



Case report

Primary recurrent orbital schwannoma treated with surgical excision and Mitomycin-C

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ABSTRACT

Purpose: Primary orbital schwannoma (POS) is a slow growing, benign encapsulated peripheral nerve sheath tumor that occurs infrequently within the orbit. Recurrence of POS is extremely rare. Previous speculations for reasons of recurrence include incomplete excision and tumor seeding.

Observations: We present the fifth case reported in the literature to date of POS that had 2 episodes of recurrences within 8 years after diagnosis, in which rapid and insidious relapses were observed after initial surgical resection. This is also the first reported recurrent POS in which topical Mitomycin-C (MMC) has been employed during surgical excision with an aim to prevent further recurrences.

Conclusions: AND IMPORTANCE: Whilst complete surgical excision remained the standard for management for most POS, when there are multiple recurrences and in cases where total excision is not possible, addition of topical MMC may be an option that may bring about tumour regression as demonstrated in our case.

1. Introduction

Primary orbital schwannoma (POS) is a benign, slow growing peripheral nerve sheath tumor (PNST) that occurs infrequently within the orbit representing 1% of all orbital tumors.¹ Recurrence of orbital schwannoma are most likely associated with neurofibromatosis type 2 (NF2) or schwannomatosis.¹ NF2 is caused by inactivation of NF2 gene which typically presents with bilateral vestibular schwannoma or other associated lesions.² Schwannomatosis is confirmed by presence of two or more non-intradermal schwannomas without features of NF2.³ Recurrence of isolated POS without evidence of NF2 and schwannomatosis is extremely rare and only 4 cases have been documented.^{4,5} We present a case of POS that had 2 episodes of recurrences within 8 years after diagnosis, in which rapid and insidious relapses were observed after initial surgical resection; to our best knowledge the first case reported in an Asian. This is also the first reported recurrent POS in which topical Mitomycin-C (MMC) was used during surgical excision to prevent recurrence.

2. Case report

A 19-year-old lady of Chinese descent presented to our service in 2011 complaining of insidious left eye painless bulging without diplopia (Fig. 1A). She declined history of trauma or dysthyroidism. Examination revealed visual acuity (logMAR) of 0.7 bilaterally. A firm, non-tender, non-pulsatile mass was palpable inferior and deep to the supraorbital rim. Exophthalmometer revealed left non-axial proptosis by 3mm. Anterior segment and fundal examination were unremarkable. No signs of optic neuropathy or thyroid eye disease were detected. Bilateral lacrimal glands and cervical lymph nodes were not enlarged. Subsequent imaging with orbital magnetic resonance imaging (MRI) revealed a large, well circumscribed, bilobed, contrast enhancing extraconal mass in the left anterosuperior orbit which measured 1.2 × 1.6 × 1.0cm (Antero-posterior (AP) x transverse (T) x coronal (C)) and 1.9 × 2.2 × 1.6cm (APxTxT) respectively extending towards the apex (Fig. 1B). Anterior orbitotomy showed two cystic encapsulated masses superior to the globe along the course of supraorbital nerve and were completely resected and biopsied (Fig. 1C). Histopathology examination revealed well encapsulated areas of spindle cells arranged in long intersecting

Abbreviation: POS, Primary orbital schwannoma; PNST, Peripheral nerve sheath tumour; MRI, Magnetic resonance imaging; CT, Computer tomography; NF2, Neurofibromatosis type 2; MMC, Mitomycin C.

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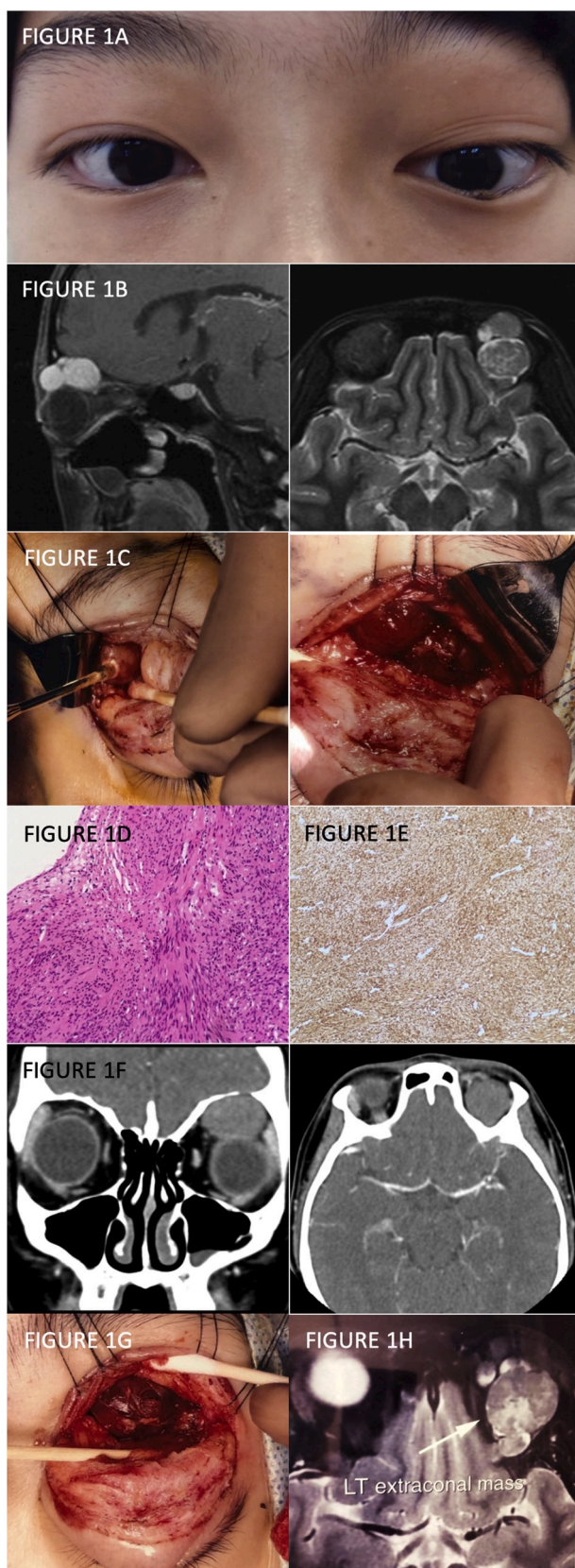
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Fig. 1. A: Primary orbital schwannoma (POS) of the left eye presented as painless non-axial proptosis and mild hypoglobus.
 B: Magnetic resonance imaging (MRI) of orbit revealing a large, well circumscribed, fusiform, contrast enhancing extraconal mass in the left anterosuperior orbit extending towards the apex.
 C: Excisional biopsy via left anterior orbitotomy showing a cystic encapsulated masses superior to the left globe.
 D: Photomicrography of Antoni A area and Verocay bodies within a schwannoma. H&E; 200X.
 E: Photomicrography of schwannoma showing diffuse S-100 immunohistochemical positivity.
 F: Computer tomography revealing recurrence of POS lying antero-superior to the left orbit just 6 weeks after first excision.
 G: Repeat excisional biopsy via left anterior orbitotomy showing an encapsulated masses superior to the left globe.
 H: MRI of the orbit showing recurrence of POS 6 years after the last surgical excision.

fascicles with nuclear palisading, which also stained positive with S-100 on immunohistochemistry (Fig. 1D and E). The diagnosis was compatible with schwannoma. Retrospective clinical examination and imaging revealed no signs indicative of neurofibromatosis type 2 (NF2).

Left eye swelling was however observed again 6 weeks after initial surgery. Orbital Computed Tomography (CT) revealed a lesion measuring $1 \times 2.3 \times 2.9$ cm (APxTxC) antero-superior to the orbit (Fig. 1F). A second excisional biopsy showed schwannoma recurrence and resection of the recurrent tumour was performed (Fig. 1G).

She enjoyed a relapse free period until 6 years later when she complained of progressive left eye bulging and diplopia in up-gaze. Orbital MRI revealed an extraconal fusiform lesion in the superior orbit measuring $2 \times 2.7 \times 4$ cm (APxTxC) in size extending towards the orbital apex (Fig. 1H). A repeat resection confirmed schwannoma recurrence. A near complete capsule and tumour removal were achieved given its apical location. MMC 0.4mg/ml impregnated gauze were applied topically at the site of excision for 5 minutes at the excision bed as a measure to prevent recurrence and postoperative scarring. MMC was rinsed with copious saline after treatment before closure.

6 months postoperatively a resurgence of supraorbital mass was noted on interval imaging. Excisional biopsy was repeated but only revealed lipo-granulomatous changes without evidence of recurrent schwannoma. Further imaging 3 months later revealed similar cystic mass within the same region, which was shown to be fibro-inflammatory tissues only on biopsy. Further scanning at 6, 12 and 18 months showed no recurrence of masses in the left orbit.

3. Discussion

Schwannoma is a benign PNST that typically affects patients from 20 to 40 years of age. Involvement within the orbit is rare affecting mostly sensory nerves that traverses within the orbit. Orbital schwannoma is usually asymptomatic but patients may present with painless proptosis, diplopia and symptoms of compressive optic neuropathy when the lesion expands.^{5,7} Definitive diagnosis is reliant on histopathological examination. Classically schwannoma demonstrate hypercellular spindle cell rich Antoni A areas and haphazardly arranged cytoplasmic Antoni B areas.⁸ Immunohistochemistry analysis supplement the diagnosis by showing positivity in S-100 and vimentin staining, which are present in Schwann cells.⁸ Complete surgical excision is the preferred choice of orbital schwannoma where feasible to prevent orbital nerve compression or intracranial extension.^{1,9} Radiotherapy is an alternative treatment but limited by unknown efficacy and collateral radiation damage.⁸

Recurrence of POS without evidence of NF2 and schwannomatosis is rare. Three cases reported in the literature describe late schwannoma recurrence at 3,6 and 22 years respectively after initial excision.^{4,5,10} Another case was a 5-year-old girl who had 2 recurrences within 1

month after each excision. Incomplete surgical excision has been attributed to rapid recurrence.¹⁰ Our patient represents the fifth reported case of recurrent POS, in which one had rapid recurrence at 1 month followed by late recurrence 6 years later. No evidence for NF2 and orbital schwannomatosis were shown, as only a single histologically confirmed lesion was found in each recurrence which all arose from the same location. We recognise that tumour seeding might have contributed to the early relapse. The second recurrence was unexpected as previous delivery of schwannoma was complete. We speculate that this may be linked with residual subclinical tumour at the orbital apex, as highly cellular schwannomas have been associated with recurrence.¹¹

MMC was applied at the second resection due to its anti-tumour nature. A potent DNA crosslinker, topical use of MMC with surgical excision in our case did not show recurrence of POS at 27 months post-operatively. This case represents the first documented use of topical MMC during surgical excision of POS that augmented clearance of tumour and seeding, as evidenced by the absence of rapid recurrence histologically. Intraoperative topical MMC was used previously for management of retrobulbar cystic type optic nerve sheath meningioma that has shown to reduce tumour recurrence, where topical MMC (4mg/ml) was applied on tumour site for 5 minutes after excision.¹² The same duration of MMC were applied over the surgical bed in our case, although one-tenth of the dose of MMC was chosen in view of vicinity to optic nerve. We speculate this new regimen can enhance tumour cell elimination in recurrent cases of POS, which may also benefit in situations where total excision is difficult. The final outcome will require longer term evaluation.

It is questionable whether topical MMC is the cause for lipo-granulomatous changes post-operatively, which exhibited as a mimicker of POS recurrence as demonstrated in our case. Orbital lipo-granulomatous lesions are rare and exhibit typical histopathological features that distinct it from non-specific inflammatory changes.¹³ One possible explanation maybe linked to direct toxicity to local tissue from MMC. Histopathology study of lipo-granulomatous tissue on biopsy did not reveal Touton cells and non-Langerhan histiocytosis indicative of orbital xanthogranulomatous disease. Previous use of MMC in optic nerve sheath tumour did not reveal complications.¹² Further study is necessary to study the effect of MMC on orbital tissues.

4. Conclusions

We report a rare case of POS which had recurrence at 1 month and 6 years after its initial surgical resection. Reasons for local tumour recurrence were unknown but possibly related to seeding and tumour load. Complete surgical excision remains the standard for management for most POS. When there are multiple recurrences and in cases where total excision is not possible, surgical resection together with topical intraoperative MMC may be an option that can bring about tumour regression as demonstrated in our case.

Patient consent

Ethics, consent and permissions

Ethics approval and consent has been obtained from the institution ethics committee. Written informed consent has been obtained from the participant for report and publishing.

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Authorship

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Author's contributions

LKCP designed, analysed, reviewed and revised the manuscript, LNKY designed, analysed and reviewed the manuscript.

CE and KTCS revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Declaration of competing interest

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CRediT authorship contribution statement

Kai Ching Peter Leung: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing - original draft, Writing - review & editing. **Nerissa Kei Yen Lam:** Data curation, Formal analysis, Investigation, Methodology, Writing - original draft, Writing - review & editing. **Edwin Chan:** Supervision, Writing - review & editing. **Tak Chuen Simon Ko:** Supervision, Writing - review & editing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ajoc.2020.100784>.

References

1. Rootman J, Goldberg C, Robertson W. Primary orbital schwannomas. *Br J Ophthalmol.* 1982;66(3):194–204. <https://doi.org/10.1136/bjo.66.3.194>.
2. Evans DgR. Neurofibromatosis type 2 (NF2): a clinical and molecular review. *Orphanet J Rare Dis.* 2009;4(1):16. <https://doi.org/10.1186/1750-1172-4-16>.
3. Merker VL, Esparza S, Smith MJ, Stemmer-Rachamimov A, Plotkin SR. Clinical features of schwannomatosis: a retrospective analysis of 87 patients. *Oncologist.* 2012;17(10):1317–1322. <https://doi.org/10.1634/theoncologist.2012-0162>.
4. Chisholm IA, Polyzoidis K. Recurrence of benign orbital neurilemmoma (schwannoma) after 22 years. *Can J Ophthalmol.* 1982;17(6):271–273. <https://www.ncbi.nlm.nih.gov/pubmed/7165843>. Accessed April 8, 2019.
5. Jensen OA, Bretlau P. Melanotic schwannoma of the orbit. Immunohistochemical and ultrastructural study of a case and survey of the literature. *APMIS.* 1990;98(8):713–723. <http://www.ncbi.nlm.nih.gov/pubmed/2206515>.
6. Kim KS, Jung JW, Yoon KC, Kwon YJ, Hwang JH, Lee SY. Schwannoma of the orbit. *Arch Craniofacial Surg.* 2015;16(2):67. <https://doi.org/10.7181/acfs.2015.16.2.67>.
7. Lam DSC, Ng JSK, To KF, Abdulah V, Liew CT, Tso MOM. Cystic schwannoma of the orbit. *Eye.* 1997;11(6):798–800. <https://doi.org/10.1038/eye.1997.208>.
8. Hanemann CO, Evans DG. News on the genetics, epidemiology, medical care and translational research of Schwannomas. *J Neurol.* 2006;253(12):1533–1541. <https://doi.org/10.1007/s00415-006-0347-0>.
9. Rose GE, Wright JE. Isolated peripheral nerve sheath tumours of the orbit. *Eye.* 1991;5(6):668–673. <https://doi.org/10.1038/eye.1991.123>.
10. Kron M, Bohnsack BL, Archer SM, McHugh JB, Kahana A. Recurrent orbital schwannomas: clinical course and histopathologic correlation. *BMC Ophthalmol.* 2012;12(1):44. <https://doi.org/10.1186/1471-2415-12-44>.
11. Dhawan A, Gupta N, D'souza P, Garg R. A rare case of benign isolated schwannoma in the inferior orbit. *Indian J Ophthalmol.* 2008;56(6):514. <https://doi.org/10.4103/0301-4738.43380>.
12. Dhoot DS, Shults WT, Ng JD. Successful use of mitomycin C to prevent recurrence of the cystic component of an optic nerve sheath meningioma. *Ophthalmic Plast Reconstr Surg.* 2008;24(3):235–236. <https://doi.org/10.1097/IOP.0b013e3181706d39>.
13. Sivak-Callcott JA. Adult xanthogranulomatous disease of the orbit and ocular adnexa: new immunohistochemical findings and clinical review. *Br J Ophthalmol.* 2006;90(5):602–608. <https://doi.org/10.1136/bjo.2005.085894>.