lacunae.

At 8 months of age, an examination under anesthesia was conducted during an unrelated surgical procedure. A wide-angle contact fundus camera (RetCam3, Clarity Medical Systems, Pleasanton, CA) was used to obtain fundus photographs and fluorescein angiography. A handheld portable spectral-domain optical coherence tomography unit (SDOCT) (Bioptigen Inc, Research Triangle Park, NC) was used to examine the structure of the lacunae, foveas, and optic discs.

Features typical for Aicardi syndrome were observed, including bilateral coloboma-like optic discs and chorioretinal lacunae (Figure 1). Fluorescein angiography (FA) demonstrated a normal venous and arterial filling phase, a normal transit time, and no vascular leakage (Figure 1). SDOCT demonstrated subretinal fluid. Within lacunae, the RPE was typically absent, and the choroid and sclera were thin (Figure 2). The hyperpigmented areas surrounding the borders of some lacunae on fundus photos were visualized as areas of increased reflectivity deep in the choroid (Figure 1B). The neurosensory retina demonstrated areas of small inner-nuclear layer cysts at the lacunar borders, and the reflectivity normally seen at the inner-segment/outer-segment junction of photoreceptors was attenuated overlying the lacunae. The coloboma-like optic discs were excavated in both eyes (Figure 3). The foveal architecture was normal.

Discussion

Aicardi syndrome (MIM 304050) is an X-linked dominant disorder for which the molecular genetic etiology has not yet been identified.² Without a specific genetic test, the diagnosis of Aicardi syndrome relies on clinical and radiologic findings. Peripapillary chorioretinal lacunae are considered typical, but other ocular abnormalities include microphthalmia, persistent pupillary membrane, chorioretinal “colobomas,” choroidal neovascularization, and optic nerve abnormalities, including hypoplasia, colobomas, morning glory abnormality, retinal detachment, and glial tissue extending from the optic disk³ (Suk KK, Lalwani GA, Murray TG, Hess D, Berrocal AM. Retinal findings in patients with Aicardi syndrome. IOVS 2010;43:ARVO E-abstract 2209).

To our knowledge, this is the first demonstration in vivo that lacunae in Aicardi syndrome are subretinal fluid-filled cavities overlying typically absent RPE. Thin choroid and sclera form the base of these cavities, and an abnormal neurosensory retina, characterized by disruption of the photoreceptors and intraretinal cysts, overlies the cavities.

Prior postmortem histopathological studies have corroborated some, but not all, of the features found in our case. Some histopathological specimens showed well-preserved neurosensory retina,⁴ whereas others showed glial tissue replacing the neurosensory retina overlying lacunae.⁵ Inner nuclear layer cysts have not been previously reported to our knowledge. Descriptions of RPE structure in postmortem histopathological studies have shown variable findings ranging from absence of RPE, attenuated RPE, or hyperplasia of RPE within lacunae.⁴⁻⁶ Prior histopathological studies have shown the choriocapillaris vessels to be decreased in caliber and number at the level of lacunae,^{5,6} consistent with our SDOCT findings showing choroidal and scleral thinning within and adjacent to the lacunae.

Literature Search

A PubMed search from 1970-2010 was performed using the following terms: *Aicardi OCT* OR *Aicardi fluorescein*.

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FIG 1.

Intraoperative fundus photographs and fluorescein angiography obtained at 8 months of age. The chorioretinal lacunae are ovoid with well-demarcated borders and clustered in the peripapillary regions. There are multiple areas of hypopigmented retinal pigment epithelium (RPE) both associated with and distinct from the chorioretinal lacunae in both eyes. Bilateral coloboma-like optic disks are also present. Late-phase fluorescein angiography images of each eye demonstrate hyperfluorescence of lacunae likely due to fluorescein pooling and hyperfluorescence at areas of hypopigmented RPE likely due to transmission defects. There was no vascular leakage in either eye.

FIG 2.

Fundus and OCT imaging of chorioretinal lacunae. Left eye fundus image (A) with magnified area at the edge of a chorioretinal lacuna and SDOCT B-scans obtained 80 μm apart at the locations denoted in the lower duplicate of the image (B). White triangles identify the hyperreflective retinal pigment epithelium (RPE) (B1-B3). In B1 there is an abrupt end to the RPE at the temporal edge of the lacuna. At the interface between adjacent lacunae in B2, there is a thin bridge of RPE. B3 shows a scan both through the interface between adjacent lacunae and within a lacuna showing a corresponding gap between attenuated RPE within the lacuna. Intraretinal cysts are present in the inner nuclear layer (white arrow). An area of increased reflectivity deep to the choroid in each scan (white asterisk) corresponds to the hyperpigmented structure adjacent to chorioretinal lacunae. C), Another lacuna and its interface with nonlacunar retina. At this interface, the neurosensory retina loses contact with the RPE (white arrow), the RPE again ends abruptly (white triangle), and the absent RPE permits increased visualization of the hyperreflective sclera nasal to it. The white asterisk denotes the cavity of subretinal fluid. The retina overlying the lacuna appears to have an intact external limiting membrane but does not have a distinct inner-segment/outer-segment photoreceptor junction.

FIG 3. Coloboma-like optic disk. Right eye fundus image and corresponding SDOCT through the optic nerve head showing marked excavation. Temporal to the disk there is hyperreflectivity (white asterisk) deep to an otherwise normal appearing retina.