

Massive Retinal Gliosis – A Rare Benign Condition Masquerading as a Malignant Intraocular Tumor: A Case Report

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ABSTRACT

Massive retinal gliosis (MRG) is a rare, benign intraocular condition resulting from reactive glial cells undergoing exaggerated repair phenomenon. A 52-year-old male presented with 6-year history of enlarging mass in the right eye, associated with progressive vision loss and worsening proptosis. He reported history of trauma to that eye secondary to a vehicular crash one year prior. Magnetic resonance imaging (MRI) of the orbits revealed an intraocular lesion with calcifications raising the possibility of a malignant tumor. Enucleation of the right globe was performed and histopathologic examination revealed the entire vitreous cavity and retina replaced by glial cells arranged in interlacing bundles and whorls with foci of calcifications, highly suspicious of MRG. This was further confirmed by a positive, diffuse, and robust cytoplasmic expression of glial fibrillary protein (GFAP). The disease is known to have favorable outcomes as no complications, such as reemergence of the mass, active bleeding, and secondary infection, were observed from the patient during subsequent visits. Distinction of MRG from other intraocular neoplasms is clinically challenging, hence biopsy is necessary. MRG should be considered as a differential diagnosis when encountering intraocular tumors, especially if there is a history of eye trauma. This is the first reported case of MRG in the Philippines.

Keywords: massive retinal gliosis, intraocular mass, retinal tumor, case report

INTRODUCTION

Massive retinal gliosis (MRG) is a rare, benign intraocular condition resulting from reactive glial cells undergoing an exaggerated repair phenomenon. It may be idiopathic; related to various disease entities such as neurofibromatosis, retinitis pigmentosa, uveitis, retinopathy of prematurity, Coats' disease, retinal detachment surgery, infection; or secondary to physical trauma.¹⁻⁵

The objective of this report is to feature an unusual intraocular tumor, which can easily be misdiagnosed as a malignant neoplasm. The significance of this case is to highlight its course and histopathological findings as it is currently challenging to clinically differentiate it from other intraocular tumors. In this report, we describe the first documented case of MRG in a Filipino patient.

CASE PRESENTATION

A 52-year-old Filipino male presented with a 6-year history of progressively enlarging mass in the right eye, associated with vision loss and proptosis. Past medical history revealed blunt force trauma to the right eye secondary to a motor vehicular crash a year before the emergence of the



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mass, yet no intervention was done. His uncorrected visual acuity in the right eye was no light perception and in the left, it was 15/200 with no improvement on pinhole. Gross eye examination revealed a fleshy, pinkish-brown, non-bleeding, and non-purulent mass with areas of scaling on the right eye (Figure 1). Hertel exophthalmometry showed a 10 mm proptosis in the right eye. Slit-lamp examination revealed a non-injected conjunctiva, clear cornea, deep and quiet anterior chamber, and corectopic pupil in the pseudophakic left eye. Further, fundus examination of the left showed a tessellated retina with staphyloma along a tilted optic nerve head, indicative of a pathologic myopic eye, hence the poor vision.

Orbital magnetic resonance imaging (MRI) with contrast demonstrated a large, irregular, heterogeneously enhancing mass measuring 3.2 cm x 2.6 cm x 2.5 cm, predominantly T1 isointense and T2 hyperintense, with scattered foci, occupying the entire right globe. The mass remained to be well-circumscribed and hyperintense before and after administration of contrast. Normal anatomical structures in the eye were not appreciated on the right (Figure 2). These findings were compatible with an intraocular neoplasm.

Because of these initial findings, the patient was scheduled for enucleation with placement of an orbital implant on the right eye. Chest X-ray revealed incidental reticulonodular densities localized in the right upper lung zone. Pulmonary tuberculosis was considered, with the intraocular mass considered to be an extrapulmonary manifestation of tuberculosis. Sputum GeneXpert assay revealed a negative *Mycobacterium tuberculosis* infection, thus the pre-planned surgery was rescheduled until he was cleared.

The patient underwent an uncomplicated enucleation of the right eye with placement of a 20 mm polymethyl methacrylate orbital implant. A 40 mm x 30 mm x 28 mm,

dusky brown, globular, non-bloody tissue with an extension of the optic nerve measuring 5 mm was removed (Figure 3).

Gross histopathologic examination showed a gritty, whitish-yellow, granular surface with an area of hemorrhage on cross-section. Microscopic examination revealed that the lesion occupied the whole vitreous cavity replacing the retina totally by spindle-shaped glial cells arranged in interlacing bundles and whorls with foci of calcifications, highly favoring massive retinal gliosis. This was further confirmed immunohistochemically by a positive, diffuse, and robust cytoplasmic expression of glial fibrillary acidic protein (GFAP) (Figure 4).

The patient was seen at 1 day, 1 week, and 1 month postoperatively. On each clinic visit, there were no signs of tumor recurrence, orbital implant exposure, or surgical site infection on a short follow-up period after surgery.

DISCUSSION

Orbital masses have diverse etiologies. They may arise from the orbit or ocular tissues, adjacent structures, or distant locations in the body secondary to metastasis. In a 10-year review of the tumors of the eye and ocular adnexa in the Philippines in 2015, most intraocular tumors documented were of malignant etiology. Of the 394 intraocular tumors reported, 21 (5.33%) cases were benign and 373 (94.67%) cases were malignant, with retinoblastoma being the most common out of the malignant cases.⁶ In this paper, we have documented a case of massive retinal gliosis, a rare benign intraocular tumor, which was not previously described locally.

MRG results from a non-neoplastic proliferation and migration of retinal Müller cells. These retinal gliocytes cover the entire thickness of the retina and interacts with all types

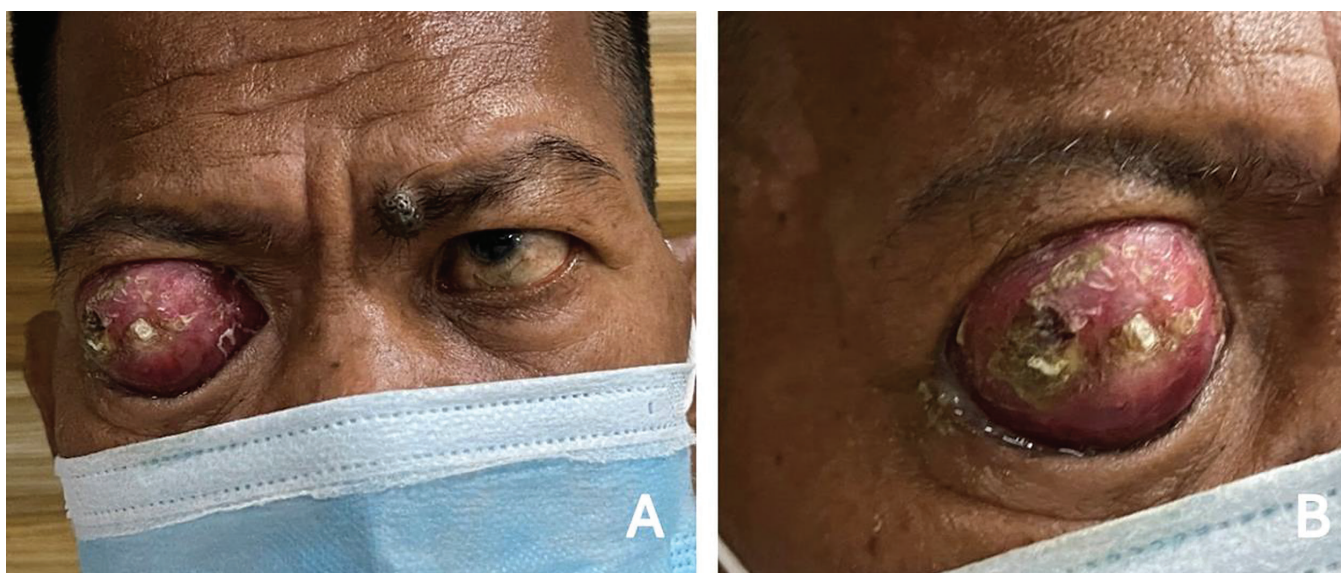


Figure 1. Gross examination reveals (A) a pink fleshy mass in the right orbit with areas of scaling and (B) proptosis. Anatomical distinction of the anterior segment of the right eye is not appreciated.

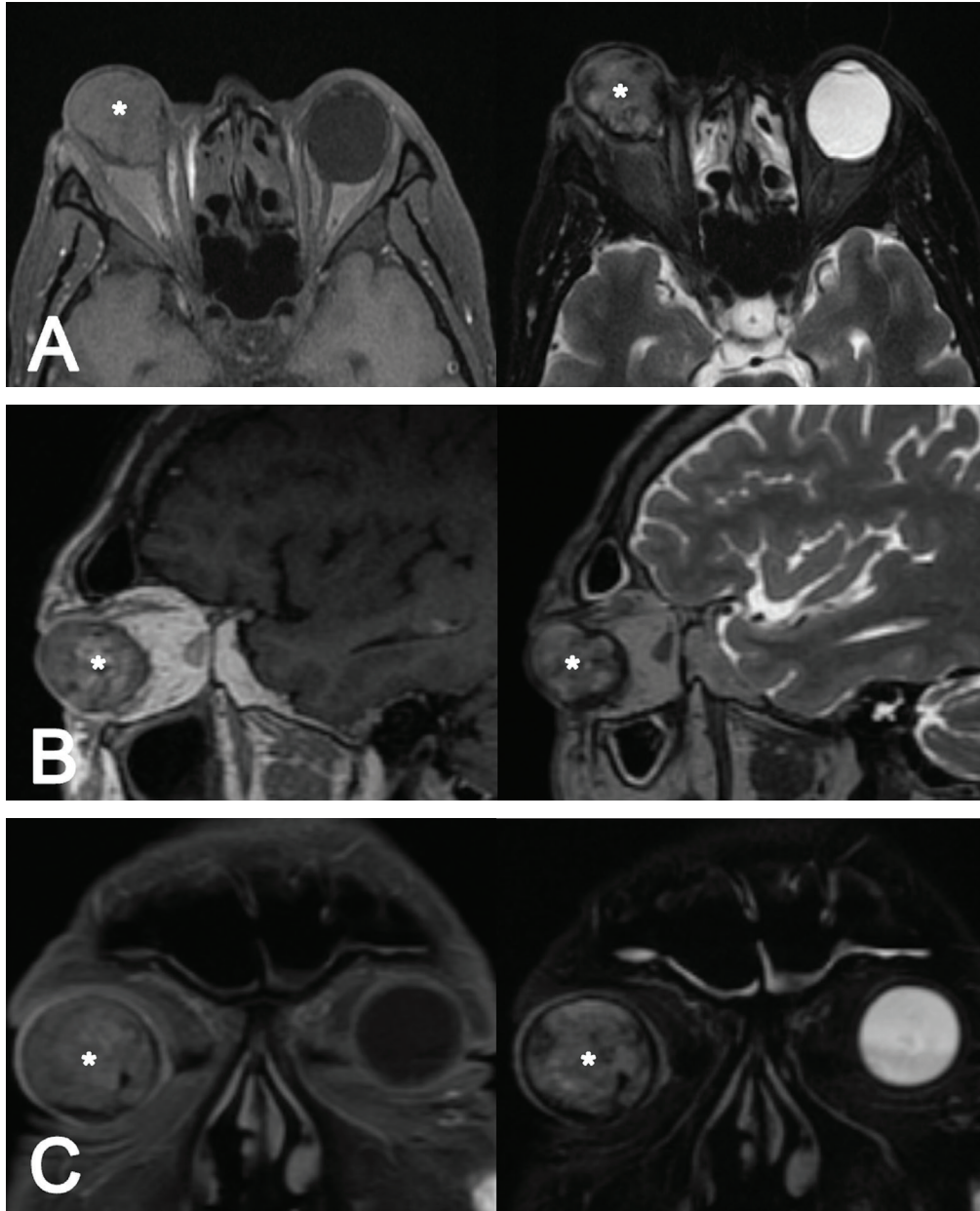


Figure 2. Orbital MRI with contrast shows a large, irregular, heterogeneously enhancing mass occupying the entire right orbit, seen on (A) axial T1 and T2, (B) sagittal T1 and T2, and (C) coronal T1 and T2 views. The signal is heterogenous but predominantly T1 isointense and T2 hyperintense, with the scattered foci of susceptibility noted within which can be reflective of calcifications (*asterisks*). The optic nerve head and extraocular muscles in both orbits are unremarkable. No enhancing mass lesion noted within the left globe.

of neuronal cells creating a soft layer of protection against mechanical trauma. Müller cells also facilitate neuronal development and plasticity due to their ability to differentiate into neural progenitors or stem cells that reproduce lost photoreceptors and neurons under pathological conditions.⁷

The onset of MRG often occurs years after a predisposing disorder such as chronic inflammation, vascular disorder, glaucoma, retinal detachment surgery, congenital abnormalities, or trauma to the eyeball.^{4,8} There are currently

no recent reports on the degree of severity of trauma, whether it be blunt or sharp, to directly cause MRG. However, in this case, the history of blunt force trauma is a significant aggravating factor to develop MRG in patients with thinned out retina from pathologic myopia.

A study by Yanoff et al. reported 38 cases of MRG, and defined three criteria for diagnosis, which were all met in our case: (a) segmental or total replacement of the retina by glial tissue; (b) abnormal blood vessels within the glial

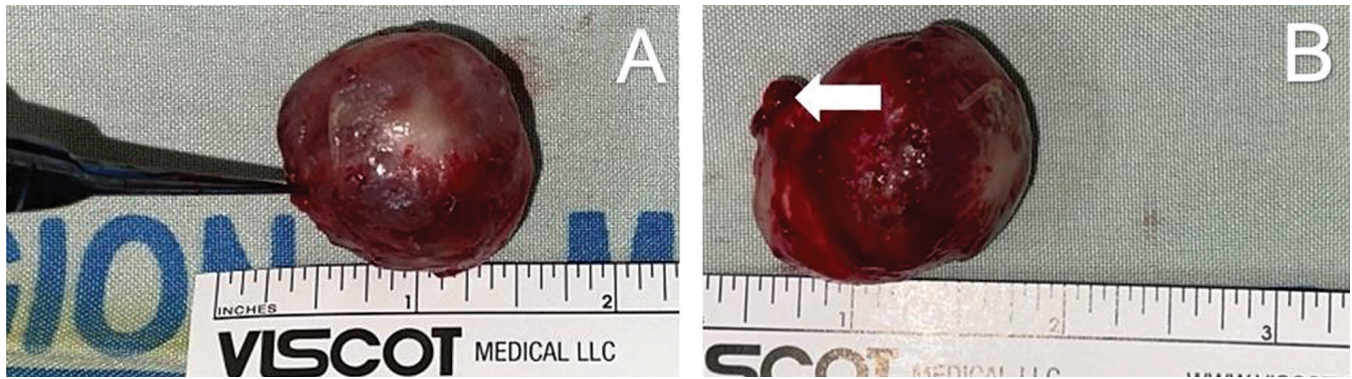


Figure 3. (A) Gross examination of the enucleated right eye shows a 40 mm × 30 mm × 28 mm dusky brown mass. (B) Extension of the optic nerve measuring 5 mm (white arrow).

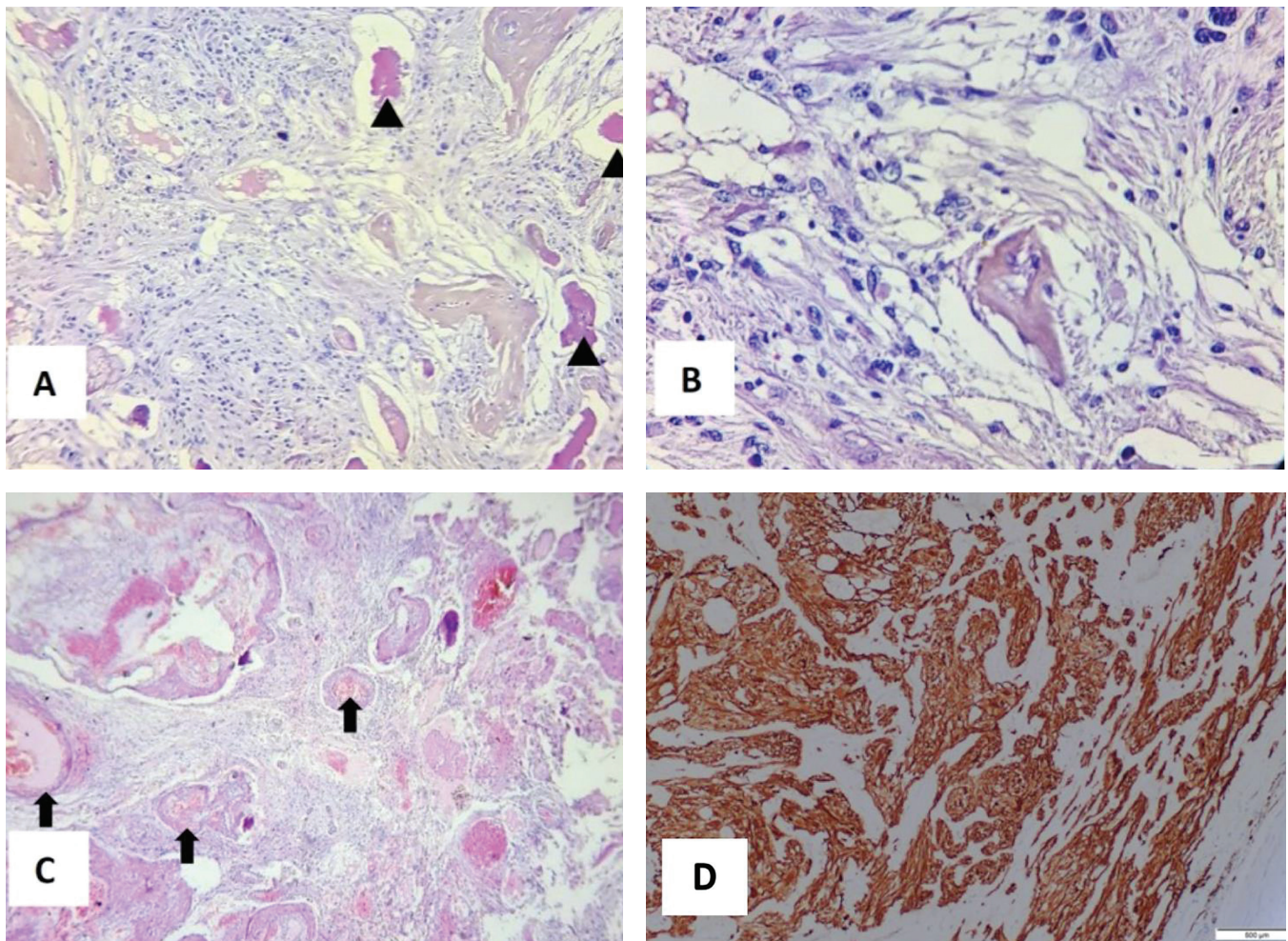


Figure 4. (A) Histologic examination shows elongated cells with abundant eosinophilic fibrillary cytoplasm and regions of blood vessels (black arrowheads) (hematoxylin-eosin, ×10). (B) High magnification showing the elongated cells; other intraocular structures cannot be identified (hematoxylin-eosin, ×40). (C) There are scattered, thin, sclerotic vascular channels with thick hyaline layer (black arrows) (hematoxylin-eosin, ×10). (D) Immunohistochemistry reveals a positive, diffuse, and strong cytoplasmic expression of GFAP (×10).

mass; and (c) obliteration of the normal retinal architecture by the proliferating glial tissue. Furthermore, immunohistochemical (IHC) study showed positivity for GFAP, hence the glial etiology.⁵

Differential diagnosis of MRG may include meningioma, uveal melanoma, astrocytic hamartoma, retinal hemangioblastomas, tumors of the retinal pigment epithelium, metastasis, and schwannoma of the ciliary nerves.^{1-5,9,10} In comparison to these disease entities, cells in MRG do not display atypia or mitosis, but express a neuron-specific enolase and glial fibrillary acidic protein (GFAP).¹¹ Uveal melanoma, which is the most common reportable intraocular tumor, was a primary consideration in this case. However, the classic clinical presentation does not correlate with our patient's presentation, that would still make this case reportable. Another differential diagnosis considered, although reported as well as a rare, benign condition, was intraocular meningioma. The aid of IHC after histopathologic analysis would either rule in or out this disease entity.

In this case, the patient had an incidental finding of pulmonary densities during his cardiopulmonary clearance prior to the procedure. This raised the suspicion of a tuberculosis infection, especially since the Philippines ranks fourth in tuberculosis incidence worldwide.¹² Although tuberculosis in the orbit is rare, this suspicion also suggested the possibility of the intraocular mass to be an extrapulmonary tuberculosis manifestation. Orbital tuberculosis is mostly documented in children, wherein the infection may masquerade as an orbital malignancy. In presentation, ocular tuberculosis may clinically appear with proptosis, bone destruction, motility dysfunction, and chronic draining fistulas. Cases that have documented intraocular tuberculosis have shown that histopathological findings may not necessarily reveal the presence of acid-fast bacilli, but usually show caseating necrosis, epithelioid cells, and Langerhans giant cells. In these cases, anti-tuberculous regimen is curative.¹³ Knowing its high incidence, ocular tuberculosis, as a cause of a state of chronic inflammation, may be a risk factor for the development of MRG. However, in this case, sputum GeneXpert was primarily done to rule out pulmonary TB for clearance to do immediate enucleation. Interferon gamma release assays (Quantiferon Gold) could have been requested to this patient to rule out Ocular TB as a cause for MRG.

Furthermore, as proof of its non-neoplastic nature, it was shown to be polyclonal in nature.⁸ Physiologically, GFAP is an intermediate filament protein primarily found in astrocytes, which are glial cells that make up most of the human central nervous system. Pathologically, such as in eye injuries or diseases, GFAP is expressed in large quantities in retinal Müller cells. Lupien et al. investigated the regulation of GFAP gene expression in human Müller cells versus glioma cell lines from the central nervous system in vitro and they found that the transcription directed by the GFAP promoter was found to be 50-times stronger in Müller cells than in either of the non-glial cell lines.¹⁴

Identifying the sequence of events from MRG is crucial and pivotal for the development of eye-sparing therapeutics. Management of most reported cases were enucleation, especially from those with history of trauma occurring years prior to growth of the tumor.^{1-3,8} Another method included endoresection, which proved to be satisfactory in providing tissue material for histopathological evaluation as well as it is limited, eyeball-sparing method of treatment in a functioning eye. Among the latest approaches that can be considered is via utilization of vitreous substitutes, such as the use of cross-linked sodium hyaluronic acid hydrogel which appeared to be protective against trauma-induced reactive retinal changes. Such method seemed to be the most promising in perspective of treatment that limit the vitreoretinal disorders, which included disruption of retinal cell layers, cell death, and gliosis.⁹ In the few documented cases of MRG, there was still no other proposed definitive management that could be done in earlier phases of the disease that could potentially be sight saving or less invasive since the cases are usually already noted at the later extensive stage, thereby still resulting to enucleation.

CONCLUSION

Although benign, the distinction of MRG from other intraocular neoplasms is clinically challenging. In this case, removal of the mass was still done since it initially presented with malignant features and there were more malignant intraocular tumors documented relative to benign cases. To confirm the diagnosis of MRG, histopathological and immunohistochemical studies are still mandatory. MRG should be considered in the differential diagnosis in cases of post-traumatic intraocular masses with calcification. The intraocular tumor in this case, initially thought to be of malignant or infectious etiology, was actually secondary to an exaggerated reactive glial process. This can therefore facilitate in making proper primary impressions leading to a diagnosis of a benign condition, rather than being quickly thought of as a malignant tumor. MRG is a quite rare condition with no available epidemiologic data on its prevalence. Given that, this is the first reported case of its occurrence in the Philippines.

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Ethics Statement and Informed Consent

This report was conducted in compliance with the ethical principles outlined in the Declaration of Helsinki of 1964, as revised in 2024. Written informed consent was obtained from the patient for the publication of the case report and accompanying images.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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