

De Novo Vestibular Schwannoma: A Report of Three Cases

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The reported growth rate of vestibular schwannoma varied widely in the literature. However, emergence of vestibular schwannoma remains unsolved. We presented three patients who had undergone previous magnetic resonance imaging (MRI) confirming the absence of tumor and were diagnosed with a unilateral vestibular schwannoma with a diameter of 18–30 mm, 6–9 years after the initial MRI. One patient had solid tumor and experienced stereotactic radiosurgery. Following stereotactic radiosurgery, continuous tumor growth led to hydrocephalus and trigeminal dysfunction, resolved by surgical removal. Other two patients had the tumor with cystic component and experienced surgical removal as first treatment. All tumors were pathologically diagnosed as schwannomas without evidence of high potential of proliferation. This is the first report of three patients with *de novo* vestibular schwannoma, showing tumor emergence and rapid growth in a short period. Considering a *de novo* aspect, the “wait and scan” policy may not be appropriate for the subset of VS such as *de novo* VS.

Keywords: *de novo*, vestibular schwannoma, acoustic neurinoma, growth rate, cystic

Introduction

Vestibular schwannoma (VS) is a benign tumor arising from Schwann cells in the vestibular component of the eighth cranial nerve. Prevalence of magnetic resonance imaging (MRI) and development of technologies enabled to detect VSs from small in sizes which led the annual incidence of diagnosed VS increasing to 0.6–1.9 per 100,000.¹⁾ Tumor growth occurs in a part of patients, and the reported growth rate is 1.9 mm/year; however, several tumors show rapid growth.^{2,3)} Reported growth incidence of sporadic VS were 17–76.6% and the incidence of treatment required were 7.4–74.5%.^{4,5)} The reported growth incidence varied among studies due to difference of definition of tumor growth and imaging quality. Although predictors of tumor growth have been explored previously, predictive factors of VS growth are still uncertain.⁶⁾ We hardly demonstrate the

tumor emergence because of limited detectability of small lesion using MRI.

We report three patients who had undergone a previous MRI confirming the absence of VS and again 6–9 years after the initial MRI, and were diagnosed with a unilateral VS with a diameter of 18–30 mm. Two consecutive MRIs of these three patients showed that the newly diagnosed unilateral, non-neurofibromatosis VSs emerged and grew in the interval between the two consecutive MRIs. Therefore, we refer to an unilateral, non-neurofibromatosis VSs as *de novo* VS. We discuss the emergence of tumor and clinical importance of *de novo* VS.

Case Reports

Case 1

Due to a minor head injury, a 75-year-old woman underwent MRI in June 2014 showing a left cerebellopontine angle (CPA) tumor (22 mm in diameter) with meatal extension, indicating VS (Fig. 1a). Past history revealed left-sided sudden sensorineural hearing loss in 1991, which led to deafness. She also had undergone MRI in 2005, which showed no tumor in the left CPA or internal auditory meatus (IAM) (Fig. 1b). These two consecutive MRIs demonstrated the emergence and succeeding rapid growth of tumor within the 9-year interval. Therefore, surgical tumor removal was considered as the first treatment option. However, due to the patient's preference, she underwent gamma knife surgery (GKS) in September 2014. The tumor margin was covered by the 50% isodose line, and 12 Gy was delivered in the periphery [tumor volume (TV), 3.9 cm³]. After GKS, the tumor progressively enlarged: TVs were 5.7 and 5.9 cm³ at 6 and 12 months after GKS, respectively. She also developed gait disturbance, unsteadiness, and left trigeminal nerve disturbance. CT scan 1 year after GKS showed progressive ventricular dilatation, indicating hydrocephalus.

She underwent tumor removal via the retrosigmoid approach 17 months after GKS. The surgical procedures for VS via retrosigmoid approach were described previously.^{7,8)} Tumor removal was done without postoperative facial palsy (>95% tumor removal). Pathological diagnosis was schwannoma showing spindle-shaped cells with palisading nuclei. Histology showed clusters of macrophages phagocytosing the hemosiderin indicating the previous intratumoral hemorrhage (Fig. 1c). Immunoprofiling showed tumor cells to stain for S-100, and <5% of MIB-1 labeling index (Fig. 1d). The tumor contained fibrosis and cell degeneration, probably due to GKS, but no atypical nuclei. After tumor removal, gait disturbance improved, and CT scans showed improvement in ventricular dilatation without shunt placement. Follow-up MRI showed no tumor recurrence 2 years after surgery and she is with no neurological deficit except for initial left deafness (Fig. 1e).

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Case 2

In March 2014, a 54-year-old man presented with diplopia and underwent MRI showing a left CPA tumor which was 18 mm in diameter (Fig. 2a). In 2008, he had undergone MRI, which showed no tumor in the left CPA or IAM (Fig. 2b). He had left-sided sudden sensorineural hearing loss in 2010, which led to moderate hearing impairment. He adopted the policy of “wait and scan,” and follow-up MRI revealed rapid tumor growth. Tumor diameters increased to 28 mm in

diameter during 5 months of follow-up. MRI revealed the development of cystic changes in the tumor, and susceptibility-weighted imaging showed a low-signal intensity area in the tumor that indicating microbleeding (Fig. 2c).

Due to rapid tumor emergence and the succeeding rapid tumor growth in 6-year interval, he was referred to our clinic and underwent surgical removal via the retrosigmoid approach. Tumor except for the small part adhering the abducens nerve (>95%) was removed resulting in complete

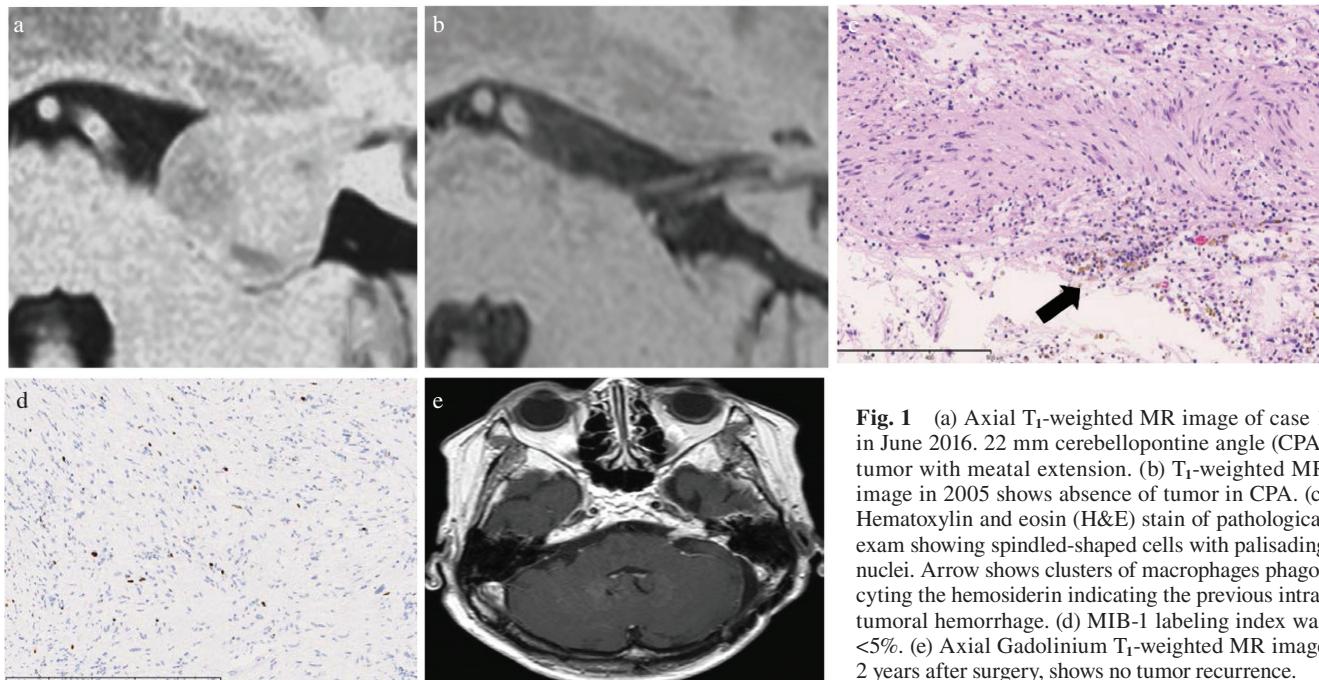


Fig. 1 (a) Axial T₁-weighted MR image of case 1 in June 2016. 22 mm cerebellopontine angle (CPA) tumor with meatal extension. (b) T₁-weighted MR image in 2005 shows absence of tumor in CPA. (c) Hematoxylin and eosin (H&E) stain of pathological exam showing spindled-shaped cells with palisading nuclei. Arrow shows clusters of macrophages phagocytosing the hemosiderin indicating the previous intratumoral hemorrhage. (d) MIB-1 labeling index was <5%. (e) Axial Gadolinium T₁-weighted MR image 2 years after surgery, shows no tumor recurrence.

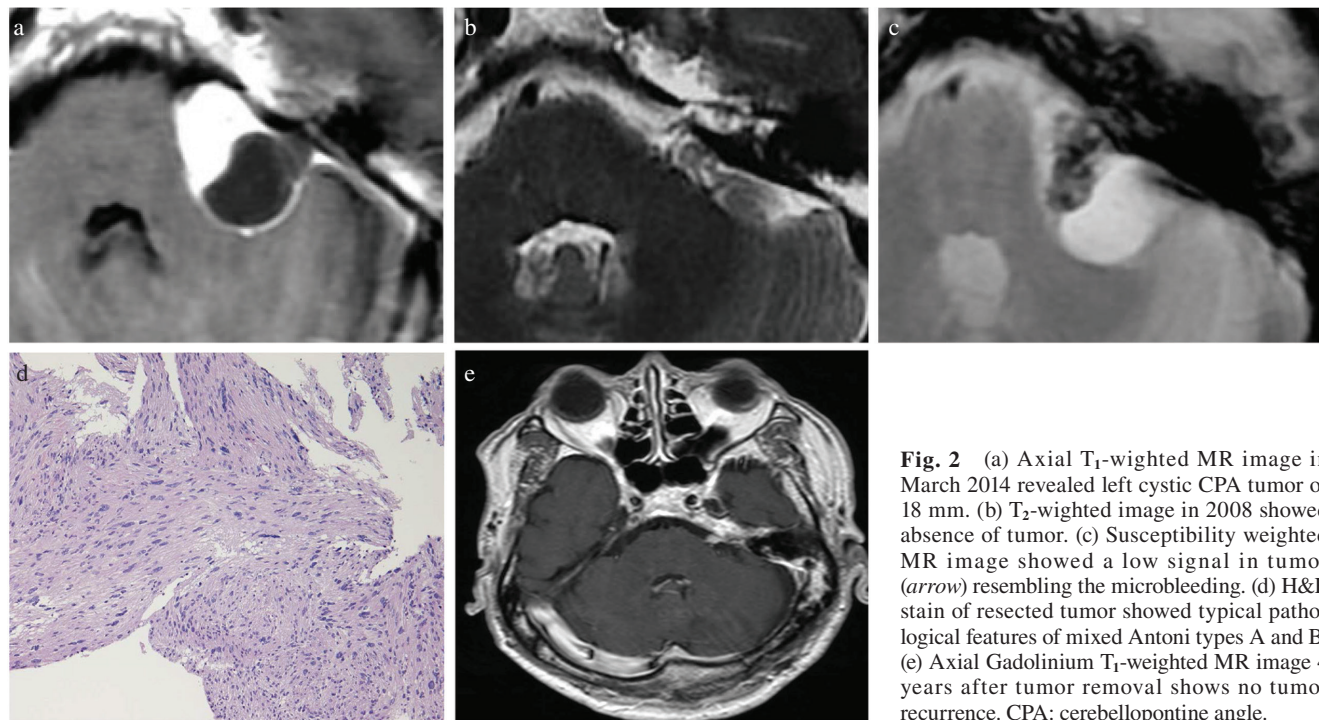


Fig. 2 (a) Axial T₁-weighted MR image in March 2014 revealed left cystic CPA tumor of 18 mm. (b) T₂-weighted image in 2008 showed absence of tumor. (c) Susceptibility weighted MR image showed a low signal in tumor (arrow) resembling the microbleeding. (d) H&E stain of resected tumor showed typical pathological features of mixed Antoni types A and B. (e) Axial Gadolinium T₁-weighted MR image 4 years after tumor removal shows no tumor recurrence. CPA: cerebellopontine angle.

preservation of facial function and no new neurological deficits, except for initial hearing loss and diplopia. Pathological findings showed typical features of a schwannoma: mixed Antoni type A and type B with <5% of MIB-1 labeling index (Fig. 2d). MRI showed no tumor recurrence 4 years after tumor removal (Fig. 2e).

Case 3

In February 2014, due to left sensorineural hearing loss, a 44-year-old man underwent MRI, which showed a cystic CPA tumor of 30-mm diameter with IAM extension (Figs. 3a and 3b). He previously underwent MRI, which showed an absence of left CPA or IAM tumor in 2008 and the tumor emergence and the succeeding rapid tumor growth in the 6-year interval (Fig. 3c). In July 2014, he underwent tumor removal, which revealed that the tumor was highly vascular and hemorrhagic and resulted in 95% tumor removal without facial palsy. Pathological diagnosis revealed a schwannoma with a mixture of Antoni A and B patterns with 5% of MIB-1 labeling index. Cellularity was slightly high, but atypical cells were not found (Fig. 3d). Follow-up MRI showed no evidence of tumor recurrence except for residual tumor during 4 years after surgery (Fig. 3e).

Discussion

We reported three patients with *de novo* VS and clarified that *de novo* VS shows the tumor emergence and the succeeding rapid growth of tumor in the short time period. As shown in Table 1, all three patients had undergone previous MRIs confirming the absence of VS, and after 6–9 years, the second MRI demonstrated a new unilateral VS with a diameter of 18–30 mm. The “wait and scan” policy of case 2 ascertained the rapid tumor growth of *de novo* VS, which

enlarged from 18 to 28 mm in 5 months. The tumor volume increased by approximately 276% in 5 months. Lees et al.⁹ demonstrated that the median growth rate was a 99.4% (interquartile range 46.5–158.8%) increase in volume per year among top quartile of fast-growing tumors. The tumor growth rate of case 2 was extremely high.

Our three cases showed intratumoral hemorrhage and/or cystic change. Vestibular schwannoma with cystic component might be associated with rapid growth.¹⁰ Factors that may predict tumor growth of above 4 mm/year are cystic and hemorrhagic features in the tumor.¹¹ The cystic formation of VSs has been attributed to repeated intratumoral hemorrhage, degenerative changes, and coalescence of microcysts in Antoni B tissue. The histopathological appearance of cystic VSs shows abnormal vessel proliferation, hemosiderin deposits along the tumor, hemosiderin-laden macrophages, and thrombotic vessels that may result in cyst formation.¹² Previous study has found that cystic VS expresses lower

Table 1 Characteristics of 3 cases

	Case 1	Case 2	Case 3
Age (years), sex	75, F	54, M	44, M
MRI interval* (years)	9	6	6
MRI findings size of newly diagnosed AN (mm)	22	18	30
Intratumoral hemorrhage	+	+	–
Cystic change	–	+	+
Patho (Antoni type)	Type A	Mixed†	Mixed†
MIB-1 (%)	5	5	5

*MRI that had shown absence of tumor, which diagnosed a new tumor.

†Pathological pattern of schwannomas types A and B.

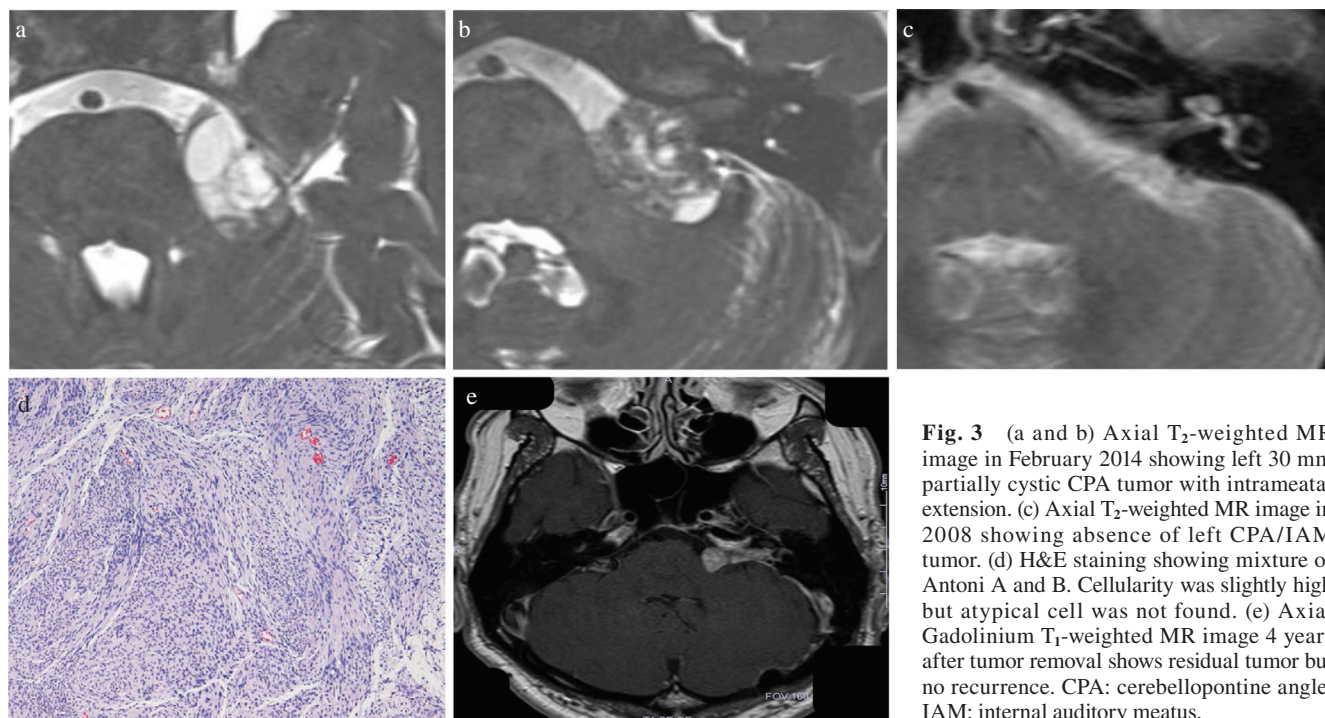


Fig. 3 (a and b) Axial T₂-weighted MR image in February 2014 showing left 30 mm partially cystic CPA tumor with intrameatal extension. (c) Axial T₂-weighted MR image in 2008 showing absence of left CPA/IAM tumor. (d) H&E staining showing mixture of Antoni A and B. Cellularity was slightly high but atypical cell was not found. (e) Axial Gadolinium T₁-weighted MR image 4 years after tumor removal shows residual tumor but no recurrence. CPA: cerebellopontine angle, IAM: internal auditory meatus.

MIB-1 index than solid VS which indicates cystic VSs emergence is caused by cyst formation, not by genuine tumor growth.¹³⁾ Moon et al.¹⁴⁾ indicated that matrix metalloproteinase-2 in cyst fluid may have a fundamental effect on tumor growth and invasion. Radiosurgery may contribute to intratumoral hemorrhage followed by thrombosis, an increase of intravascular outflow, and blood flow congestion due to tumor necrosis which may display sudden and dramatic growth.¹⁵⁾

Our report has some limitations. Though T₁ weighted image with Gadolinium administration can diagnose the small VS most effectively, initial MR images of three patients were without Gadolinium administration, and therefore might not have identified very small tumor. This report showed that the mechanism of tumor emergence and rapid growth of *de novo* VS in a short period may not be revealed by the pathological malignancy alone, but by the combination of repeated intratumoral hemorrhages and cyst formation by the coalescence and rupture of microcysts within the tumor. The pathological findings of all three *de novo* VS cases did not indicate highly proliferative features. MRI showed intratumoral hemorrhages and/or cyst formations of *de novo* VS. Previously demonstrated absence of tumor suggested the rapid growth rate. The “wait and scan” policy may not be appropriate for *de novo* VS having potential of rapid growth.

Conclusion

Considering VSs from a *de novo* aspect, the emergence of more patients with *de novo* VS and further understanding of *de novo* VS characteristics can contribute to elucidating the natural history of VS.

Spread of and improved access to MRI increased chance of confirming absence of tumor before emergence of VS. *De novo* VS may indicate the potential of rapid tumor growth, for which early intervention is considered.

Conflicts of Interest Disclosure

None of the authors have any conflicts of interest to disclose.

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