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MAIN ARTICLE

Spontaneous tumour shrinkage in 1261 observed patients with sporadic vestibular schwannoma

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Abstract

Objective: To determine the rate of spontaneous tumour shrinkage in a group of patients with sporadic vestibular schwannoma managed with a 'wait and scan' approach.

Patients: All patients with a unilateral cerebello-pontine angle tumour resembling a vestibular schwannoma were registered prospectively in a national database in Denmark. Patients registered with tumour shrinkage were identified and all computed tomography and magnetic resonance imaging scans retrieved, re-evaluated and related to the clinical data.

Results: Of 1261 observed patients, 48 displayed spontaneous shrinkage (3.81 per cent). Mean absolute shrinkage was 6.25 mm, equivalent to 52.1 per cent. Absolute shrinkage correlated with tumour size and follow-up period, whereas relative shrinkage was significantly greater for tumours which were purely intrameatal at diagnosis. There was no correlation between age and the degree of shrinkage.

Conclusion: Four per cent of sporadic vestibular schwannomas shrink spontaneously. These findings substantiate the 'wait and scan' strategy for tumours with a largest extrameatal diameter of up to 20 mm.

Key words: Acoustic Neuroma; Prognosis; Pathology; Radiology

Introduction

Vestibular schwannomas are benign tumours arising from the Schwann cell sheath surrounding the vestibular branch of the VIIIth cranial nerve.[1] In most cases, vestibular schwannoma occurs as a sporadic, unilateral tumour.[2] In recent decades, increased availability of magnetic resonance imaging (MRI) scanners and enhanced disease awareness among otologists and patients have resulted in an increase in the number of vestibular schwannomas diagnosed, especially small tumours in elderly patients with mild symptoms. Accordingly, over the last 30 years the incidence of vestibular schwannomas in Denmark (5.5 million inhabitants) has increased from 15 cases in 1976 to 110 cases in 2009, mainly due to an increase in the number of small tumours.[3] Due to small tumour size, advanced age or co-morbidity, an increasing number of patients are opting to forego active treatment in the form of microsurgery or radiotherapy. Thus, the conservative management strategy, also termed 'wait and scan', is becoming increasingly relevant.

The natural history of vestibular schwannoma is enigmatic. Only approximately 20–35 per cent of these tumours grow after diagnosis, while most remain stable in size for many years.[4] In addition, spontaneous tumour shrinkage or regression has been documented. However, publications describing tumour shrinkage have mostly been case reports or case series with a very limited number of patients.[5–8]

This paper presents a series of patients with shrinking vestibular schwannomas, drawn from a large group of consecutively diagnosed patients managed conservatively for up to three decades. We assessed the relationship between tumour shrinkage (i.e. its occurrence, rate and degree) and various clinical parameters (e.g. gender, age, and tumour size and localisation).

Material and methods

Since 1976, all patients in Denmark with a unilateral cerebello-pontine angle tumour resembling a typical vestibular schwannoma have been required by law to be referred to our centre at the ENT department in Gentofte Hospital, where their data have been entered into a national database.

Magnetic resonance imaging scans are performed at each patient's local hospital. The scan report together

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with a compact disk or digital video disk containing the scan digital file are then sent to our centre, where all scans (including diagnostic and follow-up imaging) are evaluated by one of our senior staff consultants.

Tumours were categorised according to the 2003 consensus meeting on systems for reporting acoustic neuroma results, held at Keio University, Japan, as either (1) purely intrameatal, with no size indication, or (2) intra- and extrameatal, with the size estimated as the largest extrameatal diameter, not including the intrameatal portion.[9] This system recognises that, depending on the quality of the scan, a degree of measurement error is possible. It is commonly agreed that a change of at least 3 mm indicates significant growth or shrinkage of a tumour.[9]

We conducted a database search in order to identify patients recorded between 1976 and September 2011, in order to investigate tumour shrinkage among those managed using the 'wait and scan' strategy. The inclusion criteria were the existence of follow-up imaging performed at least one year after the diagnostic scan (either MRI or, rarely, computed tomography), and the presence of registered, significant tumour shrinkage. A diminution of more than 2 mm in the largest extrameatal tumour diameter was considered to represent significant tumour shrinkage. In addition, the original scans of every patient with recorded tumour shrinkage were retrieved and re-evaluated in order to verify the change in tumour size, age at diagnosis and time of shrinkage. The size of a purely intrameatal tumour was recorded as '0' mm.

Student's *t*-test (two-tailed) and Spearman rank correlation analysis were used for statistical analyses.

Results and analysis

Patients in the 'wait and scan' treatment group were scanned as follows. After the initial MRI scan, patients were scanned once after six months, then annually for five years, then every second year for four years, and then every fifth year, until the patient either died or refused to have more examinations. Of the 1261 patients included in this study, 9.4 per cent (118) were not scanned within the last 5 years, indicating some loss to follow up.

Of the 1261 observed patients who were registered in our database between 1976 and September 2011 and who had a recorded diagnostic scan and at least one follow-up scan, 48 patients (3.81 per cent) demonstrated radiological evidence of spontaneous tumour shrinkage. Magnetic resonance images for a typical case with tumour shrinkage are shown in Figure 1. Of the 48 patients with tumour shrinkage, 25 were male (52 per cent) and 23 female (48 per cent). The mean age at diagnosis was 56.7 years and the mean total follow-up time was 9.5 years (range, 1–27 years).

As regards tumour shrinkage pattern, some tumours shrunk before the first control scan, while others grew or remained stable for some years before shrinkage occurred, as shown in Table I.

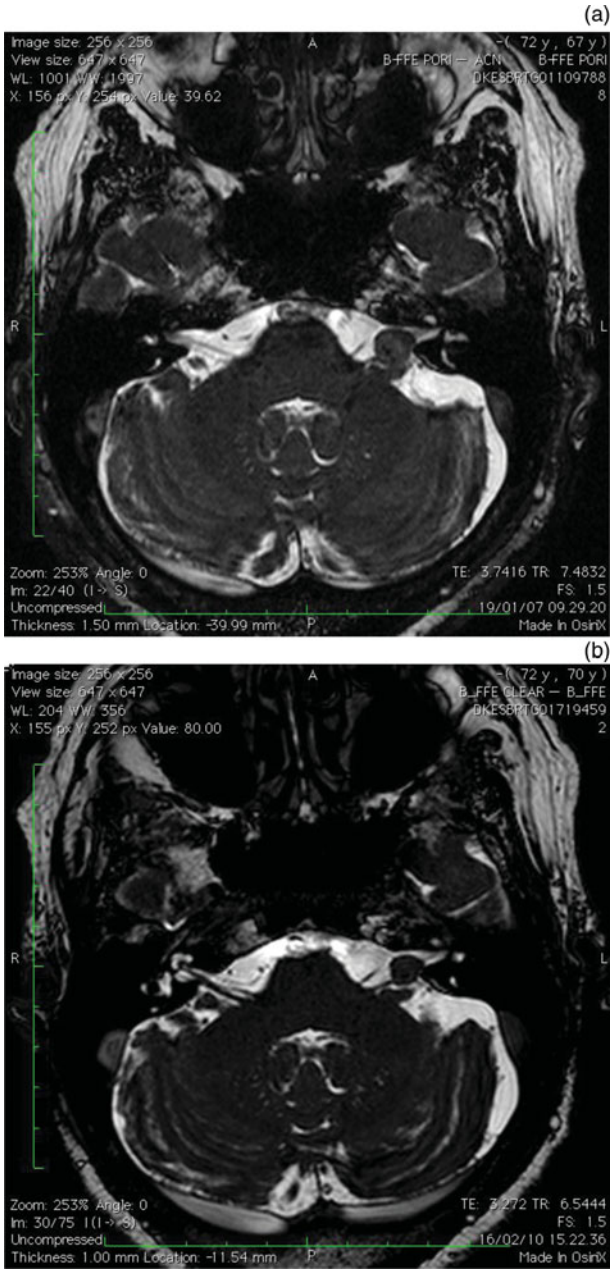

FIG. 1

Axial, T2-weighted magnetic resonance images showing spontaneous shrinkage of a left-sided cerebello-pontine angle vestibular schwannoma in a typical case over three years. Both images are at the level of the internal auditory canal, the VIIIth cranial nerve and the medial portion of the VIIth cranial nerve on the left (tumour) side, enabling proper comparison of tumour size between the images, although they do not show exactly the same features of the contralateral side because of the skew of the patient's head. Images show: (a) the tumour in 2007, and (b) the tumour in 2010, with smaller size due to spontaneous shrinkage.

The tumour size at diagnosis and at commencement and completion of shrinkage is shown in Table II. The absolute and relative tumour shrinkage, as well as shrinkage rate, are shown in Table III. The distribution of tumour size at diagnosis and at commencement and completion of shrinkage is shown in Table IV.

At diagnosis, 10.4 per cent of patients had a purely intrameatal tumour. However, all of these tumours

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TABLE I
TUMOUR SHRINKAGE PATTERN

Pattern	Patients	
	n	%
Growth then shrinkage	14	29.2
Stability then shrinkage	26	54.1
Immediate shrinkage	8	16.7

TABLE II
EXTRAMEATAL TUMOUR SIZE OVER FOLLOW UP*

Time point	Size (mm)		
	Mean	Range	SD
At diagnosis	12.04†	0–50	8.71
At shrinkage start	14.17	4–50	7.87
At shrinkage end	7.77†	0–22	6.05

*$n = 48$ patients. †$p < 0.05$, Student's *t*-test. SD = standard deviation

TABLE III
TUMOUR SHRINKAGE*

Parameter	Mean	Range	SD
Shrinkage (mm)	6.25	3–42	6.13
Shrinkage rate (mm/year)	1.55	0.2–5	1.13
Relative shrinkage (%)	52.10	18.5–100	31.22

*$n = 48$ patients. SD = standard deviation

extended extrameatally before shrinkage occurred (Table V).

Shrinkage patterns varied. The mean age at commencement of shrinkage was 62.8 years, with a mean pre-shrinkage duration of 3.9 years. The distribution of patients' ages at diagnosis and at commencement of shrinkage is shown in Table VI. Most patients were older than 50 years; patients in this age group represented 77 and 83.3 per cent of cases at diagnosis and at shrinkage commencement, respectively (Table VI).

There was no difference in absolute relative shrinkage or in the shrinkage rate between male and female patients.

There was no difference in absolute shrinkage and shrinkage rate, comparing purely intrameatal tumours versus those which were both intra- and extra-meatal. However, relative shrinkage was significantly greater ($p < 0.05$) for tumours which were purely intrameatal at diagnosis (at 86.9 per cent), compared with those which were both intra- and extra-meatal (40 per cent).

Tumour size at diagnosis and at shrinkage commencement correlated significantly with absolute shrinkage (Table VII). In addition, the total follow-up period correlated significantly with shrinkage rate and absolute shrinkage, but not with relative shrinkage. No other significant correlations were found.

TABLE IV
EXTRAMEATAL TUMOUR SIZE DISTRIBUTION

Diam (mm)	Patients (*n* (%))		
	At Dx	At shrink start	At shrink end
≤14	33 (68.8)	29 (60.4)	41 (85.4)
15–20	10 (20.8)	12 (25.0)	5 (10.4)
≥21	5 (10.4)	7 (14.6)	2 (4.2)

Dx = diagnosis; shrink = tumour shrinkage

TABLE V
TUMOUR LOCATION DISTRIBUTION

Location	Patients (*n* (%))		
	At Dx	At shrink start	At shrink end
Intra	5 (10.4)	0 (0)	12 (25)
Intra & extra	43 (89.6)	48 (100)	36 (75)

Dx = diagnosis; shrink = tumour shrinkage; Intra = intracanalicular; extra = extracanalicular

TABLE VI
AGE DISTRIBUTION

Age (yr)	Patients (*n* (%))	
	At Dx	At shrink start
≤39	4 (8.4)	2 (4.2)
40–49	7 (14.6)	6 (12.5)
50–59	16 (33.3)	9 (18.8)
60–69	14 (29.1)	15 (31.2)
≥70	7 (14.6)	16 (33.3)

Yr = years; Dx = diagnosis; shrink = tumour shrinkage

TABLE VII
CORRELATION BETWEEN TUMOUR SHRINKAGE AND PATIENT FACTORS*

Factor	Abs shrink	Shrink rate	Rel shrink
Pt age at diagnosis	0.04	0.18	0.29
Pt age at shrink start	−0.01	0.08	0.29
T size at diagnosis	0.51†	−0.34	−0.40
T size at shrink start	0.65†	−0.24	−0.35
Total FU duration	0.45†	−0.57†	0.05
Pre-shrink duration‡	−0.12	−0.26	0.01

Data represent correlation coefficients. *$n = 48$ patients. †$p < 0.01$. ‡Time between diagnosis and start of shrinkage. Abs = absolute; shrink = shrinkage; Rel = relative; Pt = patient; T = tumour; FU = follow up

Discussion

The present study reports detailed data for a series of 48 cases of tumour shrinkage identified among 1261 patients with sporadic vestibular schwannoma (3.8 per cent) observed for up to three decades. On average, patients with a shrinking tumour were 57 years of age and had a tumour of 12 mm (largest

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extrameatal diameter) at diagnosis. Some tumours shrunk before the first post-diagnostic control scan, while others grew or remained stable for some years before shrinkage occurred. At commencement of shrinkage, the mean largest extrameatal diameter was 14 mm; this reduced to 7.8 mm (i.e. a reduction of 52 per cent) on completion of shrinkage. The mean shrinkage rate was 1.6 mm/year. The occurrence and pattern of shrinkage was not related to gender, tumour size or localisation at diagnosis. However, relative shrinkage was significantly greater for tumours which were purely intrameatal at diagnosis. Absolute shrinkage correlated significantly with tumour size at diagnosis and at shrinkage commencement, and also with the total follow-up period. Although 80 per cent of patients were more than 50 years of age, there was no significant correlation between age and absolute or relative shrinkage.

This series of shrinking sporadic vestibular schwannomas is by far the largest published to date. Previously published papers on this topic have been limited by very small patient numbers, referral selection bias and/or a lack of focus on tumour shrinkage. According to the 11 previous studies of conservative management published since 1991, 3–22 per cent of patients display tumour shrinkage, over follow-up periods ranging from 1 to 12.5 years.[10–20] Summarising these reports, approximately 7.8 per cent of patients (83 of 1062 observed cases) displayed spontaneous reduction of tumour diameter. Most of these studies reported the percentage of patients displaying tumour shrinkage; however, only two papers presented additional information on these patients. Luetje described a decrease in tumour diameter in 6 of 47 observed cases, which ranged from 3.4 to 15 mm.[17] Battaglia *et al.* reported that six patients displayed a mean tumour regression of 0.74 mm/year.[11] Except for these studies, all other authors grouped tumour shrinkage patients together with no-growth cases.

- **Of 1261 observed sporadic vestibular schwannoma cases, 3.81 per cent showed spontaneous shrinkage**
- **Mean absolute shrinkage was 6.25 mm**
- **Absolute shrinkage correlated with tumour size and follow-up period**
- **Relative shrinkage was greater for intrameatal tumours**
- **These findings support a 'wait and scan' strategy for small tumours**

The causative factors affecting spontaneous tumour shrinkage are not clear, although a few theories have been proposed. Putative aetiological factors include vascular causes, the ageing process and immunologically mediated tumour cell apoptosis.[5,8] Our finding that most of our patients (approximately 80 per cent) were aged more than 50 years may support the ageing process as an aetiological factor, although we could find no correlation between age and absolute shrinkage, relative shrinkage or shrinkage rate.

The fact that 90 per cent of the tumours in our series had a largest extrameatal diameter of 20 mm or less at diagnosis was obviously due to the selection of 'wait and scan' management for (or by) patients with small and moderately sized tumours. Thus, our results may be skewed by a tumour size selection bias. However, as larger tumours are typically treated surgically due to the greater risks posed by further growth (e.g. brainstem compression), data on spontaneous shrinkage in these tumours are probably unattainable.

Conclusion

Four per cent of small to medium-sized vestibular schwannomas shrink spontaneously. The occurrence and pattern of shrinkage is not related to gender, tumour size or localisation at diagnosis. Thus, none of the investigated clinical parameters can predict the occurrence of spontaneous tumour shrinkage.

Absolute shrinkage correlates with tumour size at diagnosis and at shrinkage commencement, and also with total follow-up duration, whereas relative shrinkage is greater for tumours which are purely intrameatal at diagnosis. We could find no correlation between age and absolute or relative tumour shrinkage.

These findings support the use of a 'wait and scan' strategy for patients with tumours with a largest extrameatal diameter of up to 20 mm.

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