Massive retinal gliosis without retina

Massive retinal gliosis (MRG) is a rare, benign intraocular condition that may develop in association with long-standing eye conditions, including chronic inflammation, vascular disorders, glaucoma, trauma, prematurity retinopathy, surgery, and congenital abnormalities (microphthalmos and cyst).[1–5] It may represent a non-neoplastic reactive tissue response to retinal injury.[6] We describe an unusual case of MRG-like, which occurred 20 years after evisceration.

C.R.J., a 69-year-old white male, complained about a sensation of fullness in the left orbit for several months. He also noted that his left orbital implant had extruded a couple of days before presentation.

He had lost both eyes' vision in his youth (retinal detachment) and had undergone 2 previous surgeries before evisceration 20 years previously. He reported that a left orbital acrylic implant had extruded 7 years earlier and had been replaced by a smaller one on that occasion.

On external examination, there were bilateral anophthalmic sockets. In the left socket, a large tumour-like mass was located beneath the conjunctiva. This mass was causing some bulging of both lids.

A computed tomography scan of the orbit (taken before implant extrusion) showed that the left eyeball was deformed and enlarged. A mass posterior to spheric acrylic implant was detected. Dense calcification was noted within the mass (Fig. 1A, B). The right orbit appeared normal with spheric acrylic implant. Based on these findings and clinical diagnosis of orbital neoplasm, a biopsy of the tumour was carried out. The biopsy showed a benign glial proliferation. Definitive surgery was postponed for several months. In the meantime, the tumour increased in size (Fig. 1C, D).

We performed an enucleation of the eviscerated socket. The conjunctiva was dissected around the lesion and the scleral shell. We identified horizontal rectus muscles, which were disinserted. The tumour was dissected and cut from posterior attachments. An encapsulated mass measuring 36 mm × 24 mm × 23 mm and of irregular shape was resected. Polyethylene spheric implant No. 20 (Porex, Stryker Medpor, MI, USA) was inserted, covered by the autologous dermis. In 2 years' follow-up, there were no signs of inflammation, implant extrusion, or mass recurrence.

On gross examination, there was a greyish, soft, and heterogeneous mass that compromised intrascleral space, and in some parts there was extrascleral extension.

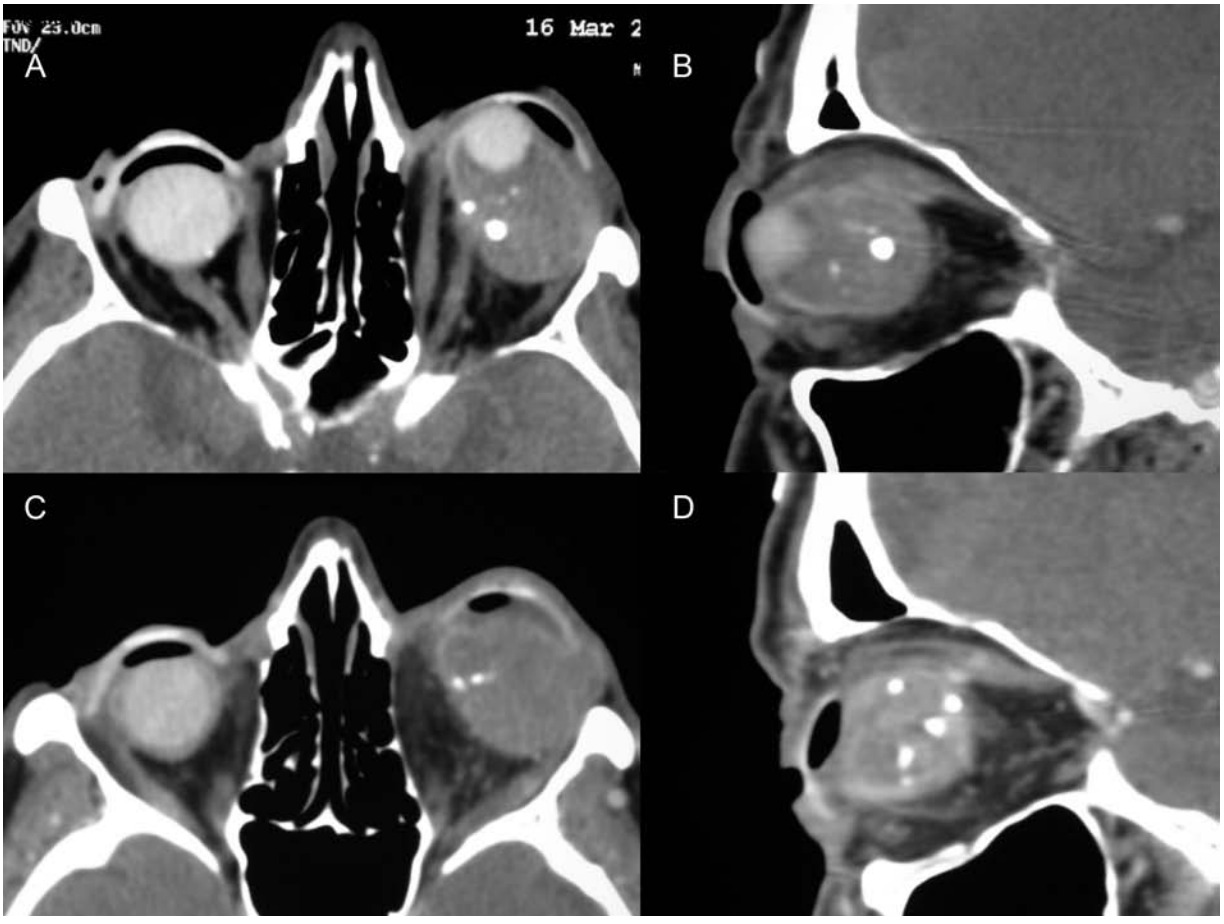

Fig. 1—Computed tomography shows deformed left socket with a mass behind implant and areas of calcification (A, B). After implant extrusion, the mass volume increased but preserved same aspect (C, D).

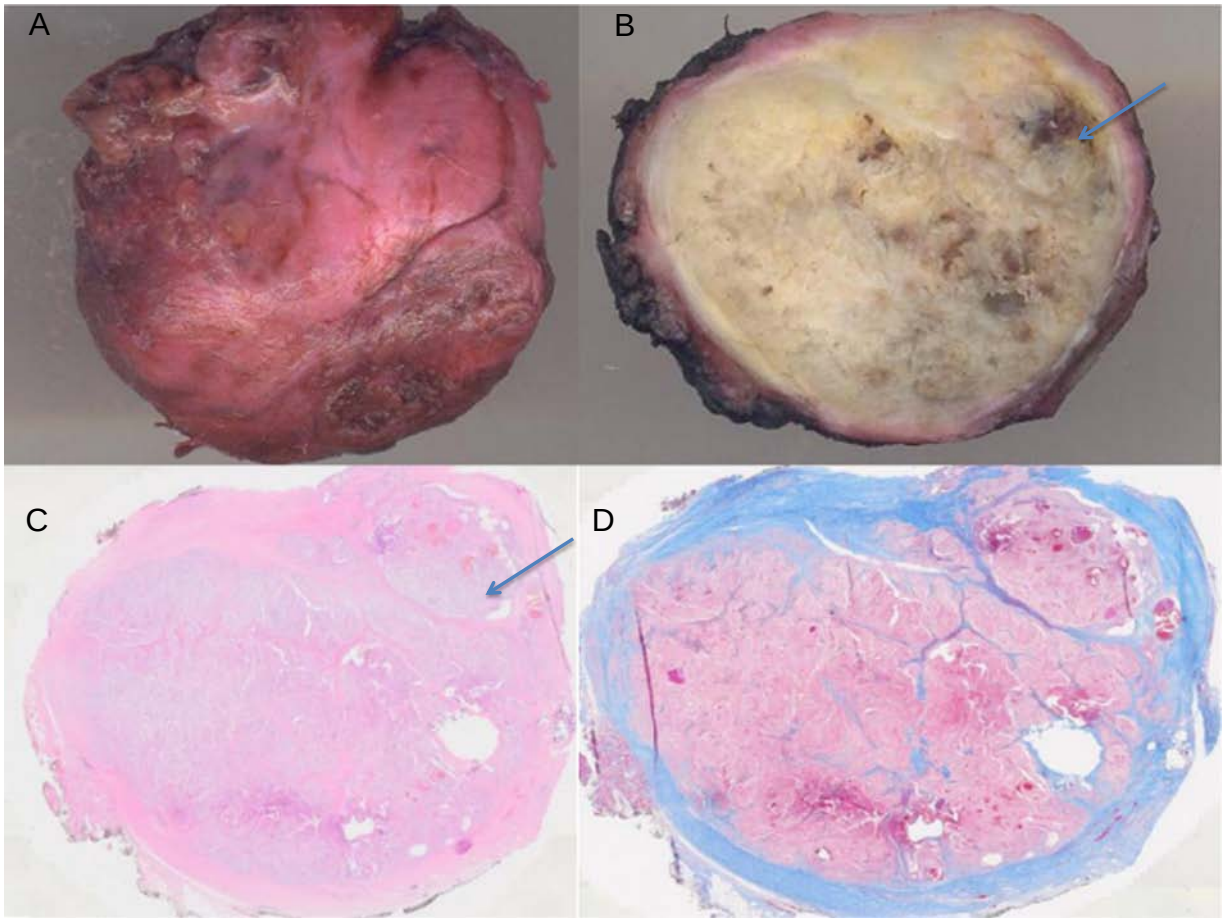

Fig. 2—Resected specimen. A mass measuring 36 mm × 24 mm × 23 mm and of irregular shape (A) compromising intrascleral space and extrascleral extension (B). Macroscopically, the entire lesion can be seen (hematoxylin and eosin) (C), and Masson's trichrome enhances scleral wall (D). Arrows point out areas of scleral ruptures.

On light microscopy, we observed the remaining scleral cavity filled by glial cells with small and round nuclei and fibrillar cytoplasm arranged in interlacing bundles and whorls (Fig. 2A–C). There was no nuclear atypia or mitosis. Large blood vessels with a thin wall and foci of dystrophic calcifications were also identified. There was an extrascleral extension of the lesion. On immunohistochemical study, all spindle-shaped cells showed intense positivity for glial fibrillary acidic protein (GFAP) (Fig. 2D) and neuron-specific enolase. The S100 protein was positive in less than 1% of cells (Fig. 3).

On the basis of the patient's history, light microscopy, and immunohistochemistry study findings, we proposed the diagnosis of MRG. MRG results from non-neoplastic proliferation and migration of retinal Müller cells.[7] It is a very rare condition. The distinction of MRG from true intraocular neoplasms can be clinically very difficult to establish. We believe that this is the first reported case of MRG after eyeball evisceration, also interesting because of extrascleral extension.

MRG onset often occurs 10 or more years after a predisposing disorder such as chronic inflammation, vascular disorder, glaucoma, trauma, retinal detachment surgery, or congenital abnormalities.[4,7] In our case, the patient had undergone many surgeries and experienced chronic inflammation that resulted in a painful blind eye leading to evisceration.

The differential diagnosis of such an intraocular lesion includes uveal melanoma, astrocytic hamartoma, retinal hemangioblastomas, tumours of the retinal pigment epithelium, metastasis, schwannoma of ciliary nerves, and vasoproliferative tumours of the retina.[1–5,8,9] This case is differentiated from these alternative diagnoses based on patient history and previous clinical examinations data and on the histopathological features and immunohistochemistry of the lesions.

Yanoff et al.[5] reported 38 cases of massive gliosis of the retina. The authors defined 3 criteria for massive gliosis of the retina: (*i*) segmental or total replacement of the retina by glial tissue; (*ii*) abnormal blood vessels within the glial mass; and (*iii*) obliteration of the normal retinal architecture by the proliferating glial tissue. The current case could not fulfil the third criteria mentioned because the patient had no retina, but we believe that proliferated cells were from the retina.

MRG cells display no atypia or mitosis but express neuron-specific enolase and GFAP. Thus, few other

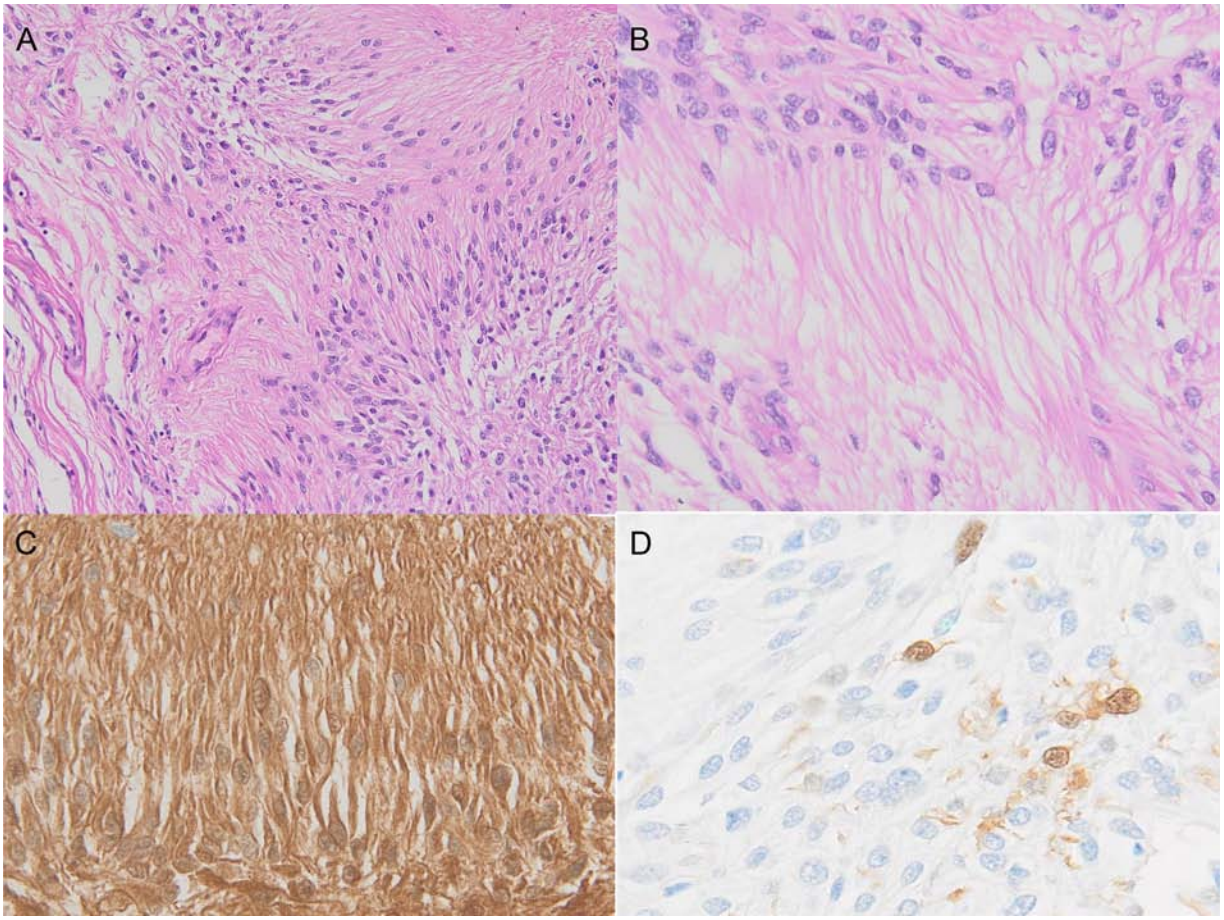

Fig. 3—All intrascleral cavity is replaced by glial cells arranged in interlacing bundles and whorls (A; hematoxylin and eosin [H&E], ×100). Individual cells are elongated, with abundant eosinophilic fibrillary cytoplasm (B; H&E, ×400). The glial cells show intense immunoreactivity for the glial fibrillary acidic protein (GFAP) (C; ×400) and focal immunoreactivity for the S100 protein (D; ×400).

entities are relevant to the differential diagnosis. Intraocular astrocytoma, a benign lesion usually appearing in healthy eyes of patients with tuberous sclerosis and neurofibromatosis, is associated with vision loss and infiltration of the choroid.[10] Intraocular schwannoma arising from the sheath of the ciliary nerves is a capsulated neoplasm containing spindle cells with elongated nuclei with hyperchromasia. When GFAP is expressed in schwannomas, it is focal and in cells around blood vessels, whereas the S100 protein is always diffusely positive.

This case is interesting because MRG occurred after evisceration. Normally, we suppose that, at evisceration, all ocular contents, including retina, are removed. On the other hand, remnants of pigmented tissues are sometimes observed near optic nerves and around exit points of vortex veins in eviscerated sockets. In fact, choroidal melanoma after evisceration can be explained by uveal remnants.[11]

Conceivably, some glial cells may have remained in the scleral shell or around the optic nerve, eventually resulting in proliferation. Extrascleral involvement may be related to scleral disruption on evisceration, biopsy procedures, and implant extrusions. At first, we suspected that it was a tumour behind the scleral shell. Surprisingly, the histologic analysis showed that the main part of the mass was within an enlarged scleral cavity. If proliferation first occurred in the orbital tissue, the mass would not be able to trespass into the sclera.

This surprising case suggests to us that, during the evisceration process, remnants of Muller glial cells can migrate and proliferate at other sites and even in the orbital space.

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Neuro-ophthalmic presentations of clival plasmacytoma

Neurologically isolated cranial mononeuropathy (e.g., sixth nerve palsy) leading to diplopia is a common presentation to ophthalmologists. Although rare, clival lesions can cause isolated unilateral or bilateral abducens palsies with or without papilledema. Intracranial plasmacytomas (ICPC) are rare tumours that constitute less than 1% of intracranial neoplasms. They may present as a solitary plasmacytoma or may be part of a systemic malignant plasmacytosis, as in multiple myeloma (MM).

We describe 2 novel cases of ICPC presenting with abducens nerve palsies. The first patient had previously treated MM, but developed new binocular diplopia with fluid and decreased hearing in the right ear. The second patient presented with bilateral abducens palsies and associated right-sided V2 hypothesia and subsequently was diagnosed with both clival plasmacytoma and MM.

A 59-year-old African-American female presented with a 3-week history of horizontal binocular diplopia. She also had a headache and "fluid sensation" in her right ear causing mild hearing loss. Her medical history included MM successfully treated with chemotherapy 3 years ago, well-controlled hypertension, and hypothyroidism. Surgical history included spinal surgery and knee replacement for degenerative joint disease 8 years previously. She denied any drug allergies and was taking levothyroxine, amlodipine, amoxicillin, and low-dose prednisone. She denied alcohol, tobacco, or drug use. Her family history was significant for colon cancer in her sister, and diabetes, hypertension, and stroke in her father. Review of systems was otherwise negative. On neuro-ophthalmic examination, best corrected visual acuity (BCVA) was 20/25 OD and 20/20-2 OS. Ishihara colour plates were 14/14 OU. Humphrey automated visual fields were within normal limits OU. Pupils measured 4 mm in dark and 2 mm in light, and no relative afferent pupillary defect (RAPD) was noted. Intraocular pressure measured 19 mm Hg OU. There was no disk edema or pallor. Her ocular motility showed a −4 deficit of abduction OD. She had an incomitant 30 prism diopter (PD) esotropia (ET) in primary gaze, which increased in right gaze and decreased in left gaze. The remainder of her ophthalmologic examination was unremarkable.

Magnetic resonance imaging (MRI) of the brain with and without contrast showed a large enhancing lesion centred in the clivus measuring 3.2 × 1.9 × 3.1 cm (Fig. 1). The mass invaded the right cavernous sinus and extended through the posterior table of the sphenoid sinus on the right with invasion of the sellar floor and superior displacement of the pituitary gland. Heterogeneous enhancement throughout the calvarium was suspicious for infiltration, and a biopsy showed ICPC. Immunohistochemistry stained positive for CD38, CD138, CD56, and antilambda. Bone marrow biopsy showed 49% lambda light chain–restricted plasma cells consistent with plasma cell myeloma. The eye was patched for symptomatic relief, and she was treated with radiation therapy and bortezomib.

An 84-year-old female presented with headache, blurry vision, and progressive binocular horizontal diplopia over 2 weeks. Her medical history was significant for stroke, hypertension, coronary artery disease, congestive heart failure, aortic aneurysm, thyroidectomy, recent acute kidney injury, renal cysts, angiomyolipoma, hiatal hernia, gastrointestinal bleeding, multiple gastric polyps, and diverticulosis. Surgical history included coronary stenting and cholecystectomy. She denied any drug allergies and was on amlodipine, atorvastatin, carvedilol, dexlansoprazole, furosemide, meloxicam, potassium, and ranolazine. She denied tobacco, alcohol, and illicit drug use. Her family history was significant for fatal abdominal cancer in her mother and fatal cerebral aneurysm in her father. On neuro-ophthalmic examination, the visual acuity was 20/60 OD and 20/25 OS. Pupils were symmetric in light and dark without anisocoria or RAPD. Intraocular pressure measurements were 13 mm Hg OU. There was no disk edema or pallor. There was a 50 PD ET in primary position, which increased in both right and left gazes.