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. Most of the intracranial schwannoma, however, arise from the sensory division of cranial nerves (CNs) including vestibular nerve followed by the trigeminal nerve. Being purely motor nerve, oculomotor nerve schwannoma (ONS) is an extremely rare tumor unless associated with Recklinghausen’s disease. The transition zone of the
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 hypesthesia in V1 after the operation.

LITERATURE REVIEW

Review of literature for cases of ONS that were treated surgically in our department.

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                                |
| Hogan et al.            | 1986 | 40  | f   | 2           | none             | headache                                |
| Bataille                | 1987 | 54  | f   | 2           | III              | Diplopia, headache                      |
| Katsumata et al.        | 1990 | 47  | m   | 1           | III              | 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 Bogdan        | 1994 | 13  | f   | 2           | III, V           | Diplopia, Ptosis                        |
| 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                                |
| Kato et al.             | 2000 | 66  | f   | 2           | II, III          | Incidental                              |
| Sarna 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              | headace, ptosis                         |
| Shamim et al.           | 2008 | 11  | f   | 2           | III              | Diplopia, blindness                     |
| Prabhu and Bruner       | 2010 | 38  | f   | 2           | III              | Headache, Diplopia, Ptosis, Dizziness   |
| Goel et al.             | 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 |
| Kato 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 |
| Shamin 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 | I/II | 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: Mide fossa, O: Orbital, CS-O: Cavernous sinus plus intraorbital, CI-CS: Cisterno-cavernous, CS-MF: CS plus midle fossa, MF-O: Mide fossa plus orbital, CO: Cisterno-orbital
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. [9] 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. [14] 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. [10] 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 [8] 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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