

Received: 2020.10.21
Accepted: 2020.11.17
Available online: 2020.12.10
Published: 2021.01.26

Massive Retinal Gliosis in an Infant Microphthalmic Globe: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

EF 1 **Rakan S. Al-Essa**
AD 1,2,3 **Hind Manaa Alkatan**
BD 2,3 **Maria A. Arafah**
BF 1,3 **Yasser H. Al-Faky**

1 Department of Ophthalmology, College of Medicine, King Saud University, Riyadh, Saudi Arabia
2 Department of Pathology, College of Medicine, King Saud University, Riyadh, Saudi Arabia
3 King Saud University Medical City, King Saud University, Riyadh, Saudi Arabia

Corresponding Author: Hind Manaa Alkatan, e-mail: hindkatan@yahoo.com, hkatan@ksu.edu.sa
Conflict of interest: None declared

Patient: **Male, 11-month-old**
Final Diagnosis: **Microphthalmos with massive retinal gliosis**
Symptoms: **Microphthalmos with no useful vision, left eye**
Medication: —
Clinical Procedure: **Enucleation, left eye**
Specialty: **Ophthalmology • Pathology**

Objective: **Congenital defects/diseases**





Background: Massive retinal gliosis (MRG) is a rare benign intraocular tumor that results from the proliferation of well-differentiated glial cells in response to long-standing pathological processes, including glaucoma, trauma, chronic inflammation, vascular disorders, and congenital anomalies. This lesion is considered to be nonneoplastic and occurs ≥ 10 years after the predisposing insult. It usually affects children and can mimic other conditions, including uveal melanomas, vasoproliferative tumors of the retina, astrocytic hamartomas, and retinal hemangioblastomas.

Case Report: We present a case of infant MRG with severe left eye microphthalmia. An 11-month-old boy was presented by his parents in the Oculoplastic Unit of a teaching university hospital with bilateral incomplete cryptophthalmos and small globes. An enucleation of the left globe was carried out to stimulate orbital bone growth and to improve the cosmetic outcome. The histopathological examination revealed a microphthalmic globe with sclerocornea and disorganized intraocular anterior segment structures. The retina was dysplastic with proliferating spindle-shaped glial cells showing fibrillar eosinophilic cytoplasm and filled most of the vitreous cavity. The glial origin of the cells was confirmed by the immunohistochemical markers (glial fibrillary acidic protein and synaptophysin), supporting the diagnosis of MRG. The optic nerve was markedly hypoplastic.

Conclusions: MRG is a rare intraocular tumor that is clinically difficult to diagnose. A definite diagnosis can be made only on the basis of a histopathological examination and immunohistochemical markers.

MeSH Keywords: **Fraser Syndrome • Glial Fibrillary Acidic Protein • Gliosis • Microphthalmos • Retinal Dysplasia**

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/929363>

 1115   1  11



Background

Massive retinal gliosis (MRG) is a rare, benign, noninvasive intraocular lesion that results from the proliferation of well-differentiated glial cells [1]. In 1918, Von Hippel reported 2 cases of a “benign growth of the retina” [2]. The term “massive retinal gliosis” was used for the first time in 1926 by Friedenwald when he described 4 additional cases [3]. In 1971, Yanoff et al. reported 38 cases of MRG and suggested that the lesion is a nonneoplastic tissue response to retinal injury initiated by several causative factors, including congenital malformations, glaucoma, neoplasia, vascular disorders, trauma, and chronic inflammatory conditions [4]. MRG can develop in association with the retinopathy of prematurity [4,5], as a complication of retinal detachment surgery [6], or as an idiopathic entity [1]. Nork et al. concluded that the cells of origin for the MRG [1] are the Muller cells, while Inayama et al. documented the polyclonal nature of the disease [7]. Here, we report a case of MRG diagnosed by routine histopathologic and immunohistochemical studies.

Case Report

An 11-month-old boy was presented by his parents in the Oculoplastic Unit of a teaching university hospital; he had a bilateral disfigurement of the periocular areas since birth. He was born after a full-term uneventful pregnancy with no significant perinatal or family history. He was otherwise healthy, with no associated systemic anomalies. The ophthalmoscopic examination of the right eye showed an incomplete cryptophthalmos and a palpable microphthalmic globe with a cyst. An examination of the left eye revealed an incomplete cryptophthalmos with a very small globe (Figure 1A). He showed no response to bright light projected separately to each eye. Magnetic resonance imaging (MRI) of the brain and orbit showed a microphthalmic right globe with a large cyst inferiorly in relation to a coloboma, a detached thick retina, and poorly identified extraocular muscles. The left eye showed more severe microphthalmia, without a cyst. The MRI showed bilateral, markedly small optic nerves consistent with hypoplastic changes (Figure 1B). Since the left globe had no visual potential and was not expected to stimulate orbital bone growth, the case was discussed with the patient’s parents. They opted to have a left globe enucleation with an orbital implant and a skin graft-wrapped conformer as the first step in the required multistage surgeries to improve the cosmetic outcome. The enucleated small globe measured 13×12×10 mm with a posterior 2-mm optic nerve, and had an anterior opaque ill-defined cornea. A histopathological examination of the globe showed an unidentifiable corneal epithelium, absent Bowman’s layer, and altered stromal lamellar architecture consistent with a sclerocornea. The Descemet’s membrane was not seen. The angle

of the anterior chamber was obscured and obliterated by the adherent, underdeveloped, disorganized iris and ciliary body tissue. The entire posterior cavity of the globe was occupied by a mass consisting of dysplastic retinal tissue and proliferating spindle-shaped glial tissue with fibrillar eosinophilic cytoplasm forming whorled fibers and a wavy pattern of growth (Figure 1C, 1D), in addition to a few focal areas of calcification. The cells expressed strong reactivity to the neural markers (glial fibrillary acidic protein [GFAP] and synaptophysin), supporting the diagnosis of massive retinal gliosis (Figure 1E, 1F). Some dilated blood vessels were present; however, no prominent vascular component was observed, and the optic nerve was markedly hypoplastic. Postoperatively, the patient made a full recovery, with complete healing of the left socket and a satisfactory cosmetic outcome.

This case report adhered to the ethical standards of the Institutional and National Research Human Ethics Committee and the 1964 Helsinki Declaration as amended in 2013. An approval is not required for this case report according to our Institute’s Review Board/Ethics Committee. The patient’s parents provided written informed consent for publishing the clinical information and accompanying images from this case report without revealing the patient’s identity.

Discussion

MRG affects children more than adults, often occurs ≥ 10 years after the predisposing insult, and all ages and both sexes are affected with almost equal frequency [4]. In the present case report, a male infant presented with MRG in association with severe microphthalmia.

Clinically, it is difficult to distinguish MRG from other intraocular neoplasms [8]. MRG often appears as a single nodule or multiple well-vascularized nodules that typically involve the peripheral retina, although it can occur anywhere in the globe [1]. The differential diagnosis of MRG includes uveal melanomas, vasoproliferative tumors of the retina (VPTR), astrocytic hamartomas, intraocular metastasis, tumors of the retinal pigment epithelium, and retinal hemangioblastomas [5,6,8,9]. MRG can be differentiated from these diagnoses by its histopathological and immunohistochemical (IHC) features, which are mandatory tools for an accurate diagnosis. However, the distinction between MRG and VPTR is more challenging, as both these entities share similar histopathological features characterized by glial and vascular proliferations. While MRG is characterized by a glial-predominant proliferation, the glial and vascular components are largely represented in VPTR, which explains its exudative nature due to fluid leakage from the prominent vasculature [5]. Irvine et al. suggested the term “reactionary retinal gliangiosis” to encompass both entities, as they belong to a

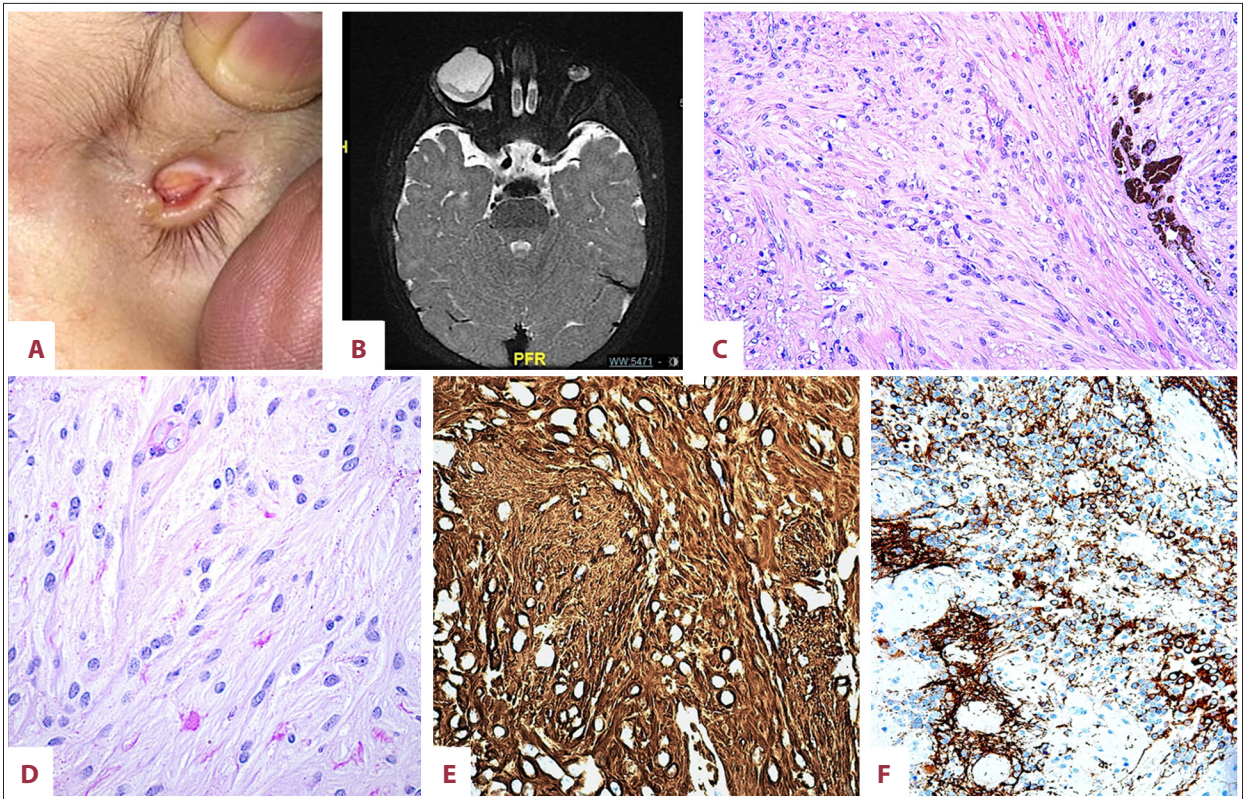


Figure 1. (A) The clinical appearance of incomplete cryptophthalmos, with a deeper small microphthalmic globe on the left side. (B) An axial T2-weighted magnetic resonance image showing a microphthalmos with a cyst occupying the right orbital cavity, and a small microphthalmic globe on the left. (C) A histopathologic image of the massive retinal gliosis with an island of ciliary body-pigmented epithelium (original magnification $\times 200$, hematoxylin and eosin). (D) A higher magnification of the proliferating spindle-shaped glial cells (original magnification $\times 400$, periodic acid Schiff). (E) Retinal gliosis showing a strong expression of the glial tissue marker (original magnification $\times 400$, glial fibrillary acidic protein). (F) Glial cells expressing reactivity to synaptophysin (original magnification $\times 200$, synaptophysin).

spectrum of benign reactive proliferations of glial and vascular tissues [10]. Histopathologically, the vascular component was not prominent in the present case.

Nork et al. demonstrated that the proliferating cells in MRG are immunoreactive for carbonic anhydrase isozyme C, which is specific for the retinal Muller cells [1]. Histologically, MRG is characterized by a nodular proliferation of uniform spindle-shaped cells with abundant eosinophilic fibrillary cytoplasm and indistinct cell borders. The spindle cells typically have minimal atypia and their glial origin can be confirmed using IHC markers, including GFAP, neuron specific enolase, and S-100 [1,7,11]. Yanoff et al. defined 3 histopathological criteria for the diagnosis of MRG: a focal or total replacement of the retina by the proliferating glial tissues, abnormal dilated blood vessels within the tumor, and an obliteration of the normal architecture of the retina by the proliferating glial tissues [4]. The histopathological and IHC findings of the present case fulfilled the proposed criteria and were consistent with the previous reports of MRG cases.

Conclusions

We report a case of MRG in a microphthalmic infant eye. This is a rare intraocular tumor resulting from the benign proliferation of well-differentiated glial cells. Clinically, the distinction of MRG from other intraocular masses is difficult and the final diagnosis can only be made utilizing tissue diagnosis and IHC studies.

Acknowledgements

The authors would like to thank King Saud University Medical City for the laboratories, materials, manpower, and the use of infrastructure in support of this case report.

Department and Institution where work was done

Ophthalmology Department and Pathology & Laboratory Medicine Department, College of Medicine, King Saud University Medical City (KSUMC), King Saud University, Riyadh, Saudi Arabia.

Conflicts of interest

None.

References:

1. Nork MT, Ghobrial MW, Pagman GA, Tso MO: Massive retinal gliosis. *Arch Ophthalmol*, 1986; 104: 1383–89
2. Von Hippel E: Uber diffuse gliose der netzhout und ihre beziehungen zu der angiomatosis retinae. *Graefe's Arch Clin Exp Ophthalmol*, 1918; 95: 173–83 [in German]
3. Friedenwald JS: Massive retinal gliosis of the retina. In: Crisp WH, Finhoff WC (eds.), *Contributions of ophthalmic science: Dedicated to Dr. Edward Jackson*. Menasha, Wisconsin, George Banta, 1926; 23–28
4. Yanoff M, Zimmerman LE, Davis RL: Massive gliosis of the retina. *Int Ophthalmol Clin*, 1971; 11(3): 211–29
5. Houston SK, Bourne TD, Lopes MB, Ghazi NG: Bilateral massive retinal gliosis associated with retinopathy of prematurity. *Arch Pathol Lab Med*, 2009; 133(8): 1242–45
6. Gelisken F, Inhoffen W, Rohrbach JM, Bartz-Schmidt KU: Massive retinal gliosis: A late complication of retinal detachment surgery. *Graefe's Arch Clin Exp Ophthalmol*, 2004; 242(3): 255–58
7. Inayama Y, Hanashi M, Yazawa T et al: Massive gliosis of the retina: Report of a case investigated by immunohistochemistry and clonality assays. *Hum Pathol*, 2005; 36(6): 702–5
8. Ditmar S, Holz FG, Volcker HE: Massive reactive gliosis of the retina. *Klin Monatsbl Augenheilkd*, 1997; 211(5): 338–41
9. Jakobiec FA, Thanos A, Stagner AM et al: So-called massive retinal gliosis: A critical review and reappraisal. *Surv Ophthalmol*, 2016; 61(3): 339–56
10. Irvine F, O'Donnel N, Kemp E, Lee WR: Retinal vasoproliferative tumors: Surgical management and histological findings. *Arch Ophthalmol*, 2000; 118(4): 563–69
11. Shiraki N, Morimoto T, Fujikado T, Nishida K: Rapid growth of massive retinal gliosis in an infant. *J Case Rep Images Oncology*, 2015; 1: 28–31