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Review Article

Management of oculomotor nerve schwannoma: Systematic review of literature and illustrative case

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ABSTRACT

Background: Oculomotor nerve schwannoma (ONS) is an extremely rare intracranial benign tumor. Till date, there is no standard treatment of oculomotor schwannoma. Here, we present an illustrative case report of ONS, perform a systematic review of literature on surgically and radiosurgically treated cases and morbidity related to both treatment modalities.

Methods: We performed a systematic review of literature for cases with ONS treated with surgery or radiosurgery using PubMed/Ovid Medline.

Results: Till date, there are 60 reported cases of ONS (45 treated surgically and seven radiosurgically) with the dominance of female gender (53%) and mean age of 35.2 years (Range 1–66). In 8% of the cases, there was no involvement of cranial nerve (CN) III and 92% of the cases CN III alone or together with CN II, IV, V, and VI. In 67% of the cases a complete resection and 33% a partial resection performed. In 73% of the cases, postoperative third nerve palsy was documented, 22% improved after surgery and in around 5% of cases, the outcome was not described. In the radiosurgically treated cases of nonvestibular schwannoma including ONS, the progression-free interval of approximately 2 years was above 90%.

Conclusion: Due to the high rate of postoperative complete oculomotor nerve palsy, a subtotal resection avoiding the nerve injury seems to be a feasible option. Radiosurgery is another option to treat small size schwannoma. A combined treatment with microsurgery followed by radiosurgery may allow effective treatment for large size oculomotor schwannoma.

Keywords: Clinical outcome, microsurgery, oculomotor nerve schwannoma, radiosurgery

INTRODUCTION

Intracranial schwannoma accounts for around 7% of all intracranial tumors.[9] Most of the intracranial schwannoma, however, arise from the sensory division of cranial nerves (CNs) including vestibular nerve followed by the trigeminal nerve.[11] Being purely motor nerve, oculomotor nerve schwannoma (ONS) is an extremely rare tumor unless associated with Recklinghausen's disease. The transition zone of the

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third nerve from central to the periphery is 0.6 mm; hence, these tumors can occur over multiple anatomical locations including interpeduncular cistern, parasellar, cavernous sinus (CS) region, orbital apex, and intraorbital. In large tumors radiologically and intraoperatively it is difficult to detect from which nerve the tumor arises; however, a selective postoperative deficit of the harboring nerve can identify its source.

Till date, around five dozens of cases of ONS have been reported in literature. Most of the cases reported in the literature have been treated surgically with a very high rate of complete third nerve palsy that adds significant morbidity. Although radiosurgery could be an alternative, only a few successfully treated cases with radiosurgery have been reported in literature.[3,6,7,10] Till date, there is no standard treatment of oculomotor schwannoma.

Hence, we review surgically and radiosurgically treated cases and morbidity reported in these cases and discusses alternative options to treat these tumors. Furthermore, we present an illustrative case of ONS treated surgically in our department.

MATERIALS AND METHODS

Case report

A 64-years-old male presented with a history of exophthalmos and blurry vision on the left side for 3 years. On examination, the patient was alert and oriented to all qualities. Visual field was intact and pupil size was normal and reactive to light. The patient showed a slight restriction of ocular movements as a sign of partial oculomotor palsy. Magnetic resonance imaging (MRI) scan showed a 5.6 cm contrast enhancing lesion on the left orbital apex with extension in the middle fossa [Figure 1a to Figure 1f]. The whole tumor was located extradural. In the medical history, patient was operated on left orbital mass through a left-sided lateral orbitotomy 36 years ago. Histological and operative finding at that time suggested a "Neurilemmoma" of V1. Ophthalmic nerve was cut on both sides of the tumor to remove the tumor completely. Pat. developed hypestesia in V1 after the operation.

LITERATURE REVIEW

Review of literature for cases of ONS that were treated with surgery was performed using PubMed, Ovid Medline, and Scopus database. We used the PRISMA checklist as a guide to achieve accepted standards for reporting system reviews. The first author performed all steps and discussed with senior author.

We used keywords "oculomotor nerve" in combination with "schwannoma" and "surgery" or "radiosurgery." A total of 141 related articles were yielded. Articles in nonEnglish language were excluded. The articles without any kind of treatment were also excluded. Finally, 60 articles were considered suitable for review.

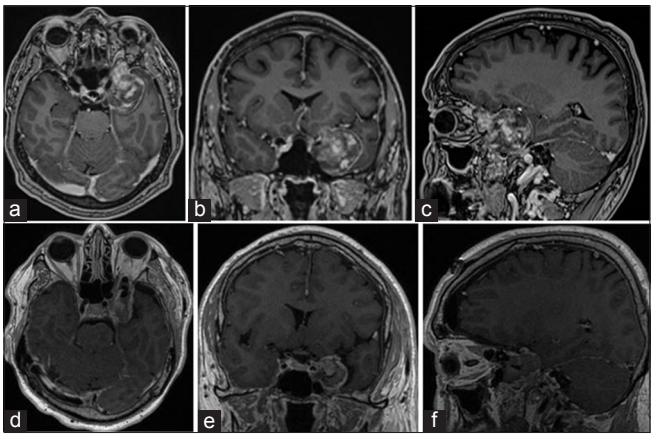

Figure 1: Preoperative (a-c) and postoperative (d-f) magnetic resonance imaging showing the location and gross total resection of tumor.

RESULTS

Surgical resection and operative findings

After exclusion of irrelevant articles according to above-mentioned exclusion criteria, 60 articles were considered to be included in our analysis. We analyzed age, size, location of schwannoma, involvement of CNs, extent of surgical resection, and the third nerve palsy after surgery. The analysis of data from included articles showed that oculomotor schwannoma is slightly more in female gender (53%) and mean age of 35.2 years (standard deviation = 19.5, range 1–66). In 8% of the cases there was no involvement of CN III and 92% of the cases there was either CN III alone or together with CN II, IV, V, and VI affected [Table 1]. 45 of the reported cases were treated with surgery and there are only 4 reports with 7 cases treated with radiosurgery. In 67% of the cases a complete resection and in 33% a partial resection performed [Table 2]. In most of the cases, the tumor was located in the interpeduncular cistern, CS, or cistern-cavernous region [Table 2]. Only a few cases with intraorbital or middle fossa location have been reported [Table 2]. Location and size of the tumor are extremely important to plan the extent of resection. Due to the large size of the tumor with a diameter of 56 mm and mass effect we preferred surgical resection that is in line with literature. Surgery was performed through a lateral supraorbital approach using OPMI PENTERO 900 microscope (Carl-Zeiz, Germany). We used this approach as we are more familiar to the approach for such tumor locations. Dura was opened in a curved fashion to inspect the presence of any tumor. In line with the radiological findings, the tumor was located in temporal fossa in extradural space compressing the temporal lobe laterally, optic nerve medially and oculomotor nerve downwards and the tumor extended toward the superior orbital fissure along the third nerve. In the present case, a subtotal resection with > 90% of tumor removal was performed. The thin layer of the tumor along the course of oculomotor nerve was left intact to avoid the axonal injury to the oculomotor nerve. Dura was closed in a watertight fashion.

Table 1: Review of literature on all cases of oculomotor nerve schwannoma.

Author	Year	Age	Sex	Label (m/f)	Involvement of CN	Symptoms
Kovacs	1927	55	m	1	III and V	Incidental
Nagamune *et al.*	1974	46	f	2	III	Diplopia
Kan *et al.*	1976	36	m	1	III	Diplopia
Huber *et al.*	1978	55	m	1	III, IV	Reduced vision
Huber *et al.*	1978	52	m	1	III	Diplopia
Huber *et al.*	1978	40	f	2	III	Reduced vision
Schubiger	1980	19	f	2	III	Headache
Broggi Franzini	1981	45	m	1	III	Hemiparesis
Hiscott and Symon	1982	58	f	2	III	Hemiparesis, drowsiness
Leunda *et al.*	1982	11	m	1	III	headache, Hemiparesis
Kansu *et al.*	1982	15	m	1	III	headache
Okamoto *et al.*	1985	52	f	2	III, V, VI	Diplopia
Ishige *et al.*	1985	64	f	2	IV, V, VI	Periorbital pain
Satoh *et al.*	1985	46	f	2	III	Headache
Nogami *et al.*	1986	40	f	2	none	headache
Bataille	1987	54	f	2	III	Diplopia, headache
Katsumata *et al.*	1990	47	m	1	III, V	Diplopia, Ptosis
Lunardi *et al.*	1990	60	f	2	III, IV	Headache
Mehta *et al.*	1990	19	f	2	none	Gait disturbance
Takano *et al.*	1990	65	m	1	III	Ptosis, diplopia
Kurokawa *et al.*	1992	55	m	1	none	Diplopia
Barat *et al.*	1992	27	f	2	None	Exophthalmos, vision loss,
Kadota *et al.*	1993	41	m	1	III	Diplopia, Ptosis
Schultheiss *et al.*	1993	65	m	1	III, V	Incidental
Niazi and Boggan	1994	13	f	2	III, V	Hemiparesis, Diplopia
Kachara *et al.*	1998	55	m	1	III	Headache
Kachara *et al.*	1998	61	m	1	III	reduced vision
Asaoka *et al.*	1999	64	f	2	II, III	Headache
Mariniello *et al.*	1999	8	f	2	III	Diplopia
Kawasaki *et al.*	1999	23	f	2	III	headache
Lingavi *et al.*	2000	23	m	1	III, IV, V	headache
Katoh *et al.*	2000	66	f	2	II, III	Incidental
Sarma *et al.*	2002	36	f	2	III	Diplopia
Hatakeyama *et al.*	2003	33	m	1	III	Diplopia
Netuka and Benes	2003	12	f	2	III	Headache
Murakami *et al.*	2005	11	f	2	III	headache, diplopia, ptosis
Bisdorf and Wildanger	2006	14	f	2	III	headache
Kozic *et al.*	2006	9	m	1	III	Diplopia, ptosis
Sener *et al.*	2006	1	m	1	III	Ptosis
Ohata *et al.*	2006	63	f	2	II/III	Diplopia, Ptosis
Tanriover *et al.*	2007	34	f	2	II/III	Headache, Ptosis, anisocoria, exotropia
Chewning *et al.*	2008	3	f	2	III	headache, ptosis
Shamim *et al.*	2008	11	f	2	III	Diplopia, blindness
Prabhu and Bruner	2010	38	f	2	III	Headache, Diplopia, Ptosis, Dizziness
Goel and Shah	2010	32	m	1	III	Headache, Diplopia, Ptosis
Goel and Shah	2010	16	m	1	III	Headache, Ptosis
Safavi-Abbasi *et al.*	2010	61	F	2	III	Diplopia
Saetia *et al.*	2011	41	m	1	II	Visual loss
Furtado *et al.*	2012	21	m	1	III	Diplopia
Furtado *et al.*	2012	25	m	1	III	Diplopia
Nagashima *et al.*	2012	5	m	1	III	Ptosis, exophthalmos
Iijima *et al.*	2013	37	f	2	III	Hydrocephalus, anisocoria, semicoma
Yang *et al.*	2013	3	m	1	None	Irritability, Convulsion
Cho *et al.*	2014	41	f	2	II	Visual disturbance
Kauser *et al.*	2014	32	m	1	III	Ptosis
Kumar *et al.*	2014	29	m	1	II, III	Diplopia, blurry vision

(Contd...)

Table 1: *(Continued)*

Author	Year	Age	Sex	Label (m/f)	Involvement of CN	Symptoms
Senapati *et al.*	2014	24	f	2	III	Diplopia, ptosis
Mariniello *et al.*	2017	16	f	2	III	Proptosis
Mariniello *et al.*	2017	51	f	2	III	Proptosis
Mariniello *et al.*	2017	38	m	1	III	Proptosis

Table 2: Review of literature on surgically treated cases of oculomotor nerve schwannoma.

Author	Year	Age	Sex	Symptoms	Involvement	Max. Division	Location	Resection (Total/pa)	III-Nerve-p	Post-operative
Schubiger	1980	19	f	Headache	III and V	30	CS	Total	No	No
Broggi Franzini	1981	45	m	Hemiparesis	III	30	CI	Total	No	ND
Hiscott and Symon	1982	58	f	Hemiparesis, drowsiness	III	40	CI	Subtotal	Yes	Yes
Leunda *et al.*	1982	11	m	Headache, Hemiparesis	III, IV	55	CI	Total	Yes	Yes
Kansu *et al.*	1982	15	m	Headache	III	4	CS	Total	Yes	ND
Okamoto *et al.*	1985	52	f	Diplopia	III	40	CS- O	Subtotal	Yes	Yes
Nogami *et al.*	1986	40	f	Headache	III	15	CI	Total	Yes	Yes
Katsumata *et al.*	1990	47	m	Diplopia, ptosis	III	15	CI	Total	Yes	Yes
Lunardi *et al.*	1990	60	f	Headache	III	35	CI	Total	Yes	Yes
Mehta *et al.*	1990	19	f	Gait disturbance	III	50	CS	Subtotal	Yes	Yes
Takano *et al.*	1990	65	m	Ptosis, diplopia	III	25	CS-MF	Subtotal	Yes	Yes
Kurokawa *et al.*	1992	55	m	Diplopia	III, V, VI	20	CS	Total	Yes	Yes
Barat *et al.*	1992	27	f	Exophthalmos, vision loss	IV, V, VI	40	CS-O	Total	Yes	Yes
Kadota *et al.*	1993	41	m	Diplopia, Ptosis	III	20	CS	Total	Yes	Yes
Schultheiss *et al.*	1993	65	m	Incidental	none	8	CS	Total	No	No
Niazi and Boggan	1994	13	f	Hemiparesis, Diplopia	III	30	CS	Total	Yes	Yes
Kachara *et al.*	1998	55	m	Headache	III, V	20	CS	Total	Yes	Yes
Kachara *et al.*	1998	61	m	Reduced vision	III, IV	40	CS	Total	Yes	Yes
Asaoka *et al.*	1999	64	f	Headache	none	15	CI	Subtotal	No	No
Mariniello *et al.*	1999	8	f	Diplopia	III	10	CS	Total	Yes	Yes
Lingavi *et al.*	2000	23	m	Headache	none	5	CI	Total	No	No
Katoh *et al.*	2000	66	f	No	None	15	CI-CS	Subtotal	No	Yes
Sarma *et al.*	2002	36	f	Diplopia	III	10	CS	Total	Yes	Yes
Hatakeyama *et al.*	2003	33	m	Diplopia	III, V	40	CI-CS	Total	YES	NO
Netuka and Benes	2003	12	f	Headache	V	28	CI-CS	Total	NO	NO
Ohata *et al.*	2006	63	f	Diplopia, Ptosis	III	30	CS-O	Subtotal	Yes	Yes
Tanriover *et al.*	2007	34	f	Headache, Ptosis, anisocoria, ex	III	20	CS-O	Subtotal	YES	NO
Shamim *et al.*	2008	11	f	Diplopia, blindness	II, III	25	O	Total	Yes	Yes
Prabhu and Bruner	2010	38	f	Headache, Diplopia, Ptosis, Dizzi	III	35	CI	Total	Yes	Yes
Goel and Shah	2010	32	m	Headache, Diplopia, Ptosis	III	40	CI-CS	Subtotal	Yes	No
Goel and Shah	2010	16	m	Headache, Ptosis	III, IV, V	30	CI-CS	Total	Yes	Yes
Saetia *et al.*	2011	41	m	Visual loss	II, III	45	CS	Total	Yes	Yes
Furtado *et al.*	2012	21	m	Diplopia	III	15	CI-O	Subtotal	Yes	Yes
Furtado *et al.*	2012	25	m	Diplopia	III	50	CS	Subtotal	Yes	Yes
Nagashima *et al.*	2012	5	m	Ptosis, exophthalmos	III	35	O	Total	Yes	Yes
Iijima *et al.*	2013	37	f	Hydrocephalus, anisocoria, sem	III	50	CI-CS	Subtotal	Yes	Yes
Yang *et al.*	2013	3	m	Irritability, Convulsion	III	13	CI	Total	Yes	Yes
Cho *et al.*	2014	41	f	Visual disturbance	II	24	CS-O	Subtotal	No	Yes
Kauser *et al.*	2014	32	m	Ptosis	III	43	CS-IO	Total	Yes	Yes
Kumar *et al.*	2014	29	m	Diplopia, blurry vision	II/III	69	CS	Subtotal	Yes	Yes
Senapati *et al.*	2014	24	f	Diplopia, ptosis	II/III	62	CS	Total	Yes	Yes
Mariniello *et al.*	2017	16	f	Proptosis	III	17	CS-CI	Total	Yes	Yes
Mariniello *et al.*	2017	51	f	Proptosis	III	20	CS	Total	Yes	No
Mariniello *et al.*	2017	38	m	proptosis	III	32	CS	Total	Yes	No
Muhammad *et al.*	2018	64	m	Exophthalmos, blurry vision	III	56	MF-O	Subtotal	Yes	Yes

CS: Cavernous sinus, CI: Cisternal, MF: Midel fossa, O: Orbital, CS-O: Cavernous sinus plus intraorbital, CI-CS: Cisterno-cavernous, CS-MF: CS plus midle fossa, MF-O: Midle fossa plus orbital, CO: Cisterno-orbital

Table 3: Review of cases of oculomotor nerve schwannoma treated with radiosurgery.

Author	Number of patients	Radiation technique	Tumor type	Clinical outcome
Kim *et al*. 2008	8 patients (2 ONS)	Gamma Knife RS	Nonvestibular schwannoma including ONS	1. Mean progression-free interval 23 months 2. No improvement of ONP in 2 cases
Nishioka *et al*. 2008	17 patients (2 ONS)	Stereotactic radiation	Nonvestibular schwannoma including ONS	1. 47% of cases improved, 53% remained unchanged 2. No side effects or worsening of symptoms
Kimmball *et al*. 2011	43 patients (2 ONS)	Gamma Knife RS	Nonvestibular schwannoma including ONS	1. Local tumor control was 97% at 1 year, 91% at 4.5 years, and 83% at 5 years 2. CN deficits 9%
Elsharkawy *et al*. 2012	36 patients (1 ONS)	Gamma Knife RS	Nonvestibular schwannoma including ONS	1. The 2-year actuarial progression-free survival was 91%

ONS: Oculomotor nerve schwannoma, RS: Radiosurgery, CN: Cranial nerve, ONP: Oculomotor nerve palsy

Postoperative outcome

Postoperatively patient developed complete oculomotor nerve palsy with ptosis and dilated the fixed pupil. On discharge from the hospital a slight recovery with almost normalized pupil size was observed. In the short-term follow-up of 3 months the partial recovery with normalized and to the light reactive pupil and a partial recovery of ptosis (could open the eye around 1 cm) was documented.

DISCUSSION

ONSs are slow growing rare tumors. There is no standard treatment strategy for such a tumor. Hence, we reviewed the existing literature for treatment modality and reported the outcome. ONS is located at the course of nerve either in cisternal (CI) space, cisterno-cavernous region, orbital apex and rarely in the orbita [Table 2]. The clinical symptoms depend on the size and location, but a certain degree of third nerve palsy is almost always present.[5] Most common symptoms include ptosis and diplopia [Table 1]. Tumor growth toward the optic nerve can cause papilledema and vision loss and in rare cases hydrocephalus.[4] Thin section MRI (1–2 mm) with gadolinium enhancement is the choice of radiologic diagnostic for visualization and evaluation of CN pathologies. In larger sized tumors, it is difficult to exactly define the origin of the tumor. In addition to specific CN palsy, the tumor growth along the course of the particular nerve is another clue for the diagnosis. In the present case, tumor was grown from the orbital apex along the third nerve occupying the space between optic and oculomotor nerve and further growth in the middle fossa toward the temporal pole [Figure 1]. Pre- and postoperative clinical outcome, radiological and intraoperative features suggest that tumor arose from the third nerve. In most of the cases in literature, tumor location is the CI or CS region [Table 1].

Due to benign nature of the tumor, a maximum resection of the tumor is the surgical goal. However, the oculomotor nerve is very fragile and can be easily injured in an attempt to complete tumor removal. Most of the surgically treated cases showed postoperative complete third nerve palsy [Table 1]. Review of current literature showed that 73% of the cases developed postoperative third nerve palsy and 22% improved after surgery. In around 5% of cases, the outcome was not described [Table 2]. Oculomotor nerve seems to be very sensitive to injury as even a partial resection in most of the cases led to postoperative ON palsy. A radical tumor resection in the CS with cutting the third nerve and grafting the sural nerve led to a partial recovery of oculomotor function.[8] The chance of nerve injury increases if the tumor is located more anteriorly toward the superior orbital fissure than in the CI region.[12] All case reports except one[2] where the tumor located in the orbital apex showed complete third nerve palsy after the operation. The reason might be that Cho and Han performed the subtotal resection to avoid the nerve injury. Hence, the extent of tumor resection may be influenced by its location. Due to the morbidity associated with third nerve palsy the alternative strategy might be the subtotal resection.[1,12] Wait and see policy might be the right choice only in patients with the asymptomatic tumor.[5] Gamma knife radiosurgery has been reported to be the effective treatment modality for oculomotor, trochlear, and abducence nerve schwannomas without risk of CN palsy.[6] However, there is only a few case series of nonvestibular nerve schwannoma in literature treated with radiosurgery. In radiosurgically treated cases of nonvestibular schwannoma series including 7 cases of ONS report approximately <10% complications [Table 3]. These small series of radiosurgery, however, include all nonvestibular schwannoma that does not completely reflect the ONS. The radiosurgical treatment results are, however, encouraging for small size tumors.[7,10] More data are needed to evaluate the superiority of radiosurgery over the microsurgery.

CONCLUSION

Due to the high rate of postoperative complete oculomotor nerve palsy, a subtotal resection avoiding the nerve injury seems to be a feasible option. Radiosurgery is another option to treat small size schwannoma. A combined treatment with microsurgery followed by radiosurgery may allow effective treatment for large size oculomotor schwannoma.

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Ethical approval

All procedures performed in this study involving human participants were in accordance with the Ethical Standards of the Research Committee of University of Helsinki and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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