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Spontaneous malignant transformation of vestibular schwannoma: a case report and review of the literature

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ABSTRACT

Background: The malignant transformation of vestibular schwannoma (VS) is a rare identity. We present a case of spontaneous transformation of VS and a short literature review.

Case Presentation: A 41-year-old female had presented to us with vertigo, tinnitus, and hearing loss. She was diagnosed with left VS and underwent surgical resection. The initial histology was reported as benign grade 1 schwannoma. She subsequently presented to the hospital with hematoma in the tumor cavity after 4 and 5 months, respectively. Her repeat magnetic resonance imaging (MRI) showed growth of the residual tumor. She underwent a second translabyrinthine excision of the tumor. The histology from the second operation showed components of malignant transformation. One month postoperatively she suffered an acute decline in her conscious level. Repeat MRI demonstrated rapid regrowth of the tumor with further hemorrhage. In view of her rapid decline and perceived futility of further intervention and respecting her premorbid wishes, further escalation of therapy was deemed inappropriate.

Conclusion: VS can transform into a malignant tumor even in the absence of radiation therapy. This may be considered in case of rapid regrowth of the tumor.

Keywords: Case report, vestibular schwannoma, malignant transformation, cerebellopontine angle tumor.

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Background

The malignant transformation of vestibular schwannoma (VS) is rare after radiotherapy and much rarer without it [1]. There are few documented cases of spontaneous transformation of a benign VS to a malignant tumor. We present such a case and with a literature review of similar previously reported cases.

Case Presentation

A 41-year-old female who had presented with a few months' history of vertigo, tinnitus, hearing loss, and ataxia was found to have left-sided VS on preoperative magnetic resonance imaging (MRI) (Figure 1). She underwent a near total resection of the tumor (about 95%) via a translabyrynthine approach. The histology was reported as schwannoma grade 1. She made good recovery from her initial operation.

Four months later, she presented as an emergency case with vomiting, left-side headaches, and unsteadiness. Her computer tomography (CT) and MRI scan showed the presence of residual tumor with surrounding hemorrhage extending to the fourth ventricle, albeit with no mass effect (Figure 2). During this admission, she improved with a course of steroids and was discharged home.

She re-presented with further headaches a month later. An urgent repeat CT brain showed further hemorrhage in the previously operated tumor along with obstructive hydrocephalus.

As it seemed unusual for recurrent bleeding to occur in the presence of an acoustic neuroma, she underwent a cerebral angiogram but this did not show any vascular abnormalities (Figure 3).

An (External Ventriculostomy Drain) EVD was inserted to relieve her hydrocephalus urgently. She had an MRI (Figure 4) and underwent a second translabyrinthine excision of left cerebellopontine angle tumor.

At operation, we noted two separate masses: one consistent with the typical appearance of a schwannoma and the other was a capsulated mass deeper within the hemorrhagic center.

On deeper dissection, we found that both the masses fused into one another.

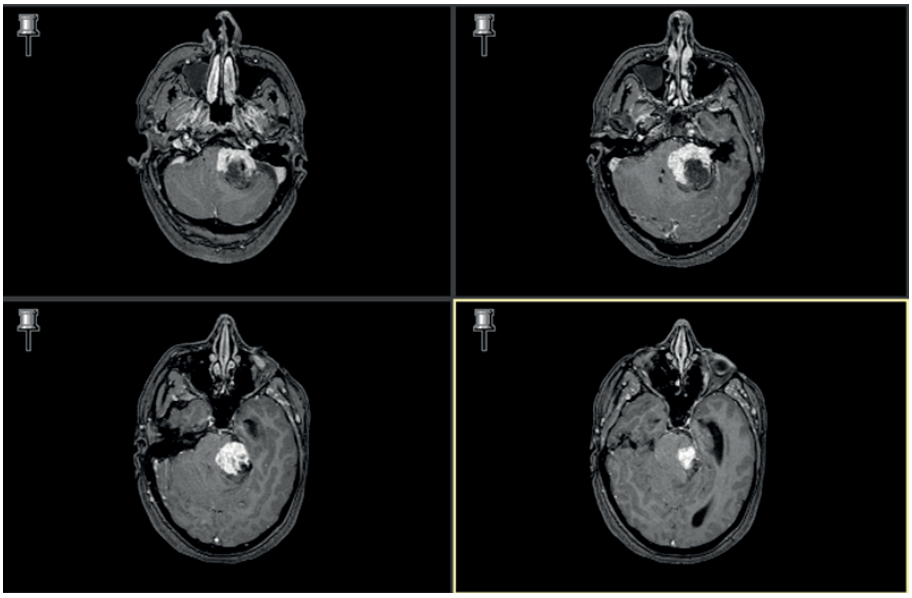


Figure 1. *Pre-op MRI (T1 with contrast) prior to first surgery.*

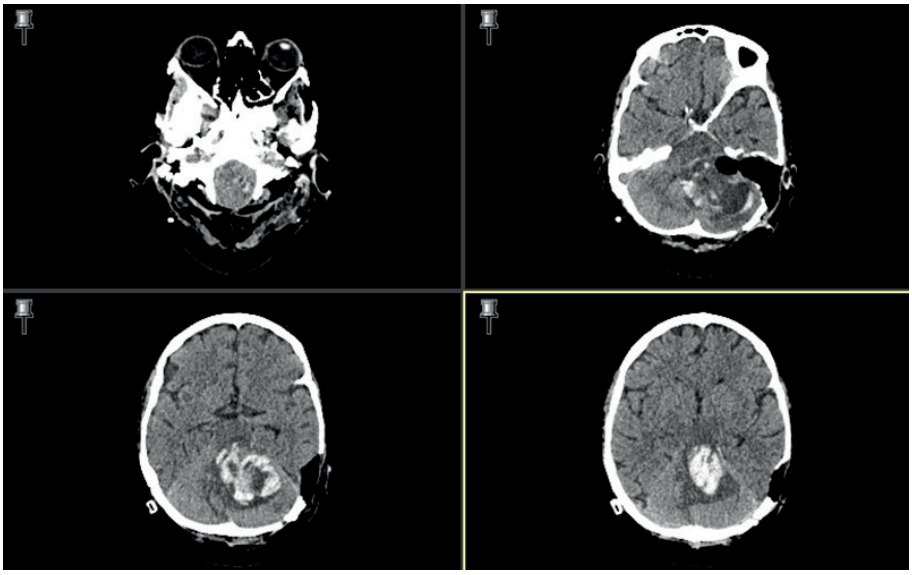


Figure 2. *CT head showing acute hemorrhage within the tumor bed with mass effect.*

Specimens of both masses were sent for histology. Postoperatively she remained stable for 5 days, but suffered a gradual decline from then on. She developed progressive bulbar symptoms and decreased mobility. One month postoperatively, she suffered an acute decline in her conscious level. Repeat cranial imaging demonstrated rapid re-growth of the tumor, now extending into the brainstem with further hemorrhage (Figure 5).

In view of her rapid decline and perceived futility of further intervention and respecting her premorbid wishes, further escalation of therapy was deemed inappropriate. She received the best supportive care and died 10 days later.

Histology

Initial histology reports a tumor composed of cells with a spindle nature including some multinucleated and slightly atypical types (interpreted as an ancient change). Although a clear biphasic appearance is not present in the rather fragmented tissue, the appearances best for those of schwannoma were WHO Grade 1.

The histology of the second resection confirmed a diagnosis of malignant peripheral nerve sheath tumor WHO Grade 3, arising within a schwannoma. There were two smears from the resection that corresponded to the different regions identified; the first had features of a typical

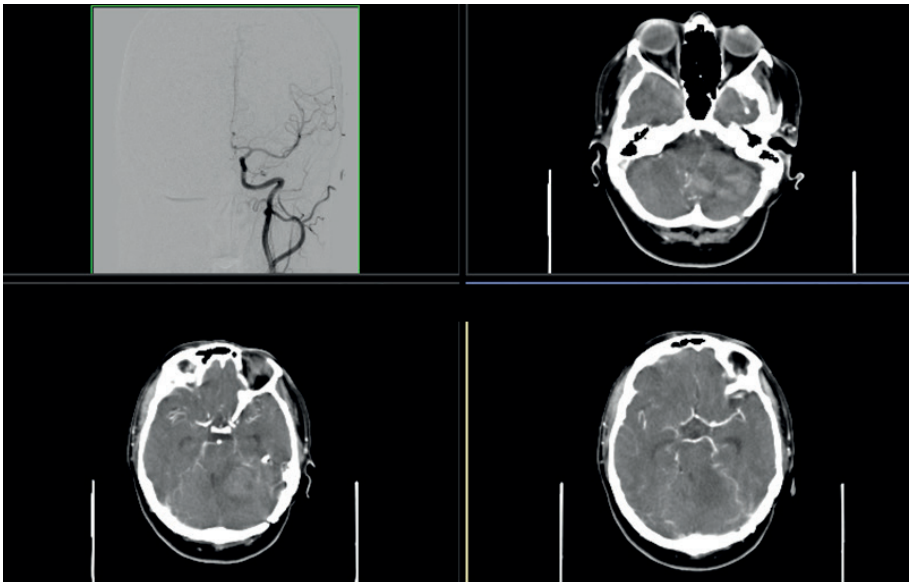


Figure 3. *Angiograms showing no associated vascular anomaly.*

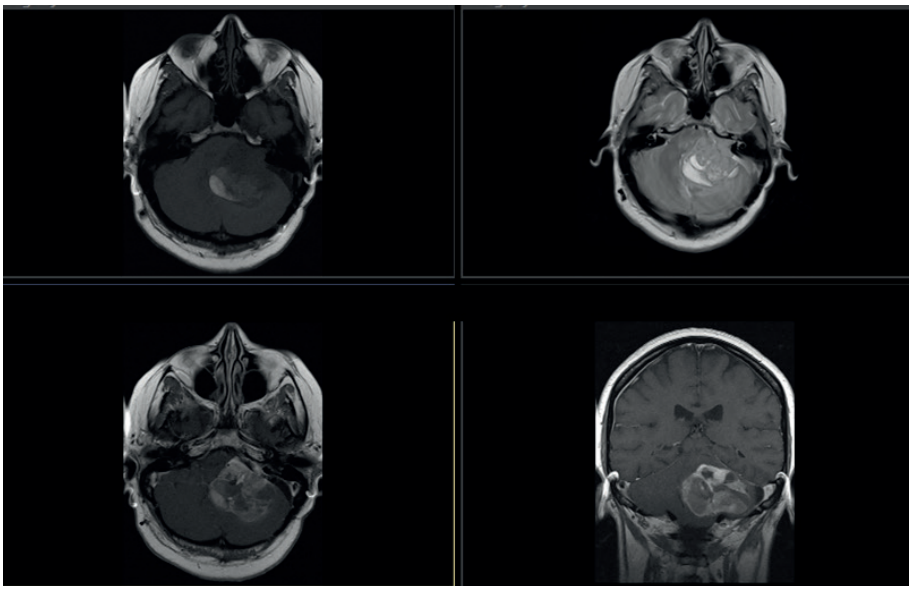


Figure 4. *MRI head T1 pre and post contrast and T2 image prior to second surgery.*

schwannoma and the second smear showed features not typical for a schwannoma, having pleomorphic atypical cells which were discohesive. Mitoses were inconspicuous. On microscopy, the sections showed a spindle cell neoplasm with alternating cellular and hypo-cellular myxoid regions in keeping with the diagnosis of schwannoma. At the edge of the fragments, the tumor displayed increased cellular density and was arranged as short intersecting fascicles giving a herring bone pattern. The cells retained the spindle shape but had large pleomorphic irregular nuclei containing coarse chromatin. Mitoses were abundant, and in some regions were as high as 25/10 HPF. Necrosis was not seen. Melanin pigment was not identified. Immunohistochemistry showed that S100 was expressed strongly in the schwannoma, but focally positive in the malignant component. Ki-67: proliferation index reached as high as 80% in the malignant tumor and is <10% in the benign component (Figures 6-9).

Discussion

Malignant VS are exceptionally rare, more so when they are spontaneous (Table 1).

Husseini et al. [1] published a literature review where they found 36 cases of malignant eighth nerve tumors. Twelve of these cases had previous radiotherapy. Only 12 cases had initial histology confirming initial benign VS. Some of these cases were able to demonstrate histological evidence of transformation from a benign to a malignant eighth nerve neoplasm without previous radiotherapy and/or (Neurofibromatosis 2) NF2 [2-4].

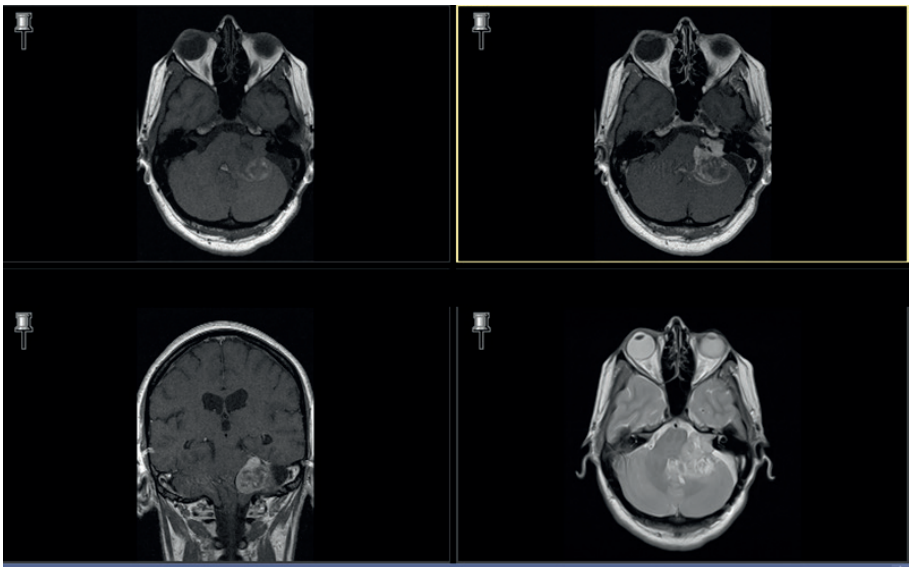


Figure 5. *MRI head T1 pre and post contrast and T2 image showing residual let acoustic neuroma with hematoma.*

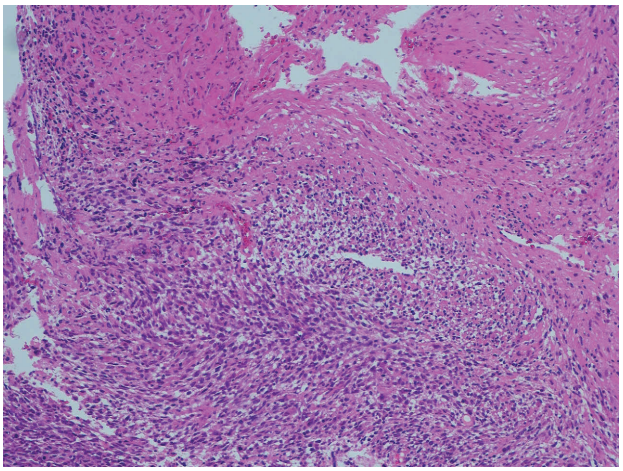


Figure 6. *H&E 100 showing Herring bone pattern in transformed areas.*

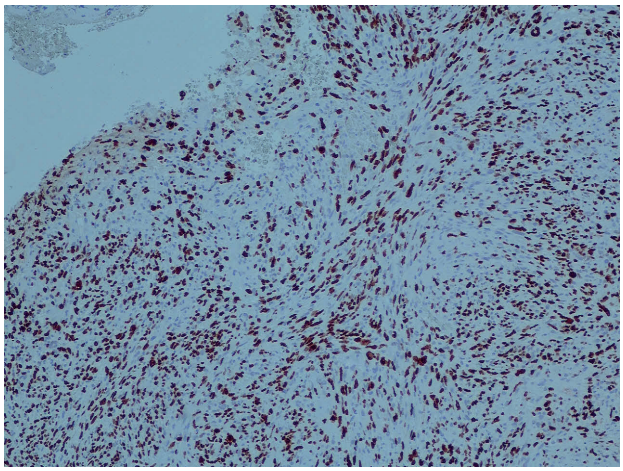


Figure 8. *Ki-67 high in malignant component.*

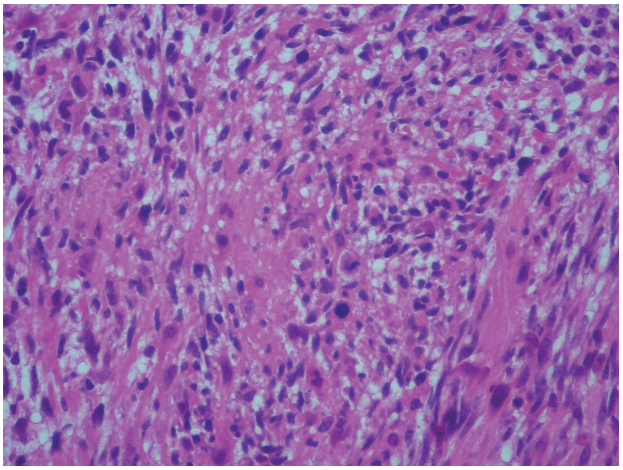


Figure 7. *H&E 200 showing mitotic figures.*

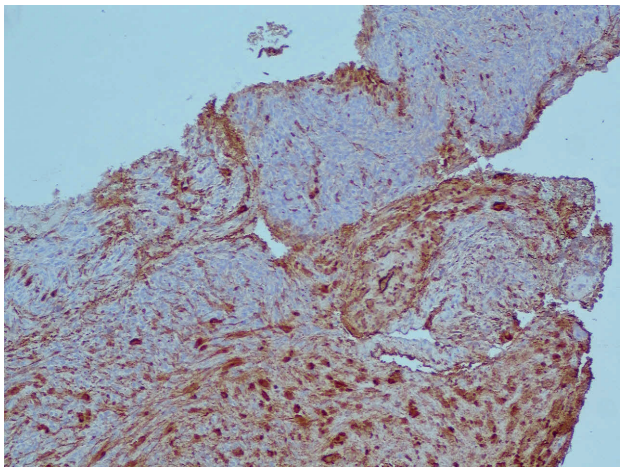


Figure 9. *S100 staining patchy in transformed area.*

Table 1. *Reported cases of spontaneous malignant transformation of VS.*

AUTHOR AND YEAR OF REPORT	AGE/SEX	SIDE	PATHOLOGY	SURVIVAL
Dastur 1967	38 years/M	L	Melanotic schwannoma	8 months
Kudo 1983	54 years/M	R	MPNST	1 month
Miller 1986	74 years/M	N/A	Melanotic schwannoma	N/A
Hernanz-Schulma 1986	2 years/F	N/A	MPNST	N/A
Best 1987	24 years/F	R	Triton	1.5 months
McLean 1990	75 years/M	R	MPNST	2 months
Han 1992	47 years/F	R	Triton	2 weeks
Maeda 1993	38 years/M	R	Triton	3 months
Mrak 1994	40 years/M	L	MPNST	36 months
Earls 1994	77 years/M	L	Melanotic schwannoma	N/A
Saito 2000	69 years/M	L	MPNST	N/A
Gonzalez 2007	43 years/F	L	MPNST	8 months
Chen 2008	62 years/F	L	MPNST	4 months
Scheithauer 2009	67 years/M	R	MPNST	1 month
Scheithauer 2009	56 years/M	R	MPNST	2 months
Scheithauer 2009	50 years/M	L	MPNST	36 months
Scheithauer 2009	32 years/M	L	MPNST	3 months
Scheithauer 2009	5 years/M	L	MPNST	N/A
Karami 2011	23 years/F	L	MPNST	27 months
Wei 2012	41 years/F	R	MPNST	NA
Bashir 2016	47 years/F	R	MPNST	42 months
Belyaev 2018	29 years/F	R	MPNST	6 months

L, left; R, right; MPNST, malignant peripheral nerve sheath tumor; N/A, not available.

The understanding that ionizing radiation plays a role in carcinogenesis has been known for some time. A study in the USA demonstrated that there is a relationship between developing secondary acoustic neuromas in those children who have had previous radiotherapy of the head and neck [5].

There are several cases presenting malignant transformation in patients treated with stereotactic radio surgery for VSs [1,3]. At this point, it would be easy to conclude that radiotherapy is a causative factor in malignant transformation of vestibular nerve tumors. However, a cohort study in the National Centre for Stereotactic Radiotherapy in Sheffield showed only one astrocytoma after gamma knife surgery for a cavernoma [6]. When specifically focusing on those patients with abnormal tumor suppressor genes [NF2 and Von Hippel Lindau (VHL) disease], they also found a glioblastoma 3 years after initial radiotherapy [7].

These results were below the national indices and NF2 patients have a 4% chance of developing gliomas. Patients who have NF2 are already at higher risk of inducing schwannoma after radiotherapy, with a recent report citing an 18.8-fold increase [8].

Lunsford et al. [9] presented 829 cases of patients with VSs treated with Gamma Knife Surgery (GSK), 62 of which had NF2. Half of those with NF2 had a malignant transformation. This apparent propensity for malignant transformation leads us to assume there is a genetic predisposition of some of these VS to become malignant. The inactivity of the tumor suppressor NF2 gene stops the production of the protein merlin, which alters Schwann cell regulation, leading to a tumor proliferation [10].

A study by Lee et al. [11] showed that those recurrent acoustic neuromas that had undergone stereotactic radiosurgery had lost the ability to express the merlin protein. A correlation between the development of sarcomas and p53 tumor suppressor gene mutations is another possible contributory factor [12]. In fact, a p53 mutation after radiotherapy in a malignant transformation has been demonstrated. Furthermore, Gonzalez et al. [3] showed that on their initial histology p53 protein expression was higher in the malignant areas, i.e., a greater presence of p53 mutation in the malignant areas, which was in a non-radiated, non-NF2 transformation.

Conclusion

The progression to malignancy is a multifactorial-based process. Safeguards should be taken in those with abnormal tumor suppressor gene diseases and the use of radiotherapy. One could also postulate that a cellular component could be used as a predictive marker as to predict the likelihood of tumor progression. Finding out the most reliable predictive marker would be a difficult one with the cases being so rare. However, with increased usage of radiosurgery, we may see more and proper studies conducted to establish cellular markers.

Therefore, even patients who have been had a near total resection and diagnosed with a grade 1 schwannoma should be carefully reviewed at regular follow up intervals to avoid missing a potential carcinogenic change.

What is new?

Malignant transformation of VS is rare. This cases represents one such rarity within months of first surgery.

List of Abbreviations

EVD External Ventriculostomy Drain
NF2 Neurofibromatosis 2
VHL Von Hippel Lindau
GKS Gamma Knife Surgery

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this case report.

Funding

None.

Consent for publication

Written informed consent was taken from the patient.

Ethical approval

Ethical approval is not required at our institution for publishing an anonymous case report.

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Summary of the case

1	**Patient (gender, age)**	41-year-old female
2	**Final diagnosis**	Malignant VS
3	**Symptoms**	Few months history of vertigo, tinnitus, hearing loss, and ataxia
4	**Medications**	Dexamethasone
5	**Clinical procedure**	Trans-labyrinthine excision of left cerebello-pontine angle tumors
6	**Specialty**	Neuro-oncology