Malignant Transformation of Vestibular Schwannoma at First Occurrence without Prior Irradiation

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ABSTRACT

Intracranial malignant peripheral nerve sheath tumours (MPNST) arising from the vestibulocochlear nerve are quite rare. Due to the increasing use of stereotactic radiosurgery worldwide for benign intracranial lesions, the literature available has primarily focused on the post-radiotherapy malignant transformation of vestibular schwannomas (VSs). To date, very few cases have been reported enlightening the occurrence of MPNST without prior irradiation or a history of neurofibromatosis. We report a rare case of cerebellopontine angle tumour in a 39-year female who presented with right-sided sensorineural hearing loss and facial palsy for four months without prior history of radiosurgery. The diagnosis was low-grade MPNST arising in the background of vs. based on mitosis, loss of H3K27me3, and radiologically infiltrative borders. The main objective of this case report was to emphasise the need for a cautious assessment of VSs with hypercellularity and atypia for mitosis, necrosis and invasion to exclude malignancy.

Key Words: *Schwannoma, malignant peripheral nerve sheath tumour, neurofibromatosis, vestibular*.

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INTRODUCTION

Malignant peripheral nerve sheath tumours (MPNSTs) constitute 2-10% of soft tissue sarcomas. In the trunk and limbs, 50% are associated with neurofibromatosis 1 (NF1) and arise from pre-existing plexiform neurofibromas. Intracranial MPNSTs, on the other hand, constitute 5% of all reported cases of MPNST and arise from the precursor, schwannoma, and in patients with neurofibromatosis 2 (NF2). The first case of MPNST of Gasserian ganglion was reported in 1978 by Hedeman *et al*.[1] Since then, very few cases of intracranial MPNSTs have been reported. Tumours of cerebellopontine angle (CPA) are even rare. To date, to the best of our knowledge, 36 cases of MPNSTs secondary to prior radiotherapy and 21 cases without prior irradiation have been reported.[2,3] The main objective of this case report is to emphasise the need for a cautious histopathological and radiological assessment of vestibular schwannomas (VSs) with hypercellularity and atypia before labelling them as benign lesions.

CASE REPORT

A 39-year woman presented with right-sided hearing loss, headache, and Bell's palsy for four months and diplopia for 2 months.

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There were no stigmata of NF2 and no family history of such a condition. No prior history of radiosurgery was reported. Neurological examination revealed diplopia, facial paralysis, and a speech discrimination score of 40%.

Gallium Gadolinium (Gd)-enhanced T1-weighted MR image demonstrated 31×30×25 mm lobulated heterogenous enhancing mass in the right CPA causing mass effect on brainstem and cerebellum. The mass was partially encapsulated with infiltrative borders extending to the foramen magnum without extension into the internal auditory canal. The left CPA was clear (Figure 1).

Microsurgical resection was attempted through the right suboccipital retrosigmoid-transmeatal approach to preserve hearing and facial nerve injury.

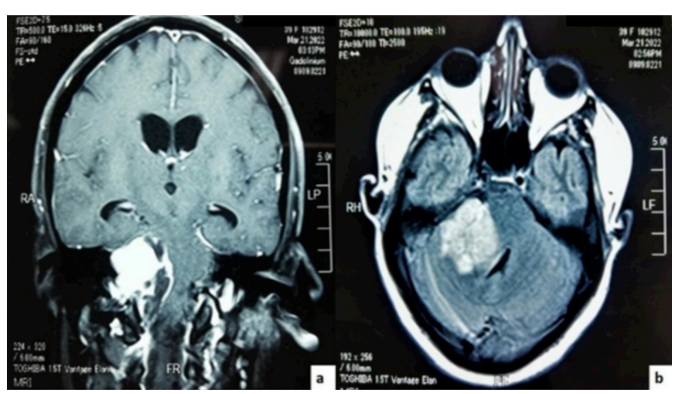

Figure 1: (a) Coronal Gd-enhanced T1-weighted MR image (b) Axial Gd-enhanced T1-weighted MR image demonstrating heterogeneously enhancing right cerebellopontine angle tumour.

Table I: Demographics and outcomes of cases of 8th cranial nerve malignant peripheral nerve sheath tumour without prior history of radiotherapy.

Primary author	Year	Age	Gender	Location	Follow-up (months)	Recurrence	Alive/ Dead
Kudo *et al.*	1983	54	M	Brainstem	4	P	A
Hernanz-Schulman *et al.*	1986	1.5	F	Left CPA	24	P	D
Best; *et al.*	-	24	F	8th CN	1.5	P	A
Mc Lean *et al.*	1990	75	M	Right CPA	2	P	D
Han *et al.*	1992	47	F	8th CN	10	P	D
Maeda *et al.*	1993	38	M	8th CN	3	P	D
Earls *et al.*	1994	77	M	Left CPA	NS	NA	NS
Gruber *et al.*	1994	61	F	Right intracanalicular	24	A	A
Mark *et al.*	1994	40	M	NS	39	P	NS
Higami *et al.*	1998	45	F	8th CN	4	P	D
Son *et al.*	2001	33	F	Left CPA	12	P	A
Suresh *et al.*	2003	46	F	8th CN	2	NA	D
Gonzalez *et al.*	2007	43	F	8th CN	8	P	D
Chen *et al.*	2008	62	F	NS	4	P	D
Scheithauer *et al.*	2009	67	M	8th CN	1	P	D
Gousias *et al.*	2010	64	M	8th CN	12	NS	A
Karami *et al.*	2011	23	F	Brainstem	27	A	D
Gong *et al.*	2012	55	F	Left CPA	5	A	A
Wei *et al.*	2012	41	F	5th CN	NS	NS	NS
Hong *et al.*	2014	25	M	CPA	24	A	A
Mathew *et al.*	2016	25	M	Left internal auditory canal	3	NA	NA
Current case	2022	39	F	Right CPA	9	A	A

NF= Neurofibromatosis; NS= Not specified; NA= Not applicable; VS= Vestibular schwannoma; CPA= Cerebellopontine angle; CN= Cranial nerve; P=Present; A=Absent; A= Alive; D=Dead.

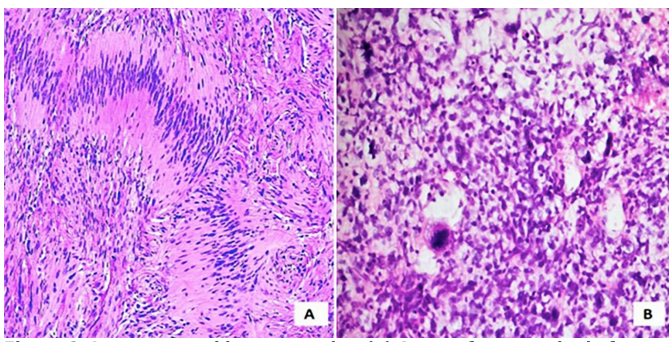

Figure 2: Intratumoural heterogeneity. (a) Areas of verocay body formation (H&E, ×40) (b) Hypercellular areas with marked atypia and mitoses (H&E, ×40).

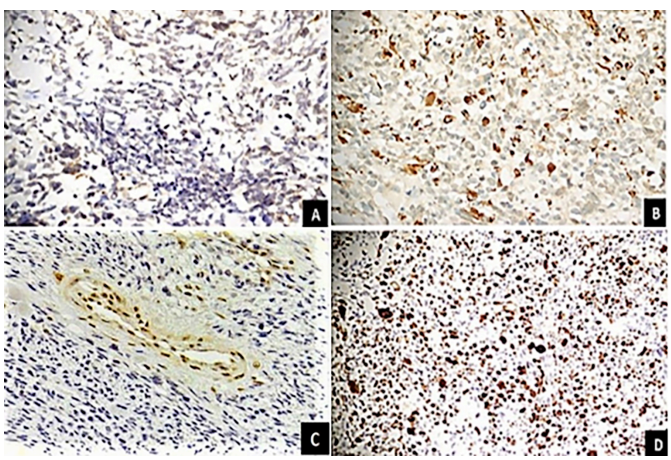

Figure 3: (a) SOX10 with focal positivity (b) S100 positive expression (c) H3K27me3 (loss of expression with positive internal control) (d) Ki-67.

Intra-operatively, there was a partially encapsulated mass with infiltrative borders at the left CPA encasing the 8th cranial nerve. The facial nerve was adherent to the tumour capsule and was attenuated. Macroscopically, the tumour was solid, vascular, and with a tendency to bleed.

The specimen was received in multiple fragments collectively measuring 25×25 mm and submitted for histopathology. Histological examination revealed intratumoural heterogeneity. Few areas showed bland spindle cell proliferation with alternating hypo and hypercellular areas and nuclear palisading. In addition, there were areas showing hypercellular spindle cells arranged in interlacing fascicles with increased perivascular cellularity. The spindle cells demonstrated nuclear condensation, bizarre multinucleated cells, and pale eosinophilic cytoplasm. Upto 4-5 mitoses/10 high-power fields (HPFs) were noted (Figure 2).

Immunohistochemistry showed SOX10 (focal +), S100 (+), DESMIN (patchy+), OLIG2 (-), GFAP (-), IDH1 (-), H3k27me3 (loss of expression), and Ki-67 of 30-40% (Figure 3). The peripheral benign lesion showed strong diffuse immunoreactivity for S100. Based on these morphological and immunohistochemical results, a diagnosis of low-grade MPNST was made.

Post-operative radiotherapy was given to the patient due to piecemeal excision. There was no radiological evidence of disease recurrence on the last follow-up scan and the patient is alive without disease after a follow-up duration of 9 months.

DISCUSSION

Schwannomas are typically encapsulated tumours arising from Schwann cells. Cellular schwannoma is a well-known variant and a real diagnostic challenge. Hypercellularity, loss of rhythmic growth pattern, atypia, and presence of mitoses must not be confused with malignancy.

The exact pathogenesis of the malignant transformation of VSs is unknown.[4] However, with respect to the pathogen-

esis, intracranial MPNSTs are divergent from MPNSTs elsewhere. The common anatomical sites of soft tissue MPNSTs are the trunk and limbs.[5] Soft tissue MPNSTs arise from pre-existing plexiform neurofibromas and are associated with NF1. In contrast, intracranial lesions develop from precursor schwannomas and are associated with NF2.

Due to the increasing use of stereotactic radiosurgery worldwide, much of the literature available has focused on radiation-induced secondary malignancies. Spontaneous malignant transformation of VSs without prior irradiation is a very rare phenomenon. To date, to the best of our knowledge, only 21 such cases have been previously reported.[6]

The present case is a rare example of MPNST arising in a background of VS in a 39-year female diagnosed at first occurrence. There was no history of prior surgery, irradiation, or association with NF.

Demographics and outcomes of cases including this case with spontaneous malignant transformation of VSs without prior history of irradiation are given in Table I. The first case was reported in 1983 by Kudo *et al*.[6] Two cases showed association with NF2. Overall, there was female predominance with 13 females and 9 males. The tumours ranged in size from 12 mm to 40 mm (mean 22 mm). Seven out of 22 cases arose from pre-existing VSs. The commonest sites of involvement were 8th cranial nerve (8/22 cases) and CPA (7/22 cases). In the present case, tumour was 31 mm in size and was located at the right CPA. The overall prognosis was poor in all these cases. Thirteen out of 22 cases showed tumour recurrence. Death due to disease occurred in 11 out of 22 cases.[6] In the present case, the patient was offered postoperative radiotherapy due to piecemeal excision. There was no radiological evidence of disease recurrence on the last follow-up scan and the patient is disease-free after a follow-up duration of 9 months.

Spontaneous malignant transformation of VS at first occurrence without prior radiation therapy is exceptionally rare and is diagnostically challenging due to morphological similarity with cellular and ancient schwannomas. Based on partial encapsulation with infiltrative borders radiologically, the presence of 4-5mitoses/10 HPFs on histological sections, absence of necrosis and loss of H3K27me3 on immunohistochemistry, a diagnosis of low-grade MPNST was favoured.

As this is a rare entity, a thorough histological examination for mitoses, necrosis and invasion is mandatory to exclude malignancy. Atypia alone is insufficient to qualify for malignancy. H3K27me3 is also a helpful immunohistochemical marker and loss of its expression is strongly suggestive of malignancy.

In conclusion, VSs with hypercellularity and atypia should be assessed with caution for mitoses, necrosis, and the presence of invasion to rule out malignancy. Radiological correlation to look for circumscribed or infiltrative borders is also mandatory before rendering a diagnosis of cellular schwannoma to avoid serious consequences in terms of the patient's management and prognosis.

PATIENT'S CONSENT:
Written informed consent was obtained from the patient to publish this case.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS' CONTRIBUTION:
MS: Contributed in analysis of the results and writing of the manuscript.
UH: Contributed to the design and implementation of the study conceived and supervised the project.
Both authors have proof-read and approved the final version of the manuscript to be published.

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