Glomus Cell Tumor of the Orbit

Glomus cell tumors are rare, benign neoplasms of the glomus body, a specialized thermoregulatory arteriovenous structure surrounded by smooth muscle-derived glomus cells and unmyelinated nerves located primarily in the dermis of the digits and palms. We describe the unique clinical, radiological, and pathological features of a large orbital glomus cell tumor necessitating exenteration for intractable pain.

Report of a Case. A 19-year-old woman developed protrusion and painful burning and throbbing of her right eye in February 2005. Initial biopsy revealed an orbital glomus cell tumor. Visual acuity was 20/30 OU. Pupillary, biomicroscopic, funduscopic, tonometric, and periorcular sensory examination results were normal with no identifiable bulbar cause for the pain. There was 3.5 mm of right proptosis (Figure 1A and B) with limited abduction and supraduction. Despite treatment with combinations of clonazepam, nortriptyline hydrochloride, gabapentin, and pregabalin and unchanged results on serial clinical examinations and magnetic resonance imaging, the patient requested tumor removal 24 months after the initial visit owing to nonparoxysmal, intractable pain that limited her daily activities.

A magnetic resonance image prior to exenteration demonstrated a large, irregular, lobulated right orbital mass measuring $2.6 \times 3.5 \times 3.3$ cm isointense to muscle on T1 weighting (Figure 1C) that diffusely enhanced with gadolinium (Figure 1D) and encased the right inferior and lateral rectus muscles anteriorly and all extraocular muscles posteriorly, causing medial deviation of the optic nerve (Figure 1C-E) and proptosis of the right eye (Figure 1C-E). No bone destruction was evident on computed tomography (Figure 1F).

Transconjunctival biopsy was performed to confirm the diagnosis before exenteration. Extensive bleeding was encountered and controlled during the biopsy. Despite good vision, the patient underwent right orbital exenteration using an orbitocranial approach for treatment of intractable pain and to prevent intracranial extension of the tumor given the malignant potential of the tumor, which fell into the category of glomus tumor of...
uncertain malignant potential as defined by Folpe et al.\textsuperscript{2} Since exenteration, she has remained pain-free and without recurrence.

Pathologically, the tumor was composed of sheets and nests of bland cells, nonencapsulated, and diffusely infiltrating. The tumor abutted the optic nerve (Figure 2A) and infiltrated surrounding orbital fat and connective tissue (Figure 2B). In some regions, sheets of cells contained small, branching vascular channels typical of glomus cell tumors (Figure 2C). In other areas, large dilated vascular channels lined by 2 to 3 layers of glomus cells (Figure 2D), typical of glomangiomas, were present. The glomus cells were uniform and round, contained eosinophilic cytoplasm (Figure 2E), and demonstrated prominent nuclear vesiculation, small regular nucleoli, no mitoses, and strong immunoreactivity for cytoplasmic \(\alpha\)-smooth muscle actin (Figure 2F) and delicate extracellular matrix rich in type IV collagen (Figure 2G). Numerous artifactual breaks that had occurred during biopsy or processing were visible (Figure 2C).

**Comment.** To our knowledge, only 2 other cases of orbital glomus cell tumors have been reported.\textsuperscript{3,4} Our case had unique clinical, radiological, histopathological, and management aspects that differed considerably from these other cases.

Unlike previous reports, pain was a critical feature of our patient’s symptoms. Numerous substance P–containing, nonmyelinated axons are found within glomus cell tumors, suggesting a potential source for the pain.\textsuperscript{5} This tumor was considerably larger and more infiltrative than other reported orbital glomus cell tumors. There was significant bleeding during the biopsy, which, while not unexpected given the tumor’s vascular nature, dif-

---

**Figure 2.** Photomicrographs showing tumor (asterisk) proximal to the optic nerve (ON) (hematoxylin-eosin, original magnification \(\times25\)) (A) and infiltrating orbital fat and connective tissue (hematoxylin-eosin, original magnification \(\times60\)) (B) containing branching microvascular channels (arrow) and a cracking artifact (CA) (hematoxylin-eosin, original magnification \(\times100\)) (C) as well as large glomus cell-lined vascular channels (VC) (hematoxylin-eosin, original magnification \(\times25\)) (D). Uniform round eosinophilic glomus cells contain vesiculated nuclei and surround capillary-sized blood vessels (arrows) (hematoxylin-eosin, original magnification \(\times400\)) (E) are immunoreactive for cytoplasmic \(\alpha\)-smooth muscle actin (immunoperoxidase/hematoxylin counterstain, original magnification \(\times400\)) (F), and are immunoreactive for surrounding extracellular type IV collagen (immunoperoxidase/hematoxylin counterstain, original magnification \(\times400\)) (G).
fers considerably from a report of an encapsulated orbital glomus cell tumor. This suggests that encapsulation or the lack thereof may be an important factor in surgical management.

Histopathologically, this tumor had characteristics of both a glomus cell tumor and glomangioma and contained smooth muscle actin typical of glomus cells. The glomus cells were surrounded by delicate type IV collagen–rich extracellular matrix similar to gastric glomus cell tumors, potentially explaining the tumor’s friability.

Finally, to our knowledge this is the first report documenting magnetic resonance imaging characteristics of an orbital glomus cell tumor: multilobulated, isointense to muscle on T1 weighting, and diffusely enhancing with gadolinium. These features aid in its differentiation from lymphoma, metastatic tumors, and other vascular tumors.

Jonathan T. Prihila, MD, PhD
Wayne T. Cornblath, MD
John M. Ramocki, MD
Lawrence J. Marentette, MD
Andrew Flint, MD
Victor M. Elner, MD, PhD

Correspondence: Dr Elner, W. K. Kellogg Eye Center, University of Michigan, 1000 Wall St, Ann Arbor, MI 48105 (velner@umich.edu).

Financial Disclosure: None reported.


COMMENTS AND OPINIONS

Assocation of Proliferative Diabetic Retinopathy With Insulin Use and Microalbuminuria

The article by Shen and colleagues reminded us of the potential role of oral peroxisome proliferative activated receptor γ-agonists, not only in the control of blood glucose, but in the delayed onset of proliferative diabetic retinopathy (PDR). The authors argue that “Rosiglitazone may delay the onset of proliferative diabetic retinopathy (PDR). The authors argue that “Rosiglitazone may delay the onset of PDR probably because of its antiangiogenic activity.” However, there are 2 major concerns to address before we seriously consider this argument, regarding the basal demographic profile in Table 1. Because this is a retrospective study, well-matched data comparing the treatment group and controls is essential before drawing any conclusions; any significant discrepancy in the patients’ profiles could be disastrously confounding to the authors’ original design. As shown in Table 1, the control patients have significantly more use of insulin than rosiglitazone group. There have been several articles in the literature suggesting that the use of insulin would induce the risk of PDR, and some authors even suggested that its potential mechanism could be insulin-related growth factor 1 (IGF-1).

Furthermore, the control group also has a higher rate of microalbuminuria than their rosiglitazone-receiving counterparts. It has also been well demonstrated that microalbuminuria is strongly associated with microangiopathy and PDR. Is there any possibility that the supposedly well-matched controls are already more likely to develop PDR because of their higher rate of microalbuminuria than the patients who are receiving rosiglitazone?

Though this is, of course, a well-designed and carefully conducted study, the authors fail to prove that the so-called delayed onset of PDR is not actually attributed to intrinsic bias in the patients’ inclusion. Therefore, we worry that a misleading conclusion is not preventable.

Shu-Hsun Chun, MD, PhD
Ai-Hsien Li, MD

Correspondence: Dr Chun, Far Eastern Memorial Hospital, 21 Nan-Ya S Rd, Section 2 Pan-Chiao, Taipei, Taiwan 02-8966-7000 (shchu@yahoo.com.tw).

Financial Disclosure: None reported.


In reply

We thank Chun and Li for their comments regarding our article. The authors express concern that there is more insulin use in the control group than in the rosiglitazone-treated group, as would clearly be expected during therapy with an insulin sensitizer. They cite 2 studies indicating that insulin itself would induce the risk of PDR through effects on IGF-1. This association remains unclear. Although some studies have shown that IGF-1 is elevated in diabetic subjects compared with nondiabetic ones, other studies have not observed this. The association between PDR and IGF-1 is also unclear. One article cited by Chun and Li demonstrated decreasing levels of free and total IGF-1 and increased levels of some IGF-binding proteins with diabetes, and concluded there was “no evidence of a direct role of free IGF-1 in the development of PDR,” although IGF-binding proteins may be involved.

Dills et al found an association between IGF-1 and PDR in patients with late-onset diabetes (P = .025), but this was