

Ectopic brain tissue in the orbit

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Abstract

Purpose The authors report findings in a 9-month-old male infant with heterotopic brain tissue in the orbit, and compare and contrast the characteristics in this patient with the few other descriptions of such lesions in the literature.

Methods Excisional biopsy of the growth was undertaken by means of an anterior orbitotomy.

Results A 9-month-old male infant had a history of congenital left 'anophthalmia' and a slowly growing mass in the left orbit. An MRI scan revealed an orbital mass with solid and cystic components. Histological study of the excised tissue was performed and revealed a choristomatous arrangement of dysplastic brain tissue with intermixed primitive retina including pigmented epithelium. There was no connection between the orbit and cranial cavity.

Conclusions The mass must be considered a rare example of heterotopic brain tissue in the orbit and is the only instance we could find in the literature in which a formed eye was absent but in which a scattered primitive ocular structure could be identified.

Key words Brain, Orbit, Choristoma, Ectopic, Heterotopic, Pigmented epithelium, Retina

The purpose of this paper is to present the clinical and histopathological findings in a patient with intraorbital dysplastic brain tissue admixed with primitive sensory retinal cells as well as retinal pigmented epithelium. Brain tissue in the orbit associated with a bony defect of the orbital wall is indicative of meningocele and encephalocele. Brain tissue in the orbit without such a connection is extremely rare, and its pathogenesis is obscure.

Case report

A 9-month-old Cambodian male infant was referred because of a history of congenital left 'anophthalmia' and progressive fullness of the left orbit. Examination revealed a ptotic left upper lid, conjunctiva protruding between the lids, and a palpable tense mobile mass within the orbit. No formed eye could be found. An MRI scan revealed an orbital mass occupying

the superior aspect of the left orbit (Fig. 1). The mass had solid and cystic components, enhanced partially with gadolinium, and bowed the orbital roof and medial wall outward. Orbital fat, optic nerve and rectus muscles were displaced inferiorly. A small heterogeneous structure was noted inferior and posterior to the cystic mass. The left orbit was small but no bony defect could be found. A CT scan was also performed and failed to reveal bony defects in the orbit.

An MRI scan also showed partial agenesis of the corpus callosum, heterotopic grey matter along the left lateral ventricular margin, and a small left cerebral hemisphere. Head circumference was initially normal, but subsequent measurements at 1–2 years of age demonstrated a circumference between the 10th and 25th percentiles.

Examination was otherwise notable for a normal right eye and orbit, a right beating nystagmus, and café au lait spots. Chromosomal studies disclosed no abnormalities. To date, no developmental syndrome has been identified with this patient. There was no family history for phakomatoses or tumours. The differential diagnoses considered included a congenital cystic eye, microphthalmia with cyst, meningoencephalocele and encephalocele.

The mass was excised via an anterior orbital approach (Fig. 2). Blunt dissection was successful in separating the mass from the conjunctiva in the lateral and medial canthal regions; the mass was adherent to the conjunctiva superiorly, and was found to infiltrate the tarsus and Müller's muscle. A sample submitted for frozen sectioning was read as dysplastic brain.

Gross examination of two specimens disclosed a tan-red, irregularly shaped, $0.4 \times 0.3 \times 0.2$ cm mass and a second tan-pink, ovoid mass measuring $2.6 \times 2.2 \times 1.1$ cm. A linear black area was evident on one end of the second specimen. On sectioning, this demonstrated a $0.4 \times 0.2 \times 0.3$ cm strip of black tissue overlying a 0.5 cm diameter pale white circular area.

Microscopic study revealed dysplastic brain tissue containing neurons of various sizes (Fig. 3). Clusters of cells with small round nuclei and a speckled chromatin pattern were found throughout the neuropil. These cells occurred in loose clusters but more frequently as rosettes

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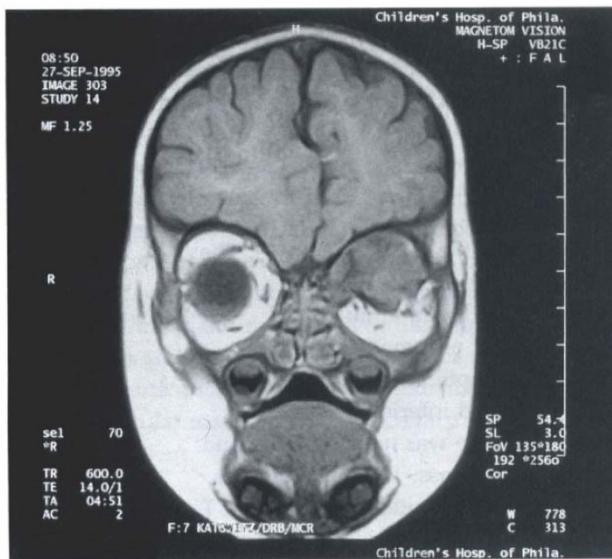


Fig. 1. Coronal MRI scan showing a mass with solid and cystic components that bows the orbital roof.

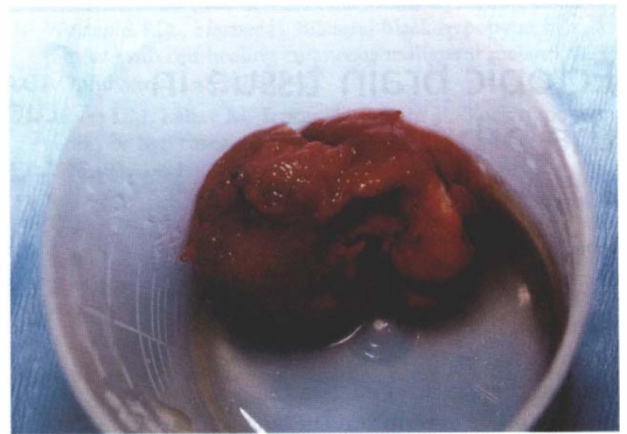


Fig. 2. Gross photograph of the mass excised from the left orbit.

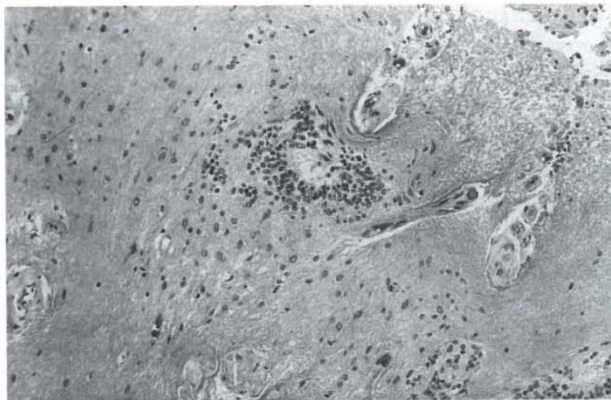


Fig. 3. Photomicrograph demonstrating a solid mass of neurons and neuropil with an interspersed population of small cells forming loose nests (haematoxylin & eosin, $\times 100$).

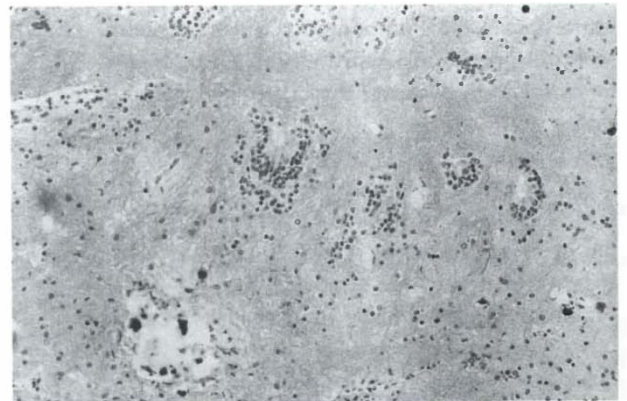


Fig. 4. Photomicrograph of the orbital mass demonstrating rosettes of pseudostratified cells and fleurettes (haematoxylin & eosin, $\times 100$).



Fig. 5. Photomicrograph of the orbital mass containing strips of pigmented epithelial cells (haematoxylin & eosin, $\times 40$).



Fig. 6. Photomicrograph of tissue demonstrating expression of retinal S antigen in fleurettes (retinal S antigen, ×40).

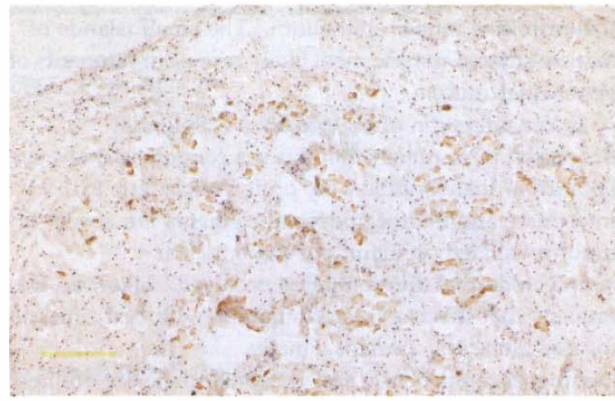


Fig. 7. Photomicrograph of tissue demonstrating expression of desmin (desmin antigen, ×40).

with a variable number of fleurettes. The cells were arranged in a pseudostratified pattern, and an internal limiting membrane and cilia were sometimes found (Fig. 4). No mitoses were seen.

In one area, cords of heavily pigmented cells resembling retinal pigment epithelium were seen (Fig. 5). Nests of pigmented epithelium were also seen in other sites. Striated muscle and apparently normal lacrimal gland were also present. Numerous calcified bodies were seen in the specimen, and this is not uncommon in cases of ectopic brain tissue.¹⁻⁴ There were no ependymal cells present in the specimen. A few oligodendroglia were found scattered in the specimen, but no evidence of myelin formation was seen. No meningeal tissues were found as part of the lesion. The specimens were systemically sampled and no rudimentary globe was identified.

Immunoperoxidase staining utilising monoclonal antibodies revealed 4+ expression of retinal S antigen by many of the small cells in loose nests, rosettes and fleurettes (Fig. 6). These same cells as well as striated muscle revealed 4+ expression of desmin (Fig. 7). These cells also strongly expressed vimentin, as did neurons,

glia and blood vessels. Neurons expressed neurofilament protein whereas there was moderate expression of glial fibrillary acidic protein in neuropil and astrocytes. Only a small percentage of cells demonstrated proliferative activity as shown by PcNA staining (Table 1). The final histopathological diagnosis was dysplasia of the eye intermixed with choristoma.

Discussion

Heterotopic brain tissue may occur outside of the cranial spinal cavity but the orbit is a rare site.^{1,2} In fact, there are only five documented examples of intraorbital ectopic brain (Table 2).¹⁻⁵

The lesion in this patient is different from those reported previously. This infant is the only one lacking a functional globe, and there are no bony defects of the orbit. Most strikingly, histopathological examination demonstrated primitive retinal and retinal pigment epithelium-like tissue within dysplastic brain tissue. The presence of fleurettes and expression of retinal S antigen allows classification of these cells as retinal in lineage.⁶ Co-expression of vimentin and desmin is remarkable in

Table 1. Immunoperoxidase staining of specimen

Monoclonal antibody	Cell types in specimen demonstrating expression	Staining
Retinal S antigen	Small cells in loose nests and rosettes; fleurettes	4+
Neurofilament protein	Neurons	4+
Glial fibrillary acidic protein	Neuropil and astrocytes	2-4+
Desmin	Striated muscle and small cell nests	4+
Vimentin	Rosettes, neurons, glia, blood vessels	4+
Proliferating cell nuclear Ag (PcNA)	Cells undergoing mitosis	Minimal

Table 2. Review of reported cases

Case no.	Author	Orbital lesion	Formed globe	Bony defects
1	Vaquero <i>et al.</i> ⁴	Mature glial hamartoma in a fibrous network	+	+ (lateral wall)
2	Call and Baylis ⁵	Heterotopic cerebellum with neuroglia	+	+ (base of ascending ramus of left zygoma)
3	Newman <i>et al.</i> ¹	Dysplastic brain with astrocytes, connective tissue, skeletal muscle, and a cyst lined by low cuboidal epithelium	+	+ (medial greater sphenoid wing; intact dura)
4	Wilkins <i>et al.</i> ²	Heterotopic brain with astrocytes and a prominent capillary network	+	+ (lamina papyracea; intact dura)
5	Elder <i>et al.</i> ³	Heterotopic brain with mature glia and neurons	+	-
6	Current case	Heterotopic brain with neurons, skeletal muscle, glia, lacrimal gland, primitive retina and retinal pigment epithelium	-	-

this primitive retinal epithelium.⁶ The small islands of mature striated muscle most likely represent remnants of extraocular muscle.

In consideration of the previous differential diagnoses, it is unlikely that this is a congenital cystic eye because in that condition the optic vesicle fails to invaginate and neuroectodermal elements are absent or undifferentiated, while in our patient clear neuroectodermal differentiation occurred.⁷ Likewise, it is unlikely that this is a microphthalmia with cyst since no formed globe was present. Finally, meningoencephalocele and encephalocele are unlikely since there was no continuity between the orbit and the cranial cavity.

Theories relative to the pathogenesis of this remarkable lesion include several possibilities: (1) herniation of normal embryonic neuroepithelium, subsequent sequestration and then parallel development, (2) transformation of dysplastic neural rests with aberrant differentiation potential, or (3) preferential development of one germ layer in a teratoma, i.e. neuroepithelium.¹ We favour the first possibility for several reasons. This infant had evidence of other central

nervous system malformations including partial agenesis of the corpus callosum, heterotopic grey matter along the left lateral ventricular margin and a small left cerebral hemisphere. An early insult in fetal development could account for all abnormalities including ectopic primitive neural tissue in the orbit conceivably disrupting formation of a normal eye.

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