Clinical Course and Prognosis of Trochlear Nerve Schwannomas

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Purpose: To delineate the disease course and prognosis of patients with mass lesions of the fourth nerve presumed to be schwannomas.

Design: Nonrandomized retrospective case series.

Participants: Thirty-seven consecutive cases of presumed trochlear nerve schwannoma from 9 tertiary university neuro-ophthalmology centers.

Methods: Cases were collected, and their clinical characteristics on presentation and follow-up are described. Inclusion criteria were brain magnetic resonance imaging (MRI) with a lesion suggestive of a schwannoma along the course of the fourth nerve. Exclusion criteria were other causes of fourth nerve palsy, such as congenital, traumatic or microvascular; normal (or lack of) initial brain MRI; lack of adequate clinical information; and disappearance of the lesion on subsequent follow-up brain MRI.

Main Outcome Measures: Demographics of patients, presence of neurofibromatosis, symptoms on presentation, vertical deviation, lesion size (on presentation and follow-up), length of follow-up, and outcomes of treatment for lesions or diplopia.

Results: Seven patients were excluded and of the 30 patients included in our series, patients were predominantly male (77%) with a mean age of 51 years (range 9–102 years). In contrast with prior case reports, almost all of our cases had a fourth nerve palsy on presentation (29/30), often isolated. Mean follow-up was 3.1 years (range 0.2 months to 11.1 years). There was no significant difference between initial and follow-up lesion size (4.4 vs. 5 mm) for patients who did not receive treatment of lesions ($P = 0.36$). Only 3 patients underwent neurosurgical resection and an additional patient received gamma-knife radiotherapy. The majority of patients (24/30) did not pursue strabismus surgery for vertical diplopia.

Conclusions: Patients with isolated fourth nerve palsy and small lesions of the fourth nerve have a good prognosis and should be followed with serial MRI scans without neurosurgical intervention unless they develop signs of brain stem compression. Most patients with diplopia and benign fourth nerve lesions typical of trochlear nerve schwannoma can adapt with either prism spectacles or no treatment at all, although strabismus surgery can be successful.

Financial Disclosure(s): The author(s) have no proprietary or commercial interest in any materials discussed in this article. *Ophthalmology 2009;116:2011–2016 © 2009 by the American Academy of Ophthalmology.*

Cranial nerve schwannomas comprise approximately 8% of all intracranial tumors, most commonly arising from the vestibular nerve, followed by the trigeminal and facial nerves.[1] Schwannomas arising from the ocular motor cranial nerves are exceedingly rare in patients without neurofibromatosis and arise from the third, followed by the fourth, and least commonly, the sixth cranial nerves.[2–35] We identified only 31 cases of pathologically identified trochlear nerve schwannomas reported in the literature.[2,3,6–31,35] Of the previously reported cases in the neurosurgical and neurology literature, only 55% of patients initially presented with trochlear nerve palsy; others presented with symptoms of headache (44%) or brain stem compression (40%).[2–32,35] Only 6 (14%) of the reported cases presented with an isolated fourth nerve palsy (with no other symptoms or signs).[3,4] Before the widespread use of magnetic resonance imaging (MRI), small lesions of the fourth cranial nerve were usually not recognized and the clinical course was unknown.[3] Although this condition is suspected to be benign, no long-term follow-up study has been performed. This study aimed to delineate the disease course and prognosis of patients with fourth nerve palsy related to presumed fourth nerve schwannoma.

Materials and Methods

Consecutive cases of presumed trochlear nerve schwannoma were retrospectively collected from 9 tertiary university neuro-ophthalmology centers. Each investigator identified patients with fourth nerve palsy, and these patients were included if the initial brain MRI scan revealed a lesion suggestive of a schwannoma (mass lesion isointense with normal brain parenchyma on noncontrast images, well-demarcated gadolinium enhancement) along the course of the fourth nerve,[3] and at least 1 follow-up MRI scan showing persistence of the lesion.

ISSN 0161-6420/09/$–see front matter
doi:10.1016/j.ophtha.2009.03.054

Exclusion criteria included other causes of fourth nerve palsy, such as congenital, traumatic or microvascular, and normal (or lack of) initial brain MRI scan. Additional exclusion criteria included lack of adequate information on the patients and disappearance of the lesion on subsequent follow-up brain MRI.

For statistical analysis, paired Student *t* test and correlation coefficients were determined using Microsoft Office Excel spreadsheet software (Microsoft Corp, Redmond, WA).

Results

Information on 37 cases was provided the investigators, and 7 cases were excluded from analysis (2 with no baseline MRI; 2 with no enhancement of the lesion on follow-up MRI; and 3 with insufficient clinical information). Fourteen of the 37 cases were identified from 366 patients with fourth nerve palsy at Emory University (3.8%). The clinical characteristics of 7 of these patients have been reported.[4,5]

The majority of included patients were male (23/30; 77%), with a mean age at diagnosis of 51±17 years (range, 9–102 years). The onset of diplopia was sudden in 14 of 30 patients (47%) and less commonly gradually progressive (11/30; 37%) or relapsing/remitting (5/30; 17%). Isolated palsy of the fourth nerve was present in 20 of 30 patients (67%). Headache was present in 7 of the 30 patients (23%). Twenty-two of the 30 patients (67%) had a median follow-up of 2.1 years (range, 0.2–11.1); 17 patients (57%) had 1 or more years of follow-up.

All patients except 1 had a fourth nerve palsy on initial examination. The 1 patient without a documented fourth nerve palsy before diagnosis had a large (5 cm) lesion located in the left cavernous sinus and middle cranial fossa, found incidentally on a head computed tomography performed after the patient was in a motorcycle accident. Median duration of diplopia before diagnosis was 6.9 months (range, 1–113 months) (Table 1). Seventy percent (21/30) of tumors were located on the right side, and with the exception of the patient above, most enhancing lesions of the fourth nerve were located in the ambient or peri-mesencephalic cistern. All cases were isolated solitary tumors. Only 1 patient in our series had neurofibromatosis.

In the 13 included Emory University cases, the lesions were not initially detected by outside radiologists in 7 cases. The lesions were identified only after reviewing (in 5 cases) or repeating (in 2 cases) the MRI scans. Figure 1 shows a typical example of a small lesion of the fourth nerve in patient 14. The median initial size (in longest dimension) of trochlear nerve-enhancing lesion on brain MRI scan was 5.5 mm (range 2–50 mm) (Table 1). With the exclusion of the 2 large lesions (20 and 50 mm), the average size of the smaller lesions was 5 mm.

The median vertical deviation initially present in primary gaze was 4 prism diopters (range, 0–16 prism diopters) (Table 1). For the 13 Emory University cases, Table 2 displays the vertical

Table 1. Presumed Trochlear Nerve Schwannoma: Diplopia and Lesion Details

Patient No.	Duration of Diplopia before Diagnosis (mos)	Initial Vertical Deviation in Primary Gaze (Prism Diopters)	Initial Size (mm)	Follow-up Size (mm)	Adaptation with Prisms	Strabismus Surgery
1	36	2	6	12	Yes	NA
2	3	NA	NA	NA	NA	No
3	18	NA	NA	No change (unavailable size)	NA	NA
4*	1	2	4	2	No	Yes
5*	21.4	4	2	2	Yes	No
6*	1	1	5	NA (small)	NA	No
7*	15.2	2	NA	Slightly more apparent	NA	No
8	0	NA	50	s/p surgery	NA	No
9	4.3	8	3	2; no change	NA	No
10*	3.6	2	3	1	NA	No
11	10.7	6	6	NA	NA	No
12	3.3	6	8	NA	NA	No
13*	8.4	6	10	10	Yes	Yes
14	15.8	4	3	9	NA	Yes
15	6.9	0	20	s/p surgery	NA	No
16	24	5	NA	Small; unchanged	Yes	No
17	24	NA	NA	NA	NA	NA
18	12	NA	NA	NA	Yes	NA
19	9	NA	2	NA	No	NA
20	3	1	NA	NA	NA	NA
21	4	NA	NA	NA	NA	NA
22	1	NA	2	s/p gamma knife	NA	NA
23	40	NA	4	3	Yes	Yes
24	9	NA	2	4	NA	No
25	4	6	2	2	Yes	No
26	6	10	3	NA	No	No
27	113	NA	5	NA	NA	NA
28	1	NA	3	NA	No	No
29	2	NA	6	7	NA	Yes
30*	Unknown	16	6	6	No	Yes

NA = not available.
*Previously reported.[4,5]

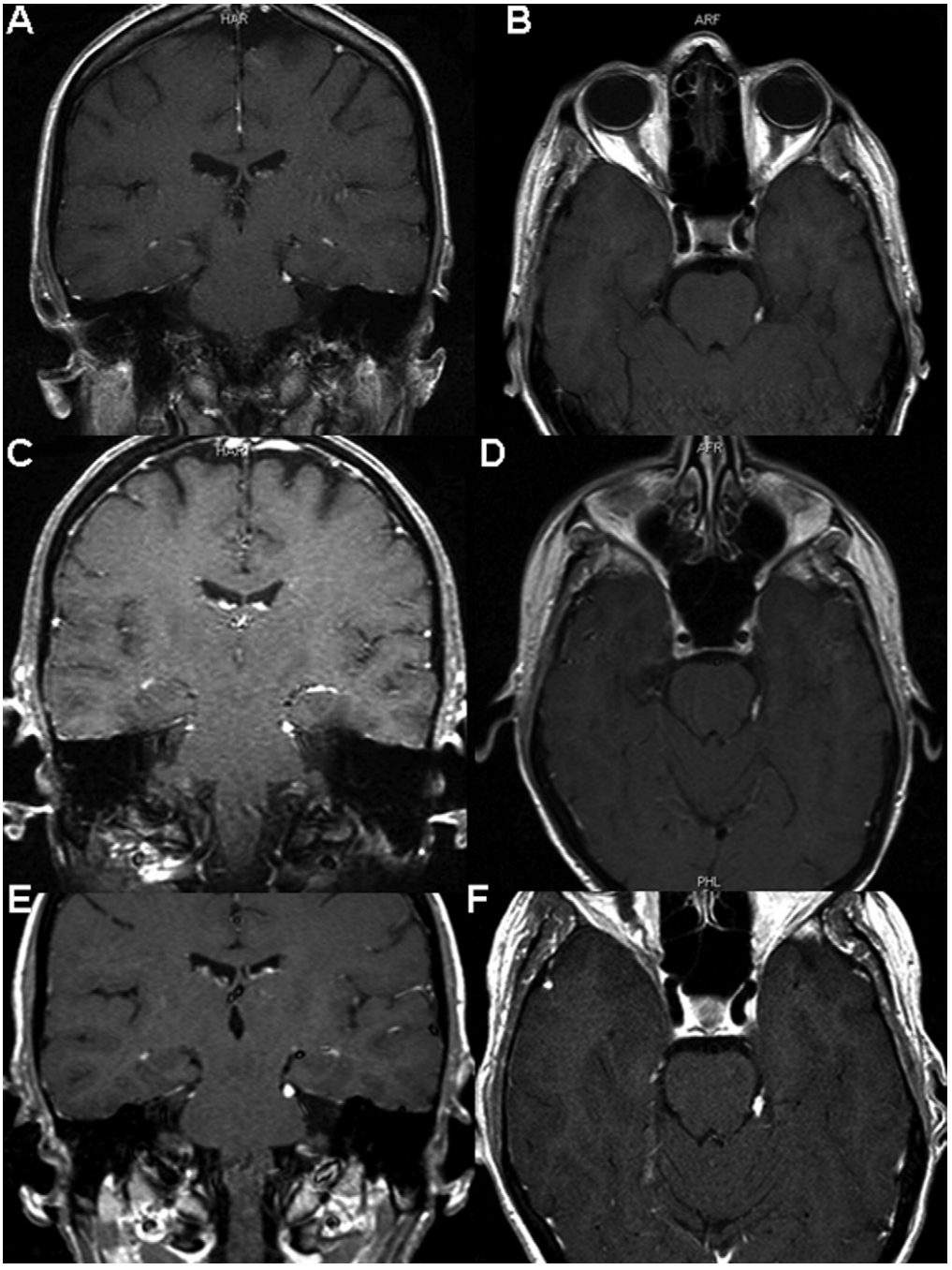

Figure 1. T1-weighted MRI scan from patient 14 showing gadolinium contrast enhancement of the left cisternal segment of the fourth nerve in 2002 **(A, B)**, 2005 **(C, D)**, and 2007 **(E, F)**. The lesion remained essentially stable in size over a 5-year follow-up period.

deviations in primary gaze measured on first presentation and at follow-up. Five of these 13 patients initially worsened at the 6- to 24-month follow-up. Five patients also either remained stable or improved during the follow-up period. For the 7 patients with both initial and latest follow-up measurements (who did not pursue strabismus surgery), no statistically significant difference was found ($P = 0.39$).

There was no correlation of age with tumor size or of tumor size with vertical deviation measured in primary gaze ($R^2 = 0.04$ and 0.007, respectively). By excluding patients with neurosurgical intervention (n = 2) or gamma-knife radiotherapy treatment (n = 1), the median follow-up size was 5 mm (range, 1–12 mm). By using a paired Student *t* test, no statistical difference ($P = 0.36$) was found between initial and follow-up lesion sizes (in the 11 untreated patients with both sizes available for comparison).

In regard to treatment, adaptation with spectacle prisms was achieved by 23% of patients (7/30). Six patients (20%) pursued strabismus surgery for relief of diplopia. The range of vertical deviation in primary gaze immediately before strabismus surgery ranged from 3 to 16 prism diopters (Tables 1 and 2). Median follow-up for the patients who pursued strabismus surgery was 3.6 years (range, 1–10.2 years), whereas overall median follow-up (for

Table 2. Emory University Vertical Deviation Measurements in Primary Gaze on Diagnosis and Follow-up

Patient No.	Vertical Deviation on Presentation (Prism Diopters)	6-mo Follow-up	1-yr Follow-up	2-yr Follow-up	≥3-yr Follow-up
4	2	NA	NA	NA	3 (s/p strabismus surgery after last follow-up)
5	4	5	8	8	2
6	1	NA	NA	NA	NA
7	2	0	10–12	NA	NA
9	0	0	NA	1–2	NA
10	2	6–8	NA	NA	NA
11	16	NA	NA	NA	NA
12	6	NA	NA	NA	NA
13	6	6	6	0 (s/p strabismus surgery)	2
14	4	NA	14	0 (s/p strabismus surgery)	0
15	0	0	0	NA	NA
16	3	6	0	NA	NA

NA = not available.

the 30 patients) was 2.1 years. Two patients (6.7%) adapted with no treatment.

Discussion

Schwannomas of the ocular motor cranial nerves in patients without neurofibromatosis are rare.[3] We could identify only 44 cases of trochlear nerve schwannomas reported in the literature, 31 of which have been pathologically confirmed (Murakawa T, personal communication, 1988; Mee EW, personal communication, 1993).[2,3,6–29,34] Previous reports have stated that fourth nerve schwannomas mainly occur in middle-aged women;[7] however, in our review of the literature, 56% of the reported cases occurred in men (Murakawa, personal communication, 1988).[2–5,8,12,13,15,19–21,28,29] In our series, the lesions were also predominantly found in men (77%). The mean age in prior reports was similar to that in our series (46 vs. 51 years). In contrast with our patients, the majority of the cases previously reported underwent neurosurgical resection (30/44, or 68%), compared with only 3 of 30 (10%) of our patients (Murakawa, personal communication, 1988; Mee, personal communication, 1993).[2,3,6–15,17–26,29,34] Follow-up was longer among our cases than in previously reported series.[2–7,9,10,12,13,15,17–20,24,26,28,33]

Celli et al[2] suggested that the combination of hemiparesis, cerebellar ataxia, and sensory findings with an extra-axial mass at the tentorial notch was more indicative of fourth nerve schwannoma than the presence of a fourth nerve palsy.[2,7–15] However, more recent evidence suggests otherwise. Only 14 of the 44 prior case reports (31%) had at least 2 of these findings, and 13 of these patients were neurosurgically treated (Murakawa, personal communication, 1988).[2,3,6,7,10–15,20,29] Fourth nerve palsy was present in 55% (24/44), with 68% experiencing diplopia as one of the presenting symptoms.[2–4,6,8,9,11,14,15,20,24,26,28,34] Isolated fourth nerve palsy (with only headache allowed as another symptom) was present in 25% of prior reported cases.[3,4,8] Some have theorized that the lower frequency of documented fourth nerve palsy in these cases is due to the schwannoma displacing and twisting some of the fourth nerve fibers rather than completely compressing and destroying the axons.[2,6,7,8,16] Others have suggested that these schwannomas may be dural based or may originate from the trigeminal nerve, especially because one of the other more frequently reported signs is facial hypesthesia.[6]

In our series, all but 1 patient had a fourth nerve palsy on presentation and 67% (20/30) had no other symptoms or signs. The higher frequency of fourth nerve palsy among our series likely in large part reflects a neuro-ophthalmology service bias: Our services receive more referrals for diplopia, whereas prior cases were reported mostly by neurosurgeons who likely receive referrals for cases with more severe symptoms and signs, such as brain stem compression. It is now customary practice for neuro-ophthalmologists investigating a fourth nerve palsy that does not recover and has no known cause to look specifically for a fourth nerve lesion on MRI or repeat the scans if there was inadequate visualization of the course of the fourth nerve. As noted previously, the lesions can be missed,[3] particularly if no gadolinium is used and the interpreter is not aware of the course of the fourth nerve or the underlying clinical findings. Approximately half of the lesions at Emory University were not initially detected on MRI. In our total series of 30 cases, lesions on presentation were smaller on average and remained stable in size compared with the previously reported cases (8.1 vs. 18.8 mm, respectively).[8,9,11,12,14,19–23,26–30,34]

Cranial nerve schwannomas can be classified as cisternal, cisternocavernous, or cavernous.[2,16] The most common location for trochlear schwannomas is cisternal (85%) (Murakawa, personal communication, 1988).[2–15,17–21,23,24,27,29] MRI has become the gold standard for distinguishing intra- and extra-axial lesions of the brain stem.[2,3,7,9,13,15,17] Gentry et al.[3] described specific MRI diagnostic features of primary benign trochlear nerve neoplasms: The MRI scans must include the brain stem, ambient cistern, cavernous sinus, and orbit; the location must be intrinsic to the fourth nerve; and the lesion must be well demarcated, usually isointense to normal brain parenchyma on noncontrast images with

intense contrast enhancement, and usually homogeneous but may be cystic or heterogeneous.[3,6,7,10,18–23] Thin (3–4 mm) sections of high spatial resolution T1-weighted coronal images are best for evaluation of the cisternal segment of the trochlear nerve.[3] The presence of neurofibromatosis type 1 or 2 or multiple cranial nerve lesions would make schwannoma highly likely as the cause for a fourth nerve palsy.[3]

One limitation of our study is that MRI scans were performed at various academic centers with different scanners, protocols, and radiologists. Uniformity across these parameters may yield even more cases. In addition, although long-term follow-up was reasonable (median 2.1 years), some patients did not have follow-up (8/30, 27%), and not all patients were followed for the same length of time (range, 0.2–11.1 years). Some lesions were so small, they may not have been detected on follow-up MRI scans.

Nonetheless, it is still important to follow these patients because these lesions may have growth potential and rarely may even have malignant transformation.[3,35] The majority of patients will remain stable, as evidenced in our series. No significant difference ($P = 0.36$) was found between initial and follow-up lesion size.

In conclusion, patients with isolated fourth nerve palsy and small lesions of the fourth nerve have a good prognosis and should be followed with serial MRI scans without neurosurgical intervention unless they develop signs of brain stem compression. Surgical resection will almost always cause a permanent fourth nerve palsy (Murakawa, personal communication, 1988).[2,3,6,8–15,17–21,24,26,28,34] Most patients with diplopia and benign fourth nerve lesions typical of trochlear nerve schwannoma can adapt with prism spectacles or no treatment at all. Correction of strabismus may be performed for selected cases, although it should be acknowledged that the vertical deviations may spontaneously improve over time or even progress.

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Footnotes and Financial Disclosures

Originally received: December 15, 2008.
Final revision: March 27, 2009.
Accepted: March 31, 2009.
Available online: August 21, 2009. Manuscript no. 2008-1500.

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Financial Disclosure(s):
The author(s) have no proprietary or commercial interest in any materials discussed in this article.

Supported in part by a departmental grant (Department of Ophthalmology) from Research to Prevent Blindness, Inc., New York, New York, and by CORE grant P30-EY0 6360 (Department of Ophthalmology) from the National Institute of Health, Bethesda, Maryland. Dr. Newman is a recipient of a Research to Prevent Blindness Lew R. Wasserman Merit Award.

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Since this article was accepted, another series of 2 cases was published (Petrela E, Hodge CJ, Hahn SS, et al. Stereotactic radiosurgery in two cases of presumed fourth cranial nerve schwanoma. J Neuro Ophthalmol 2009; 29:54–7.).