



ARTICLE

Orbito-cranial schwannoma—a multicentre experience

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OBJECTIVES: To describe the features, management approaches, and outcomes of orbito-cranial schwannomas.

METHODS: Retrospective review of ten patients with orbito-cranial schwannomas managed in six orbital services over 22 years. Data collected included demographics, presenting features, neuroimaging characteristics, histology, management approach, complications, and outcomes.

RESULTS: Mean age of the patients was 41.4 ± 19.9 years, and 6 (60%) were females. The majority presented with proptosis (90%), limited extraocular motility (80%), eyelid swelling (60%), and optic neuropathy (60%). Most lesions (80%) involved the entire anterior-posterior span of the orbit, with both intra- and extraconal involvement. All tumours involved the orbital apex, the superior orbital fissure, and extended at least to the cavernous sinus. Surgical resection was performed for all. Seven (70%) of the tumours were completely or subtotally resected combining an intracapsular approach by an orbital-neurosurgical collaboration, with no recurrence on postoperative follow-up (6–186 months). Three underwent tumour debulking. Of these, two remained stable on follow-up (6–34 months) and one showed progression of the residual tumour over 9 years (cellular schwannoma on histology) necessitating stereotactic radiotherapy (SRT) for local control. Adjuncts to the orbito-cranial resection included perioperative frozen section ($n = 5$), endoscopic transorbital approach ($n = 2$), and image-guided navigation ($n = 1$). Post-surgical adjuvant SRT was used in three subjects.

CONCLUSIONS: These results highlight the possibility of successful surgical control in complex orbito-cranial schwannomas. A combined neurosurgical/orbital approach with consideration of an intracapsular resection is recommended. Recurrence may not occur with subtotal excision and observation may be reasonable. Adjunctive SRT for progression or residual tumour can be considered.

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INTRODUCTION

Schwannomas uncommonly occur in the orbits and account for 1–2% of all orbital tumours [1–3]. The typical primary orbital schwannoma is localised and well-circumscribed [3, 4], however an orbito-cranial presentation has been documented [5]. In these cases extracapsular total resection, which is the mainstay therapy for localised lesions, is challenging and risks significant morbidity [5, 6].

There is little information regarding the management approach for orbito-cranial schwannomas. Furthermore, the outcome in the context of incomplete surgical excision is not well established. The current multicentre case-series presents the clinical and diagnostic imaging features, surgical and adjuvant management approaches, and outcomes in ten patients with orbito-cranial schwannomas.

METHODS

Data were collected retrospectively from consecutive adult patients with orbito-cranial schwannomas attending one of six orbital centres, between

August 1998 and April 2020. This study received Institutional Review Board approval and adhered to the tenets of the Declaration of Helsinki.

Included patients were adults (>18 years) with histologically proven orbito-cranial schwannoma. Junctional lesions (e.g. apical lesions abutting the superior orbital fissure but not extending into the cavernous sinus [SOF]) were not included in this series. Data collected included patient demographics, presenting symptoms and signs, duration of symptoms, neuroimaging type (MRI, CT), neuroimaging characteristics of tumour, histology, management course (including surgical approach and radiation therapy), treatment related complications, length of follow up, and clinical status at the last follow up.

RESULTS

Demographic and clinical features

The mean age of the patients was 41.4 ± 19.9 years (median 32, range 19–76 years), and 6 (60%) were females (Supplementary Table 1). All patients had unilateral involvement, of which 7 (70%) were right sided. The most common clinical signs on presentation were proptosis (90%), limited extraocular motility (80%), and

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Table 1. Tumour characteristics, management and outcomes in ten patients with orbito-cranial schwannomas.

Case	1	2	3	4	5	6	7	8	9	10
Orbital location	Inferior; Apical/ Intraconal	Superior; Apical to mid-orbit/ Intraconal	Diffuse; Apical to anterior orbit/ intra- and extra-conal	Superior; Apical to anterior orbit – intra- and extra-conal	Superior; Apical to anterior orbit /intra- and extra-conal	Diffuse; Apical to anterior orbit/ intra- and extra-conal	Superior; Apical to anterior orbit/ intra- and extra-conal	Medial diffuse; Apical to anterior orbit/ intra- and extra-conal	Superior; Apical to anterior orbit/ intra- and extra-conal	Diffuse; Apical to anterior orbit/ intra- and extra-conal
Intracranial involvement	Cavernous sinus	Cavernous sinus	Cavernous sinus	Cavernous sinus and Meckel's cave, anterior fossa	Cavernous sinus and Meckel's cave, Anterior fossa	Cavernous sinus	Cavernous sinus	Cavernous sinus	Cavernous sinus and Meckel's cave	Cavernous sinus and Meckel's cave
Size in cm	2.8	4.5	5.9	6.5	5.8	4.4	2.6	6.4	8	6.5
Surgical approach	Neuro-orbital /Orbitofrontal craniotomy	Neuro-orbital/ superior orbitotomy with image-guided pterional craniotomy	Orbital/Eyelid sparing exenteration	Neuro-orbital- ENT/ Eyelid sparing exenteration and pterional craniotomy with orbitozygomatic extension	Neuro-orbital/ Exenteration and frontotemporal craniotomy	Neuro-orbital/ Lateral orbitotomy with pterional craniotomy	Neuro-orbital/ Superior orbitotomy with pterional craniotomy	Orbital/ Lateral orbitotomy with bone window	Neuro-orbital/ Lateral orbitotomy with bone window combined with endoscopic transorbital approach	Neuro-orbital/ Lateral orbitotomy with bone window combined with endoscopic transorbital approach
Capsular relation	Intracapsular	Intracapsular	Extracapsular	Orbital; Extracapsular; Ethmoidal and intracranial; intracapsular	Extracapsular	Intracapsular	Intracapsular	Extracapsular	Extracapsular	Intracapsular
Frozen section control	No	Yes	No	No	Yes	Yes	Yes	No	Yes	No
Surgical extent	Subtotal	Subtotal	Debulking	Subtotal	Debulking	Subtotal	Complete	Debulking	Complete	Subtotal
Radiotherapy	No	No	SRT 54 Gy	SRT 54Gy	SRT 20 Gy (9 years post-op)	SRT 45 Gy	No	No	No	No
Post-op VA	10/30 (unchanged)	20/20 (unchanged)	NPL (unchanged)	NPL (unchanged)	NLP (reduced)	20/30 (unchanged)	20/20 (improved)	20/25 (unchanged)	20/50 (improved)	20/20 (unchanged)
Complications/ Sequelae	Diplopia, mydriasis	Diplopia (resolved), forehead/temporal paresthesia (resolved)	None	Forehead and parietal paresthesia	None	Diplopia (corrected)	Mydriasis (partially improved)	Forehead paresthesia	Forehead paresthesia	Total 3rd nerve palsy (partial improvement); Forehead and infraorbital paresthesia
Radiological status at final follow-up	No progression	No progression	No progression	No progression	Stable (4 months post SRT)	No progression	No evidence of residual disease	No progression	No evidence of residual disease	No progression

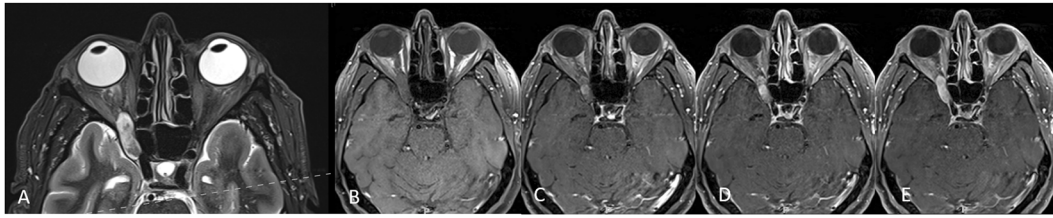


Fig. 1 MRI images of subject #1. (A) T2 fat suppressed axial image showing an oblong well defined lesion extending from the right intraconal space into the superior orbital fissure and the anterior cavernous sinus. The lesion shows heterogeneous T2 hyperintensity. (B–E) T1 axial Dynamic Contrast Imaging showing rapid enhancement.

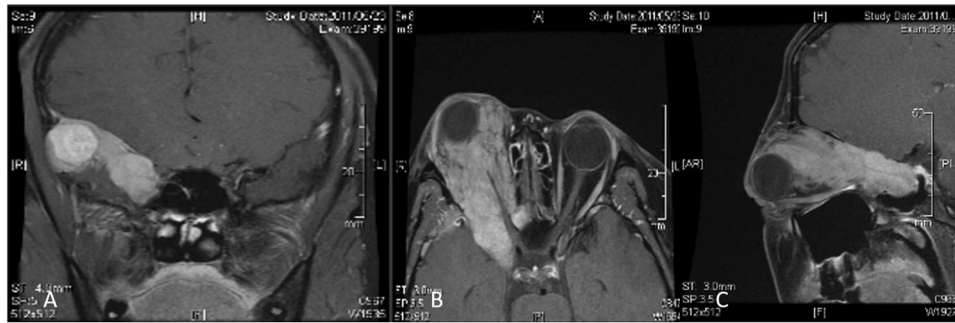


Fig. 2 MRI images of subject #5. T1 fat suppressed post contrast (A) coronal, (B) axial and (C) sagittal images showing a diffuse enhancing lesion with extensive intracranial extension through bony walls destruction.

eyelid swelling (60%, Supplementary Table 1). Six (60%) patients had signs of optic neuropathy with reduced VA ranging from 20/30 ($n = 3$), through 20/70 ($n = 1$), to no perception of light ($n = 2$). Commonly reported symptoms included blurring of vision (60%), headache (50%), orbital pain (50%), and diplopia (50%). The reported insidious onset of symptoms was a mean of 44.3 ± 66.1 months (median 12, range 2.5–180 months). One subject (#2, Supplementary Table 1) had familial schwannomatosis. An intradural T12/L1 schwannoma was surgically resected 6 years after surgery for the orbito-cranial tumour.

Tumour characteristics

The orbital location of the tumour was mainly superior in 5 (50%) of subjects, involving all orbital quadrants in 40%, and mainly inferior in one (Table 1).

The mean size of the tumours (maximal length) was 53.4 ± 1.73 mm (median 58.5, range 26–80 mm). Most lesions (80%) involved the entire anterior-posterior span of the orbit, with both intra- and extraconal involvement (Table 1).

All tumours extended at least to the cavernous sinus (CS) by SOF expansion (Fig. 1). Four lesions extended beyond the CS to involve Meckel's cave and/or the middle cranial fossa. Two of these additionally extended to the anterior cranial fossa and the paranasal sinuses/nasal cavity via orbital roof and medial wall bone destruction, respectively (Figs. 2 and 3).

Because of the extent of the tumours, the nerve of origin was not readily identifiable, likely involving more than one branch at the time of orbito-cranial presentation.

MRI imaging with and without contrast was available for 8/10 subjects, in three of which CT was also conducted. In two subjects only CT was performed. On MRI all tumours were T1 isointense. Six (out of 8) were T2 hyperintense, and two showed heterogeneous T2 intensity. All displayed marked enhancement that proved to be early and rapid on dynamic contrast imaging (available for two subjects, Fig. 1). Most of the tumours (8/10) were well-circumscribed, while 2 were diffuse (Figs. 2 and 3). Only three had a homogenous appearance, the majority (70%) appearing heterogeneous. Three lesions were multi-lobular with degenerative/multi-cystic changes (Fig. 4).

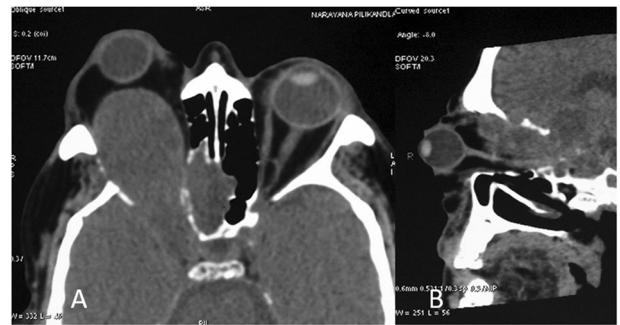


Fig. 3 CT images of subject #4. (A) Axial and (B) sagittal (non-contrast, soft tissue windows) images of subject #4 showing a diffuse lesion extending from the right orbit by bony walls destruction into the cavernous sinus, anterior cranial fossa, and nasal cavities.

Management and outcomes

Histological diagnosis proved low-grade schwannomas in all but one subject (#5). This patient underwent initial surgery for orbital tumour debulking due to ongoing pain, in which low-grade schwannoma was shown on histology. Over the next six years, the orbital and intracranial involvement significantly progressed along with increasing pain and discomfort (Fig. 2), prompting a joint orbital-neurosurgical resection. At that stage the histological features suggested a cellular schwannoma with 10% MIB-1 positive cells [7].

In eight (80%) of the subjects, surgery entailed a joint orbital and neurosurgical collaboration (Table 1). In one subject an ENT collaboration was additionally needed for the resection of ethmoidal/nasal cavity extension (subject #4, Fig. 3). The orbital approach was in most cases a lateral orbitotomy or superolateral orbitotomy, with ($n = 3$) or without a bone flap. In three subjects an eyelid sparing exenteration was performed. The neurosurgical craniotomy approaches included orbitofrontal, orbitozygomatic, frontotemporal, and pterional with ($n = 1$) or without ($n = 3$) image guidance. In two subjects an endoscopic transorbital

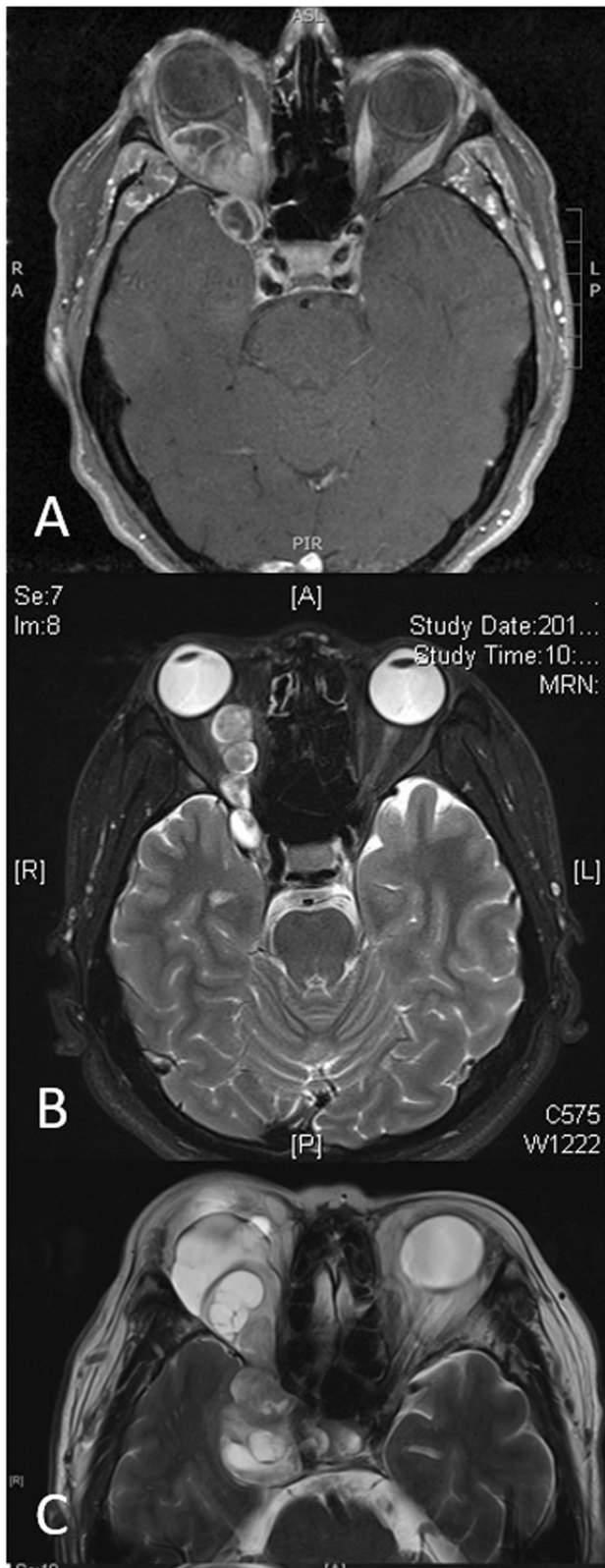


Fig. 4 Multi-lobular orbito-cranial schwannomas with degenerative/cystic changes. **A** Axial T1 fat suppressed, post contrast image of subject #6 showing mural enhancement. **B** Axial T2 images of subject #8 and **(C)** subject #9.

approach was utilised for the intracranial resection. Perioperative frozen section control was used in five (50%) of the cases. In five subjects the tumour resection was intracapsular, in four subjects extracapsular, and in one subject the orbital resection was extracapsular while the intracranial resection was intracapsular. In three subjects adjuvant fractionated stereotactic radiotherapy (SRT) was employed, with accumulative doses of 45 Gy ($n = 1$) and 54 Gy ($n = 2$).

Two of the patients underwent complete resection of the tumour, confirmed by frozen section and lack of residual disease on subsequent MRI (Supplementary Fig. 1), with no recurrence at 36 months and 49 months of postoperative follow up, respectively.

Five subjects had subtotal resection (with neurosurgical collaboration) with minimal residual disease, and with no recurrence on postoperative follow up (at 6, 8, 12, 108, and 186 months, respectively). Two patients had only the orbital component resected by orbital surgeons (i.e. tumour debulking) with evidence of residual tumour. There was no postoperative tumour progression at 6 months and 34 months, respectively. Another patient that underwent (neuro-orbital) debulking (subject #5, Fig. 2) had slow progression of a residual CS tumour over 9 years of postoperative follow-up, for which she recently (4 months) had SRT (20 Gy) treatment. The mean post-surgical follow-up was 56.5 ± 61.3 months (median 35, range 6–186 months).

There were no reported intraoperative complications. The postoperative visual acuity did not change compared to baseline in seven (70%) of the subjects, improved by two lines in one subject, and by one line in another (Table 1). In subject #5 an exenteration was performed despite preserved visual acuity, due to the abovementioned considerations. Other postoperative sequelae are detailed in Table 1.

DISCUSSION

It is recognised in the neurosurgical literature that trigeminal schwannomas epicentered intracranially, and particularly the CS, may infrequently invade the orbit. Categorisations of such presentation included “dumbbell-shaped tumour in the middle fossa and the extracranial orbital space” (ME1) [8], type D extracranial extension [9–11], or referred to as “(cavernous) peripheral subtype” [12, 13]. Nonetheless, this series is the first to focus on the management of schwannomas epicentered in the orbit with an intracranial extension. These cases presented to the orbital service due to predominant orbital involvement and significant ophthalmic manifestations, such as compressive optic neuropathy, proptosis, and limitation of extraocular movement. Because of the rarity of this presentation, the orbital surgeon may have very little experience in the management of extensive orbito-cranial tumours. Thus, being aware of the management approaches and experience collated herein from six orbital centres may benefit the orbital surgeon encountering such complex schwannomas.

The ophthalmic literature is mostly dedicated to primary orbital schwannoma. It is typically a localised, well-circumscribed, noninvasive, encapsulated tumour that can be completely or near-completely excised, and rarely recur [1, 3–5, 14]. There were, however, previous orbital schwannoma series reporting that tumours extended to the SOF in up to a quarter to one-third of cases [1, 5, 15, 16]. The course of extension corresponds to the most common orbital origin from the ophthalmic branch of the trigeminal nerve [1, 5]. Nevertheless, many of these represent junctional tumours (without intracranial involvement), thus some can be resected using a traditional extraperiosteal approach via lateral or superolateral orbitotomy [17].

The current series represents orbito-cranial schwannomas with relatively extensive orbital involvement. Most lesions (80%) occupied the entire anterior-posterior span of the orbit, with both intra- and extracranial involvement. All tumours involved the orbital apex, the SOF, and extended at least to the CS intracranially (4 involved Meckel's cave and/or middle cranial fossa). Despite this, in 70% of cases complete or subtotal resection was achieved, with significant debulking in the rest. There were no intraoperative complications (e.g. CSF leak). Postoperative sequelae were sensory (paraesthesia), motor (ophthalmoplegia/diplopia), or autonomic (mydriasis) deficits, in some cases with subsequent improvement. These were reported even following excision of localised orbital schwannomas [1, 5, 18], however are expected to be more common following SOF and CS surgical manipulation. All cases but one remained stable in up to 6–186 months, including those with residual tumours. Although in some subjects longer follow up is warranted in order to establish stability, these results highlight the possibility of successful surgical control in complex orbito-cranial schwannomas.

Infrequent occurrences of orbital schwannomas that were unable to be completely removed due to orbital apex involvement, SOF and/or CS extension have been reported. Cantore et al. [16] described one case (out of 9 orbital schwannomas) that extended beyond the SOF to involve the "skull". It was managed by intracapsular debulking using an ultrasonic aspirator. Rose et al. [1] described 6/25 orbital schwannomas that extended to the SOF, limiting complete resection. Neurosurgical collaboration was not mentioned. Nevertheless, even with incomplete resection, there has been no evidence of progression in up to 23 years of follow-up. They proposed that surgical debulking alters the growth pattern by removal of tumour growth factors [1].

In a recent series by Yong et al. [5], 3/18 orbital schwannomas involved the orbital apex, one case involved the SOF, and four extended to the CS. In total, only one of these cases, a tumour that involved the orbital apex, was completely excised (via superolateral orbitotomy). Of the four cases with CS involvement, two underwent initial debulking of the orbital portion of the tumour, requiring neurosurgical intervention (via pterional craniotomy) a few years later due to progression. One other case was debulked via lateral orbitotomy, and the last case underwent SRT without surgical management. Subsequently, all of them showed stable tumours in 3 to 19 years of follow-up [5]. Nevertheless, based on their experience the authors suggested that a larger residual tumour bulk has a higher risk of recurrence, thus surgery should aim for the maximum possible removal [5]. The neurosurgical literature supports this notion, as incomplete resections of intracranial trigeminal schwannomas are associated with a greater recurrence rate [19, 20].

In this series, complete or subtotal, intracapsular excision was attained in three cases via lateral or superior orbitotomy combined with pterional craniotomy. Image-guided navigation was used in one (of the three). In a fourth case subtotal resection was achieved via an extracapsular exenteration combined with an ethmoidal (ENT) and a pterional intracapsular excision. A pterional approach was previously advocated in a case of orbital schwannoma involving the SOF and CS, enabling complete surgical removal [13]. In another of our cases an orbitofrontal craniotomy was performed enabling subtotal intracapsular resection. This approach was previously utilised in a case of orbital oculomotor nerve schwannoma extending to the CS, enabling complete intracapsular removal [21]. Two additional cases underwent a lateral orbitotomy (with bone window) combined with an endoscopic transorbital (intracapsular) approach, achieving complete or subtotal removal, respectively. This is a recent advance in endoscopic skull base surgery, allowing access to the lateral orbit, apex of the orbit, anterior cranial fossa, and middle cranial fossa. It was shown to achieve successful resection of tumours, including trigeminal schwannomas, while minimising significant morbidities such as CSF leaks or ophthalmic complications [22, 23].

Noteworthy, SRT was employed in three of our subjects as adjuvant post-surgical treatment, and in a fourth subject for local control of a progressing CS residual tumour. Radiosurgery is an established treatment of intracranial trigeminal schwannomas with reported local control rates as high as 91–100% [6]. SRT offers the biological advantages of dose fractionation. It was reported as a sole treatment modality, after subtotal resection, and after recurrence following initial surgical resection, and similarly has shown local control rates of 95–100% [6, 24, 25]. It was advocated as an adjunct to surgical resection in symptomatic high-risk cases, including large tumours, recurrences, and CS involvement, as well as for enhancement of progression-free survival in cases of subtotal excision [6]. SRT (gamma knife) as sole treatment has been reported to be effective in two cases of solitary, well-circumscribed orbital apex schwannomas [26]. Yong et al. [5] reported the use of SRT in an orbito-cranial schwannoma deemed not amenable for surgical resection. The current experience supports the possible benefit of adjuvant SRT in surgically resected orbito-cranial schwannomas. However, further studies are warranted in order to establish its role.

In conclusion, based on the multicentre experience in the management of orbito-cranial schwannomas, the orbital surgeon can consider these approaches when encountering these rare presentations. Firstly, an orbital-neurosurgical collaborative approach, increases the feasibility of complete or subtotal tumour removal. An intracapsular resection may decrease the risk of collateral damage and should be strongly considered, particularly for the intracranial component. Perioperative frozen section control and image-guided navigation may aid in some cases. In schwannomas with extensive orbital involvement, orbital exenteration may be warranted. Finally, post-excision adjuvant SRT can be considered, as well as for local control of residual tumour progression.

SUMMARY

What was known before

- Schwannomas of the orbit usually present as localised and well-circumscribed tumours approachable to surgical resection.
- Schwannomas that occupy the deep orbital apex, and particularly cases of intracranial extension, represent a surgical challenge.

What this study adds

- This is the first series dedicated to describe the presentation, characteristics, management, and outcomes of orbito-cranial schwannomas.
- An orbital-neurosurgical collaborative approach, increases the feasibility of complete or subtotal tumour removal.
- Post-excision adjuvant radiotherapy can be considered.

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AUTHOR CONTRIBUTIONS

YS: analysis and interpretation of data, drafting of paper and critical revision. VJ: conception or design of the work, acquisition of data, and critical revision. TD: conception or design of the work, acquisition of data, and critical revision. AH: conception or design of the work, acquisition of data, and critical revision. DM: conception or design of the work, acquisition of data, and critical revision. AW: conception or design of the work, acquisition of data, and critical revision. AY: conception or design of the work, acquisition of data, and critical revision. PS: conception or design of the work, acquisition of data, and critical revision. KIW: conception or design of the work, acquisition of data, and critical revision. TH: conception or design of the work, acquisition of data, and critical revision. BP: conception or design of the work, acquisition of data, and critical revision. KD: conception or design of the work, acquisition of data, and critical revision. DS: conception or design of the work, analysis and interpretation of data, and critical revision.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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