• Letter to the Editor •

Dual histologic variants of schwannomas in orbital schwannomatosis

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Dear Editor,

We present an extremely rare case of orbital schwannomatosis with dual histologic variants. Schwannomas are tumors resulting from the slow proliferation of Schwann cells located in peripheral nerve sheaths[1]. They are commonly seen in middle-aged individuals but had been reported in patients 20-70 years of age. The presence of multiple schwannomas in the body has often been associated with neurofibromatosis (NF). However, schwannomatosis is considered in the absence of coexisting criteria diagnostic of NF. Schwannomatosis is a rare genetic disorder with an annual estimated incidence of 0.58 cases per 1 000 000 persons and usually manifests in the 2nd-3rd decade of life[2]. A set of criteria to diagnose schwannomatosis proposed by Baser *et al*[3] is summarized in Table 1.

Schwannomas found within or adjacent to the orbit are rare and represent only 1% of all orbital neoplasms[4]. A lone schwannoma in the orbit without association to NF is called primary orbital schwannoma[5]. Having multiple orbital ones is often NF-associated. However, it is extremely rare to have multiple orbital schwannomas without fulfilling any criteria diagnostic of NF, or orbital schwannomatosis.

This is a case of a 25-year-old Filipino female with a 3y history of gradually progressive proptosis of the right eye and enlarging mass at the superomedial anterior orbit of the same side. There were associated blurring of vision of the right eye, 7/10 pain in right orbit, and diplopia on all gazes. She had no pre-existing medical conditions and there was no similar condition indicative of NF1 or 2 in the family. On examination, the best-corrected visual acuity (BCVA) were 20/50 on the right eye and 20/20 on the left eye. A proptosis of 4 millimeters (mm) was measured by exophthalmometry. A 10×5 mm^2 nodular, solitary, non-movable, and non-tender mass was palpated at the superomedial anterior orbit with an inferolateral displacement of the right globe. There was resistance to retropulsion. There was no relative afferent pupillary defect. Limitations in extraocular muscle movement in the right eye were graded at -1 on all gazes. Intraocular pressures were at 14 mm Hg for both eyes. Anterior and posterior segments were unremarkable. The fundoscopy was unremarkable. There was no Lisch nodule in the iris or cataract seen. The principles outlined in the Declaration of Helsinki were followed. Written informed consent was obtained from the patient for this case presentation.

On systemic examination, she had no clinical evidence indicative of NF1 or 2 (*e.g.*, café-au-lait macules, axillary or inguinal freckles, and palpable mass in any part of her body aside from the orbit). Cranial and orbital computed tomography (CT) revealed multiple well-circumscribed intraconal and extraconal isointense masses in the right orbit (Figure 1). The intraconal mass measured 15×23×15 mm^3 and was indenting the right globe posteriorly and displacing the intraorbital optic nerve segment medially. It had a central cystic component with fluid level. The extraconal mass measured 18×11×8 mm^3, dumbbell-shaped, well-circumscribed, isointense, and was in the superomedial extraconal space. There was no other mass suggestive of meningioma or optic nerve glioma. There was also no mass appreciated in the vestibulocochlear nerve.

She underwent excision of the tumors through a lateral orbitotomy. Two orbital masses were removed from the superomedial anterior orbit measuring 6×8 mm^2 and 8×16 mm^2, light

Table 1 Diagnostic criteria for schwannomatosis

The patient must not fulfill any criteria set to diagnose NF type 1 (NF1) or 2 including having no evidence on imaging of unilateral or bilateral vestibular schwannoma, no first-degree relative diagnosed with NF2, and no gene mutation identified that is related to NF2.	
Definite	>30 years of age and having two or more nonintradermal schwannomas (one proven histologically), or one histologically proven schwannoma and having a first-degree relative meeting the prior criterion
Possible	<30 years of age and having two or more nonintradermal schwannomas (one proven histologically), > 45 years of age and having two or more nonintradermal schwannomas (one proven histologically), or schwannoma on imaging and having a first-degree relative meeting the criteria for definite schwannomatosis

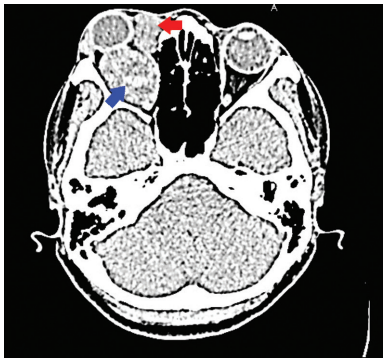

Figure 1 Plain computed tomography scan Axial view shows a large intraconal mass displacing the optic nerve medially with a central cystic area with fluid level (blue arrow). There is also superomedial isointense extraconal mass distinct from the intraconal lesion (red arrow).

pink, and with smooth pseudocapsules. The larger intraconal mass measured 20×25 mm^2 and was similarly encased in a pseudocapsule. The three excised lesions appeared to be distinct from each other. Histopathology read the tumors into two different types: schwannoma with myxoid degeneration (two superomedial anterior orbital masses), and schwannoma with degenerative atypia/ancient schwannoma (intraconal mass; Figure 2). On 6th week post-operative follow-up, her BCVA in the right eye improved to 20/25 and proptosis was resolved. She was advised to follow-up annually.

This is the 4th, youngest, and 1st case of orbital schwannomatosis with two histologic types of schwannomas. Review of the literature showed only three other patients with orbital schwannomatosis[6]. Koktekir *et al*[6] reported a case of a 59-year-old male with two orbital masses on imaging with no associated NF findings whom they diagnosed as a case of orbital schwannomatosis. However, on excision, only one mass was removed with the smaller mass on the imaging as just a possible part of it making the case a probable primary orbital schwannoma. Although two more masses were removed 5y after, these could have been recurrences from the initial mass as both were excised from the same area[6]. Similar to the other reported cases, our patient presented with gradual proptosis, enlarging mass in the superior to medial anterior orbit with resulting hypoglobus, had multiple extra- and intraconal masses on imaging, had no findings associated with NF, and responded well to surgical excision[6].

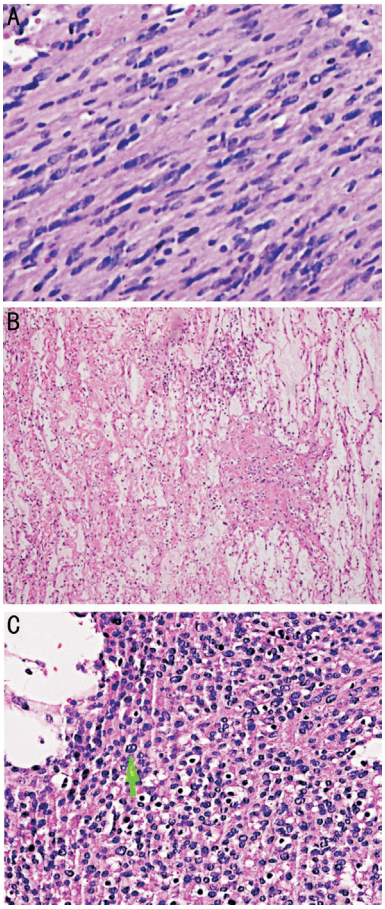

Figure 2 Histopathologic sections of the extraconal masses exhibited A: Antoni A, high cellularity and nuclear palisading; B: Antoni B, less cellularity and has loosely arranged cells and were read as classical schwanomma; C: The intraconal mass showed degenerative atypia in a high-power view (green arrow) typical of ancient schwannoma.

However, none of the cases reported having different types of histologic variants. Schwannoma has four major histologic variants: the classical/conventional type which is characterized by encapsulation and the presence of Antoni A composed of hypercellular spindle cells and Antoni B showing hypocellular myxomatous pattern; the relatively uncommon cellular type found in the vertebrae and exhibits Antoni A; the plexiform type commonly found in the skin and also exhibits Antoni A; and the melanotic type found in spinal roots, contains epithelioid cells and melanin and has potential to be malignant[1]. Additional variants include ancient schwannoma

characterized by unusual hyperchromatic nuclei in the absence of mitoses. This is a rare variant and has been reported in the orbit only once[7]. Our patient presented both with classical and ancient schwannomas.

Specific identification of the nerve origin is difficult due to the anatomic complexity of the orbital soft tissues. However, the location of the extraconal masses in all the cases can be suggestive that the schwannomas developed from the supratrochlear, infratrochlear, or the supraorbital nerve[8]. CT and magnetic resonance imaging (MRI) are helpful for tumor localization. MRI can also show capsular enhancement and circumferential enhancement surrounding regions of cystic degeneration in the ancient subtype of schwannomas[9]. MRI is also necessary to ensure that there is no vestibular mass diagnostic of NF2. If present, ophthalmologists, who can be the first to see the patient, have to also screen for cataract and glaucoma. The patient also has to be assessed for other NF2 manifestations such as hearing loss, numbness, and weakness of the extremities and appropriate referrals shall be made.

Even though orbital schwannomas are usually asymptomatic, surgery is a mainstay in its management[5-6]. Schwannomas are commonly well-circumscribed, encapsulated solitary masses that adhere to the nerve, but can be separated from the nerve origin with careful dissection to avoid nerve transection. Early surgical excision is desired to avoid the sequelae of tissue compression. Schwannomas become symptomatic by compressing adjacent structures[5]. Compression of the globe leads to proptosis and the optic nerve to the blurring of vision. Its space-occupying effect can result in diplopia from limiting extraocular movement and to eye pain[5-6]. Complete surgical excision of the mass is desired, as incomplete excision may lead to tumor recurrence similar to the other patient reported by Koktekir *et al*[6]. For our patient, despite complete excision of masses, regular surveillance of tumor recurrence is necessary since recurrence was reported to be common in orbital schwannomatosis.

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