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Natural Progression and Factors Predicting Growth of Retroperitoneal Schwannoma

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Background: Although knowledge of the natural history of retroperitoneal schwannoma, including growth rate, would be useful when determining the indications and timing of surgical treatment for such nonpalpable tumors, the existing evidence is unclear. We examined the natural history of retroperitoneal schwannoma and assessed whether magnetic resonance imaging (MRI) and clinical findings predict future growth.

Methods: Among patients with retroperitoneal schwannoma treated in our department during the period from January 1, 2015 through December 31, 2015, eight who underwent follow-up assessment by MRI and did not undergo tumor resection for longer than 1 year were enrolled. Changes in lesion size were examined in relation to selected clinical and MRI findings. In cases of pressure erosion in the vertebral body, change in the size of the intraosseous region was compared to change in the size of the whole lesion.

Results: Median absolute growth rate (AGR) was 1.9 cm^3 per year, median relative growth rate (RGR) was 5.6% per year, and median tumor volume doubling time (VDT) was 3.1 years. AGR, RGR, and VDT were not associated with any clinical variable. RGR and VDT values in the intraosseous region were about twice those of the whole lesions.

Conclusions: The growth rates of retroperitoneal schwannomas varied. Additionally, no MRI or clinical findings predicted growth of retroperitoneal schwannoma. Therefore, careful follow-up is necessary for this tumor type, especially for lesions with bone erosion. (J Nippon Med Sch 2020; 87: 13–16)

Key words: peritoneum, schwannoma, natural progression, tumor growth, doubling time

Introduction

Schwannomas account for about 5% of benign soft-tissue tumors. They can occur at any age during adulthood and most frequently develop in the head, neck, and limbs, followed by the posterior mediastinum and retroperitoneum[1]. Retroperitoneal schwannoma is frequently a chance finding on computed tomography (CT) and magnetic resonance imaging (MRI) and, because it is asymptomatic in most cases, is often followed-up without resection. However, surgery is sometimes indicated when the tumor exerts pressure on adjacent organs or peripheral nerves. Knowledge of the natural history of the tumor, including growth rate, would be helpful in determining the indications and timing of surgery for such nonpalpable tumors. However, the natural history of schwannoma is unclear. We attempted to clarify the natural history of schwannomas and to determine whether MRI and clinical findings can predict tumor growth.

Materials and Methods

This retrospective study was approved by our institutional review board and was conducted in accordance with the Declaration of Helsinki (Rl-05-H34). We followed the procedure for disclosure of retrospective observational research information (opt-out) of Nippon Medical School.

Patients

Among the patients with retroperitoneal schwannoma

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Table 1 Clinical characteristics of patients

Patient no.	Age	Sex	Nerve	Symptoms	F/U (months)
1	73	M	T12	-	38
2	40	M	L5	-	12
3	61	M	L3	-	88
4	87	M	L1	-	26
5	74	M	L4	-	29
6	61	F	L4	-	83
7	59	F	L3	-	18
8	75	F	Sciatic	Pain	58

T: thoracic, L: lumbar, F/U: follow-up period, M: male, F: female

treated in our department during the period from January 1, 2015 through December 31, 2015, we enrolled eight who underwent follow-up assessment by MRI and did not undergo tumor resection for longer than 1 year. The demographic characteristics of the patients are summarized in **Table 1**. All had lesions discovered by chance by CT or MRI. In one lesion, the diagnosis was confirmed histologically after needle biopsy. Two other lesions were later resected because the tumor exerted severe pressure on adjacent organs (the spine and kidney), after which the diagnoses were confirmed histologically. The diagnoses for the other five tumors were comprehensively confirmed by a single bone and soft-tissue oncologist who analyzed imaging and clinical findings.

Methods

Lesion size was determined by using the available MR images. The following lesion characteristics were investigated in the initial MR image: demarcation, cystic degeneration[2], target sign[3], and compacted adjacent major organs. Cystic degeneration was defined as only that distinguishable by MRI. Clinical findings were reviewed retrospectively by evaluating patient medical records. Change in lesion size was examined in relation to age, sex, lesion size on the initial MRI, presence of symptoms, cystic degeneration, and target sign. In cases of pressure erosion in the vertebral body, change in the size of the intraosseous region was compared to change in size of the whole lesion.

MRI

MR images were obtained for all lesions by using a 1.5-T device. Slice thickness was 3.0 to 6.0 mm, and the slice gap was 4.1 to 8.0 cm. Axial and either sagittal or coronal images were obtained for all eight lesions. Both T1-weighted spin-echo imaging (pulse sequences: 110-600/9-20 [TR/TE]) and T2-weighted spin-echo or fast spin-echo imaging (pulse sequences: 2200-6667/87-206 [TR/TE]) were performed for all lesions. A fat suppression technique was used when imaging all eight lesions, and postcontrast images were obtained for five lesions.

Measurements and Calculations

Tumor volume was calculated as a measure of size. The long diameter was defined as the major axis in the axial plane, the short diameter was defined as the longest line orthogonal to the major axis in the axial plane, and height was defined as the length orthogonal to the axial plane. Volume was calculated by using a formula for determining the volume of an ellipsoid, namely[4],

$$\text{Volume (cm}^3\text{)} = \frac{\text{Long diameter}}{2} \times \frac{\text{Short diameter}}{2} \times \frac{\text{Height}}{2} \times \frac{4\pi}{3}$$

Absolute growth rate (AGR), relative growth rate (RGR), and tumor volume doubling time (VDT) were used as indicators of volume changes[5]. AGR was calculated by dividing the difference between the volume on the initial MR image ($V_{initial}$) and the volume on the latest MR image (V_{latest}) by the number of years, as follows:

$$\text{AGR (cm}^3\text{/year)} = \frac{d\text{V (}la\text{test-initial)}}{t}$$

RGR was calculated by using exponentiation, as follows:

$$\text{RGR (\%/year)} = \left(\sqrt[t]{\frac{V_{latest}}{V_{initial}}} - 1 \right) \times 100$$

VDT was calculated using the natural logarithm, as follows[5]:

$$\text{VDT (years)} = \frac{Log2}{\log \text{Vlatest} - \log \text{Vinitial}}$$

Statistical Analysis

Age and initial volume were examined in relation to AGR, RGR, and VDT by using Spearman rank correlation coefficients. Sex, presence of symptoms, cystic degeneration, and target sign were examined in relation to AGR, RGR, and VDT by using the Mann-Whitney U test. If tumor volume did not increase, AGR and RGR were recorded as zero. A two-sided p value of <0.05 was con-

Table 2 Magnetic resonance imaging findings and lesion growth rates

Patient no.	Target sign	Cyst	Main growth element	Initial volume (cm^3)	Latest volume (cm^3)	AGR (cm^3/year)	RGR (%/year)	VDT (years)
1	-	+	Cyst	213.1	385.8	54.5	20.6	3.7
2	+	+	Non-cyst	6.0	6.5	0.5	7.9	9.1
3	-	-	—	14.3	11.7	0.0	0.0	–25.5
4	-	+	Non-cyst	269.7	288.5	8.7	3.2	22.3
5	+	+	—	24.5	23.1	0.0	0.0	–28.0
6	+	+	Cyst	93.7	307.1	30.8	18.7	4.0
7	+	-	Non-cyst	10.0	15.0	3.4	31.5	2.5
8	-	+	—	230.4	221.8	0.0	0.0	–88.5
Median	—	—	—	59.1	122.5	1.9	5.6	15.7

Cyst: cystic degeneration, AGR: absolute growth rate, RGR: relative growth rate, VDT: tumor volume doubling time

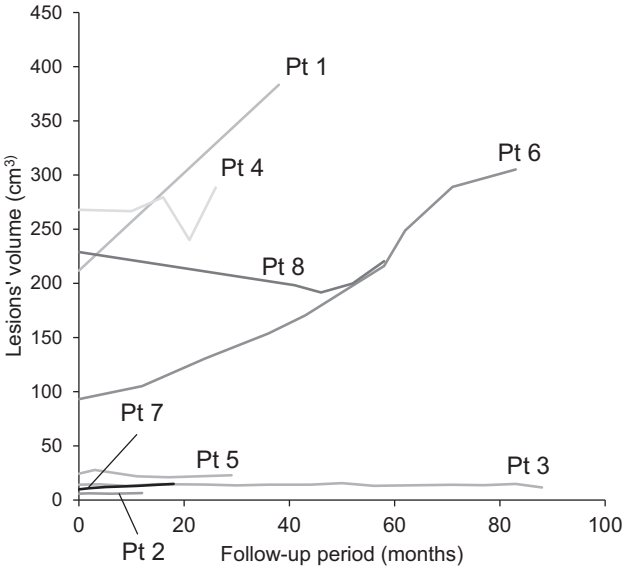

Fig. 1 Volume changes over time in all lesions.

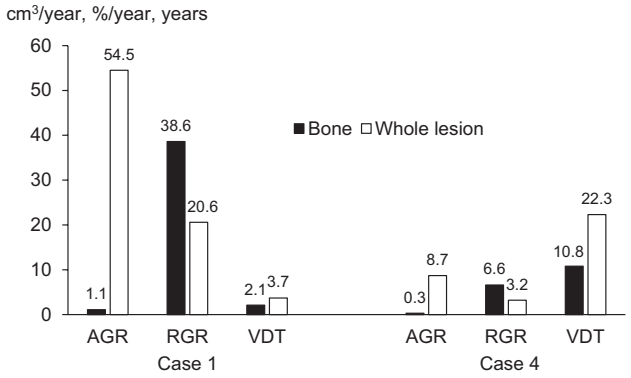

Fig. 2 Absolute growth rate, relative growth rate, and tumor volume doubling time in bone lesions and whole lesions in patients 1 and 2.
AGR: absolute growth rate, RGR: relative growth rate, VDT: tumor volume doubling time.

sidered significant. All statistical analyses were performed with the MS-Excel statistical software package (BellCurve for Excel, ver. 2.15, 2017; Social Survey Research Information Co., Ltd., Tokyo, Japan).

Results

The target sign and cystic degeneration were noted in four and six lesions, respectively (**Table 2**). Of the six lesions that increased in volume, enlargement of the cyst on MRI was the primary cause of the increase in two lesions.

MRI findings and measurement and calculation results are shown in **Table 2** and **Figure 1**. Median initial volume was 59.1 mm (range, 6.0-269.7 mm), median AGR was 1.9 cm^3 per year (range, 0-54.5 cm^3 per year), median RGR was 5.6% per year (range, 0% to 31.5% per year), and median VDT was 3.1 years (range, –25.5 to +2.5 years).

AGR, RGR, and VDT were not associated with age, sex, initial tumor volume, presence of symptoms, target sign, or cystic degeneration. Pressure erosion in vertebral bodies was observed in cases 1 and 4. RGR and VDT values in the intraosseous region were about twice those of the whole lesions (**Fig. 2**).

Discussion

This study identified two types of retroperitoneal schwannoma: those that gradually increased in size and those that did not. However, it was difficult to distinguish these types by examining clinical findings or MR images. In fact, some tumors had an RGR as high as 31.5%, while others shrank (median RGR, 5.6%). A previous study reported an average RGR of 5.3% per year (range, 0% to 27% per year) for spinal schwannoma[4], which is nearly identical to our result. That study reported that heterogeneous findings in T2-weighted and

contrast-enhanced T1-weighted images were suggestive of growth and that enlargement of the cystic portion was the main cause of tumor growth. Our results also suggest that increased cystic degeneration is the main cause of tumor growth in some but not all cases. Studies of vestibular schwannoma have not identified clinical findings associated with future growth[6,7].

Another important result of the present study is that the rate of lesion growth may be faster in the intraosseous region than in the whole lesion, as was noted in two of the present cases. In both cases, the growth rate of the intraosseous region was about twice that of the whole lesion, perhaps because of sustained remodeling of bone. Increased bone loss leads to bone fragility and requires surgery. Retroperitoneal schwannomas resulting in incipient bone erosion require careful follow-up and assessment of surgical timing.

This study has many limitations. It was retrospective, the number of lesions was small, the follow-up period was short, about 60% of lesion diagnoses were not confirmed histopathologically, and measurements were made by a single examiner. Despite these limitations, this appears to be the first report on growth rates of retroperitoneal schwannoma, a rare disease. Moreover, we observed that growth might be faster in the intraosseous regions of lesions.

In conclusion, it is unclear whether MRI and clinical findings can predict retroperitoneal schwannoma growth, and there is a need for continuous observation. For lesions with bone changes, careful follow-up is necessary. To identify factors associated with growth, future studies will need to investigate more lesions and increase the duration of follow-up. Examination of histological findings obtained at biopsy may aid in identifying growth factors.

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