

Case Report

Orbital tumor associated with a microphthalmic eye and colobomatous cleft: Pilocytic astrocytoma (glioma) or massive retinal gliosis



Rita Van Ginderdeuren^{a,*}; Rafael Scot^b; Ilse Mombaerts^c

Abstract

A 11-year-old boy with congenital microphthalmos of the right eye presented with gradual protrusion of his ocular prosthesis. MRI showed an orbital mass adjacent to the microphthalmic eye. After removal of the eye and the orbital soft tissue mass a gliotic mass, resembling a pilocytic astrocytoma WHO grade 1 (glioma) was diagnosed. Through a colobomatous cleft in the eye the tumour spread in the orbit. There were no clinical signs of neurofibromatosis 1. This case showed a very rare association between a microphthalmic and colobomatous eye and pilocytic astrocytoma, grade 1. However a far advanced and infiltrative massive retinal gliosis cannot be definitively excluded as differential diagnosis.

Keywords: Orbit, Pilocytic astrocytoma, Glioma, Massive retinal gliosis, Congenital microphthalmos, Colobomatous cleft

© 2018 The Authors. Production and hosting by Elsevier B.V. on behalf of Saudi Ophthalmological Society, King Saud University. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). <https://doi.org/10.1016/j.sjopt.2018.02.011>

Introduction

This case report highlights the unique presentation of protrusion of an ocular prosthesis as the sign of an infiltrating unknown gliotic tumour. This underscores the need of orbital imaging with new ocular prosthesis problems and the importance of a specialised histopathologic examination of all resected tissue.

Case report

An 11-year-old boy was referred with a 2-year history of progressive painless protrusion of his right ocular prosthesis

(Fig. 1). At birth, he was diagnosed with clinical anophthalmos of the right eye and a small cleft of the soft palate. Specific questioning did not reveal a family history of eye problems and other congenital disorders. On clinical examination the anophthalmic socket displayed a soft, pink subconjunctival mass and a shallow inferior fornix. The midface had a normal symmetrical appearance. There were no ocular or systemic clinical signs of neurofibromatosis type I (NF1). The examination of the left eye gave normal results.

Magnetic resonance imaging (MRI) of the orbit showed a microphthalmic eye with identifiable extraocular muscles and optic nerve. (Fig. 2) There was a well-defined, multilobulated orbital mass located anteroinferior to the microphthalmic eye. Adjacent to the orbital mass, there was bowing

Received 28 November 2017; received in revised form 11 February 2018; accepted 11 February 2018; available online 9 March 2018.

^a Dept of Ophthalmology, and Pathology, Kapucijnenvoer 33, UZ Leuven, B3000 Leuven, Belgium

^b Pathology Department, University Hospitals Leuven, Gasthuisberg, Herestraat 49, 3000 Leuven, Belgium

^c Ophthalmology Department, University Hospitals Leuven, Kapucijnenvoer 33, 3000 Leuven, Belgium

* Corresponding author. Fax: +32 13 323177.

e-mail address: Rita.vanginderdeuren@uzleuven.be (R. Van Ginderdeuren).



Fig. 1. (Top) Clinical photograph of the patient with protruding prosthesis at the right side. (Bottom) Same patient, without prosthesis. A pink subconjunctival mass was visible.

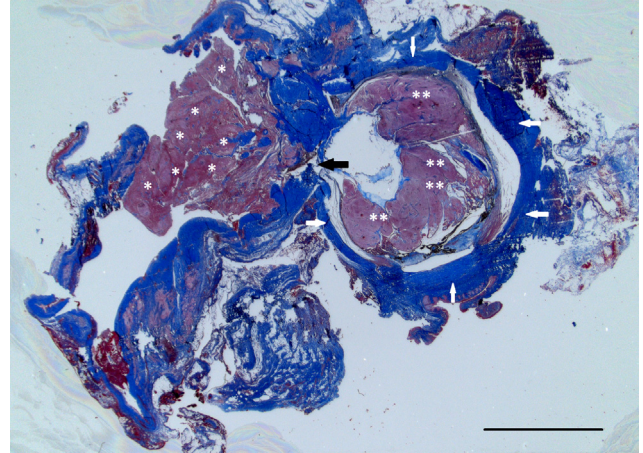


Fig. 3. Overview of biopsy specimen with orbital gliotic tumour (*) and retinal tumour (**) in red color; sclera (white arrow) and fibrous tissue in blue color; coloboma (black arrow); pigment epithelium remnants in black. (Trichroom stain, bar = 5 mm).

of the medial orbital wall without sinus invasion. Previous radiologic scans taken at birth were not available. Via anterior orbitotomy through conjunctival incision, a large, soft orbital mass without capsule and strongly adherent to the microphthalmic eye was removed en-bloc with the eye. A spherical acrylic ball covered with donor sclera was implanted and the shallow inferior fornix was restored with deepening sutures.

On pathologic examination, the specimen consisted of a soft tissue mass and a small rudimentary eyeball with a diameter of 10 mm with a colobomatous opening at the posterior sclera. (Fig. 3) The cornea lacked Bowman's layer and the Descemet's layer was reduced to irregular endothelial cells. The anterior chamber lacked a pupil, lens and trabecular meshwork, and the posterior chamber was absent. The iris displayed normal dilator myofibers and a pigmented posterior surface with irregular ingrowths of clumps of pigmented epithelial cells. The ciliary body and retinal pigmented epithelium were normally developed, and the choroid was thickened. Overall, the content of the eye was filled with sheets of spindle shaped cells with fibrillar eosinophilic cyto-

plasm and long oval, large nuclei, focally atypical with inhomogeneous distribution of chromatin and large nucleoli (Fig. 4). Rosenthal fibers were present. The rudimentary optic nerve was partially replaced by bundles of collagen fibers. Examination of the soft tissue orbital mass, which was adherent to the eyeball, revealed eosinophilic spindle shaped cells similar to those in the eyeball. There was abundant calcification, and old hemorrhages and hyalinized blood vessel walls were found.

The retinal and orbital tumor cells stained homogeneously strongly positive for glial fibrillary acidic protein (GFAP) (Fig. 4). MIB-1 (Ki67-proliferation index or cell-cycling marker) was positive in approximately 1–4% of tumor cells. There were no immunoreactivity for p53 and mutated IDH1 (isocitrate dehydrogenase 1). Genetic analysis after DNA extraction did not show BRAF-mutations. The histological findings were in compliance with pilocytic astrocytoma WHO grade I originating from the retina, but, because of negative

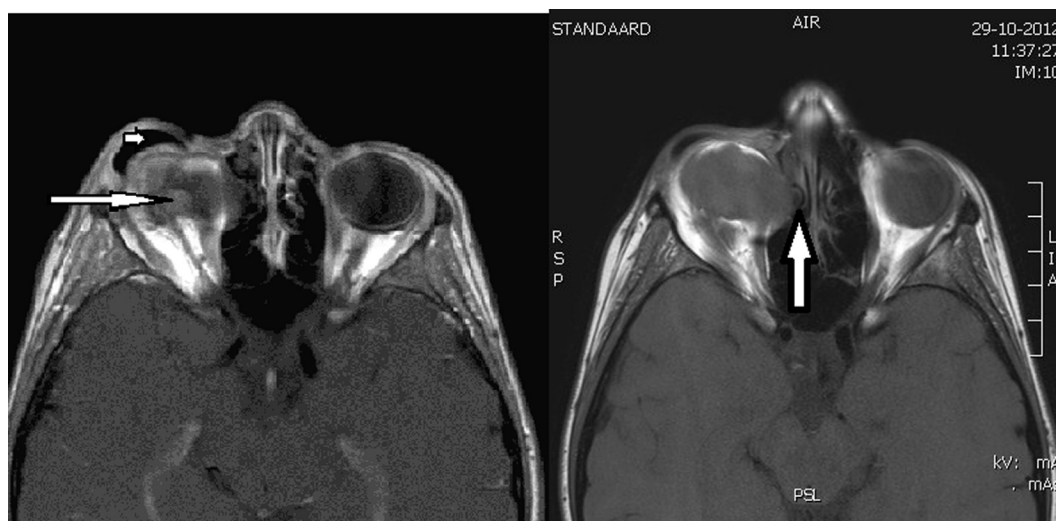


Fig. 2. MRI scan of the orbit, axial views. (Left) Microphthalmic eye (long arrow), with preserved lacrimal gland, horizontal rectus muscles and optic nerve structures. Notice the ocular prosthesis. (short arrow). (Right). Well-delineated, multilobular orbital mass in the microphthalmic socket. Notice the bowing of the medial orbital wall (arrow). There is limited image quality owing to orthodontic braces.

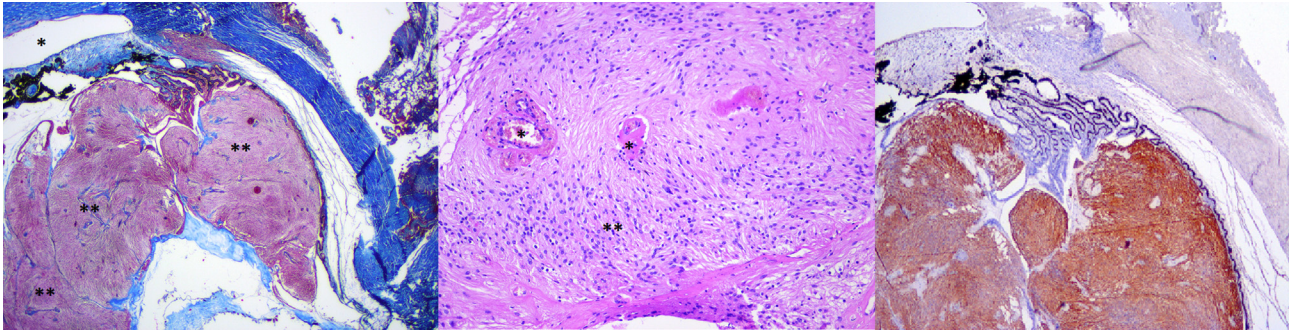


Fig. 4. Histological picture of microphthalmic eye with pilocytic astrocytoma. Left: (*) anterior chamber, (**) intraocular pilocytic astrocytoma, (Trichroom stain, original magnification $\times 16$). Middle: Intraocular pilocytic astrocytoma with bundles of bipolar cells and hyalinized bloodvessels (*), Rosenthal fibers (**), (HE stain, original magnification $\times 100$). Right: The tumor was staining homogeneously with the brown stained glial fibrillary acid protein (gfap immunostaining, $\times 25$).

molecular testing, prominent reactive retinal gliosis was another possible diagnosis. At follow-up four years later, the patient was doing well without evidence of local recurrence.

Discussion

A boy with congenital unilateral microphthalmos presented with an orbital mass with histologic features of pilocytic astrocytoma and/or retinal gliosis. Using light microscopy, low-grade intraocular astrocytoma is indistinguishable from massive retinal gliosis.¹⁻⁴

Massive retinal gliosis is a rare intraocular condition that results from the non-neoplastic proliferation of well-differentiated retinal glial cells and may develop in association with congenital malformations. It can occasionally fill the entire content of the eyeball, mimicking a neoplastic process.^{1,4} We believe that gliosis in our patient may have invaded the orbit through the colobomatous defect of the eyeball. While a negative or a Mib1 rate $<1\%$ of cells is commonly reported, we found however a higher Mib1 rate, this being indicative of a higher amount of cells in the active cell cycle.⁴ This may explain the recent growth of the mass.

Pilocytic astrocytomas, are low-grade astrocytomas (WHO grade I) and are typically encountered in young persons under the age of 20 year. They can arise in any area with resident astrocytes, such as the 3th/4th ventricle, brain stem, cerebellum and spinal cord. On histopathologic examination, the tumor is characterized by intermingling, eosinophilic slender cell processes. Rosenthal fibers, which are thick elongated eosinophilic structures likely representing clumped intermediate filament proteins, are typically present. The term *pilocytic* refers to the hair-like appearance of the bipolar tumor cells.⁵ Findings of BRAF mutation and P53 expression support the diagnosis of astrocytoma but are not always present (ref). In the orbit, astrocytes normally reside in the optic nerve. Optic nerve pilocytic astrocytoma is in 30% of the cases associated with NF1, in which case the multifocal, diffuse and chiasmatic growing pattern is virtually pathognomonic.⁵ Isolated, non-NF1 gliomas account for the majority of the optic nerve gliomas restricted to the orbit alone.⁶ The clinical behaviour of non-NF1 orbital astrocytoma is a slow growing tumor, with occasionally a rapid growth rate. The treatment implies surgical excision in the case of complete vision loss. Radiotherapy and/or chemotherapy is

considered when there is evidence of tumor growth or visual deterioration, or surgical excision is not possible. In this patient, the orbital non-NF1 astrocytoma may have derived from the retina of the microphthalmic eye. The tumor was likely present since several years, clinically supported by a well-developed bony orbit, which is atypical of congenital clinical anophthalmos. The radiologic finding of orbital wall expansion provided additional evidence of a long standing mass. The tumoral growth to a critical volume interfered with the ocular prosthetic fitting, which lead to the diagnosis.

To our knowledge, there is only one similar case reported in the English literature. In 1974, Bonner and Ide described new born child with optic nerve astrocytoma associated with microphthalmos and orbital cyst.⁷ The astrocytoma, however, presented in the orbit and not intraocular. The authors believed that the microphthalmos was caused by the mass effect from the orbital tumor. In 1982, Taylor made the interesting observation that congenital malformation of the optic nerve can be associated with, and hence likely caused by, an optic nerve glioma.⁸ In the Spanish literature, another case is reported by Rodriguez-Francia et al., of a 30-year old man with a colobomatous blind right eye and a microphthalmic left eye associated with retinal and optic nerve astrocytoma.⁹

In conclusion, we report an unusual case of glial retinal tumour growing through a colobomatous opening and infiltrating the orbital content. This mass can be interpreted as non-NF1 related low-grade pilocytic astrocytoma in congenital microphthalmos, and/or as infiltrative massive retinal gliosis. This case underscores the need of orbital imaging in patients with new ocular prosthetic problems in a long standing anophthalmic socket.

Conflict of interest

None of the authors have a conflict of interest.

References

- Jakobiec FA, Thanos A, Stagner AM, Grossniklaus HE, Proia AD. So-called massive retinal gliosis: A critical review and reappraisal. *Surv Ophthalmol* 2016;**61**(3):339-56. <https://doi.org/10.1016/j.survophthal.2015.12.002>.
- Grossniklaus HE, Lenis TL, Jakobiec FA. Retinal Reactive Astrocytic Tumor (Focal Nodular Gliosis): The Entity Also Known as Vasoproliferative Tumor. *Ocul Oncol Pathol* 2017;**3**(3):161-3. <https://doi.org/10.1159/000455149>.

3. Hudson LE, Mendoza PR, Yan J, Grossniklaus HE. Reactive retinal astrocytic tumor (focal nodular gliosis): A case report. *Ocul Oncol Pathol* 2017;**3**(1):1–7. <https://doi.org/10.1159/000448042>.
4. Inayama Y, Hanashi M, Yazawa T, Mitsui H, Kimura A, Ito D. Massive gliosis of the retina: report of a case investigated by immunohistochemistry and clonality assays. *Hum Pathol* 2005;**36**(6):702–5. <https://doi.org/10.1016/j.humpath.2005.04.013>.
5. Ironside J, Moss T, Luis D, Lowe J WR. Diagnostic pathology of nervous system tumours. In: Churchill Livingstone; 2002:53–120.
6. J R. Optic Nerve Glioma. From Diseases of the Orbit: A Multidisciplinary Approach. (Wilkins LW& ed.). Philadelphia: Philadelphia; 2003.
7. Bonner J, Ide CH. Astrocytoma of the optic nerve and chiasm associated with microphthalmos and orbital cyst. *Br J Ophthalmol* 1974;**58**(9):828–31, <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1215032&tool=pmcentrez&rendertype=abstract>. Accessed March 3, 2015.
8. Taylor D. Congenital tumours of the anterior visual system with dysplasia of the optic discs. *Br J Ophthalmol* 1982;**66**(7):455–63, <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1039822&tool=pmcentrez&rendertype=abstract>. Accessed April 28, 2015..
9. Rodríguez-Francia P, Sánchez-Tocino H, García-Cantera M, Martín-Castillo J. Optic nerve pilocytic astrocytoma with retinal involvement. *Arch Soc Esp Ophthalmol* 2005;**80**(12):733–6, <http://www.ncbi.nlm.nih.gov/pubmed/16372218>. Accessed April 28, 2015..