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Case Report

Pathology Section

Case of an Intramedullary Ancient Schwannoma of the Brainstem Mimicking Astrocytoma: A Rare Clinical Presentation with a Diagnostic Dilemma

PRAJNA DAS[1], MUKESH KUMAR PRADHAN[2], RUCHI MITTAL[3], KANAKLATA DASH[4], NARENDRA KUMAR DAS[5]

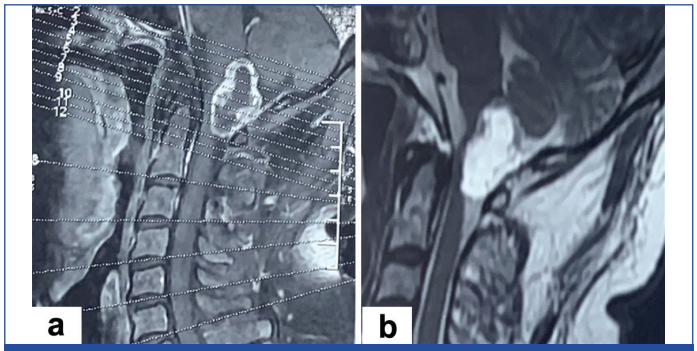
ABSTRACT

Schwannomas are common benign tumours arising from the myelin sheath of peripheral nerves. These tumours are usually located in the intradural and extramedullary regions. The common sites are cervical (58%) and thoracic region (32%), followed by the lumbar region (10%). Intramedullary location is rare and if present, is usually associated with neurofibromatosis 1 and 2 (NF-1 and 2). Intramedullary brainstem schwannomas without NF are uncommon, and to the best of the authors' knowledge, only 19 cases have been reported to date. It was first described by James Watson Kernohan, an Irish-American pathologist, in 1931. The rarity of these tumours in this location is due to the absence of Schwann cells in this area. There are several hypotheses postulating the presence of these tumours in this location. The exact cause is not yet known. The authors here present a case of intramedullary brainstem ancient schwannoma with an unusual clinicoradiological presentation, which raised suspicion of Glioma with the possibility of Astrocytoma. The patient presented with right-sided neck stiffness and shoulder pain for a period of four months. Total excision of the tumour was performed, and the postoperative period was uneventful with clinical improvement in the patient. Histomorphology raised the suspicion of a tumour of glial origin with the possibility of Astrocytoma; Immunohistochemistry (IHC) helped in reaching the definitive diagnosis of Ancient Schwannoma. Thus, a combined approach of clinicoradiological, as well as histomorphology and IHC, is essential for a definitive diagnosis of these tumours. Future multicentric studies are required to elucidate the pathogenesis of the location of these tumours.

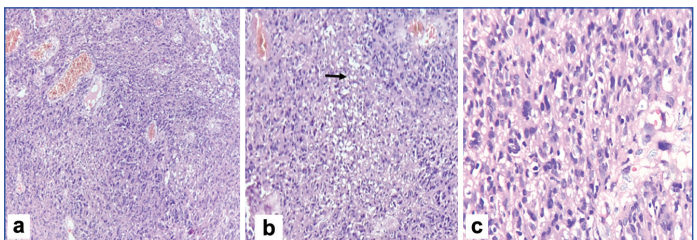
Keywords: Histopathology, Immunohistochemistry, Intradural

CASE REPORT

A 46-year-old male presented to the neurosurgery outpatient department with chief complaints of right-sided somatic as well as neuralgic shoulder pain and neck tightness for four months, associated with a two-month history of headaches. There was no significant family history. He was admitted to the neurosurgery ward for further evaluation. Physical examination revealed stable vitals with a Glasgow Coma Scale of E4V5M6. Bilateral pupils were of the same size and reactive to light with normal vision in both eyes. The muscles in all four limbs had normal power, but the power of the trapezius muscle was 4/5. Based on these clinical features, a Contrast-Enhanced Magnetic Resonance Imaging (CE-MRI) of the spine was advised, which showed an exophytic, lobulated, peripherally enhancing lesion involving the posterior part of the right hemimedulla and the cervicomedullary junction with mild extension to the upper cervical part [Table/Fig-1]. The provisional radiological diagnosis was astrocytoma. The complete blood count, liver function test, and renal function tests were within normal limits. All other routine investigations were normal, and there was no abnormality on the chest X-ray. Surgery was planned, and a total excision of the tumour along with the C1 arch was performed by midline suboccipital craniotomy. The excised specimen was sent to the Department of Pathology for histopathological evaluation. The tissue was received in multiple pieces. About 3-µm thick formalin-fixed paraffin-embedded tissue blocks were prepared, and Haematoxylin and Eosin stained sections were examined. Histopathological examination of the biopsy tissue showed tumour fragments with partial circumscription. There were predominantly cellular areas with small foci of hypocellularity [Table/Fig-2a]. Focal microcystic areas were also seen [Table/Fig-2b]. The tumour cells were arranged mostly in diffuse sheets and vague fascicles. These cells were ovoid to polygonal to spindled, having a moderate amount of fibrillary cytoplasm and indistinct cell outlines. The cellular areas showed a moderate degree of nuclear pleomorphism, dense nuclear chromatin, and inconspicuous nucleoli [Table/Fig-2c]. There were

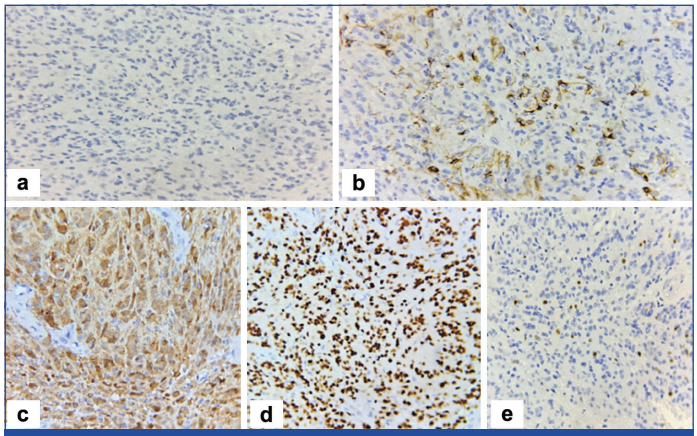


[Table/Fig-1]: Contrast-Enhanced Magnetic Resonance Imaging (CE-MRI): T2-weighted sagittal (a) and axial (b) images showed exophytic lobulated peripherally enhancing mass involving posterior part of right hemimedulla and cervicomedullary junction with mild extension to upper cervical region.



[Table/Fig-2]: a) Tumour is predominantly cellular and focally hypocellular comprising of oval to spindle cells having moderate amount of fibrillary cytoplasm with indistinct cell outlines along with interspersed capillaries (H&E, X200); b) Focal microcystic areas in between tumour cells (H&E, X200) (arrow); c) Tumour cells show moderate degree of nuclear pleomorphism (H&E, X400).

interspersed hyalinized blood vessels [Table/Fig-2a]. The mitotic count was 1/10 HPF. Endothelial cell proliferation and necrosis were not present. With these morphological features, a differential diagnosis of glioma (anaplastic astrocytoma), ancient Schwannoma, and cellular meningioma was considered. IHC was advised for further typing of the tumour. It revealed negative expression of Epithelial Membrane Antigen (EMA) and patchy (15%) expression of Glial Fibrillary Acidic Protein (GFAP) [Table/Fig-3a,b]. The tumour cells showed diffuse and strong expression of S100 and SOX10 [Table/Fig-3c,d]. Ki-67 showed a proliferation index of 2-3% [Table/Fig-3e]. The diagnosis of intramedullary ancient Schwannoma of the brainstem was confirmed. The patient was managed conservatively, and the postoperative period was uneventful. He was discharged in a haemodynamically stable condition with no neurological deficits. He is doing well at about 10 months of follow-up.



[Table/Fig-3]: Immunostaining: a) EMA- Negative in tumour cells (IHC, X200); b) GFAP- Patchy membranous positive in tumour cells (IHC, X400); c) S100- Strong cytoplasmic expression by tumour cells (IHC, X400); d) SOX10- Strong nuclear positive expression by tumour cells (IHC, X200). e) Ki-67- <5% (IHC, X200).

DISCUSSION

Spinal tumours comprise 15% of all Central Nervous System (CNS) tumours [1]. Intradural and extramedullary schwannomas of the spinal cord account for about 10% of all spinal tumours [1]. Intraparenchymal as well as intramedullary locations of schwannomas are extraordinarily rare [2]. They comprise 1.1% of spinal schwannomas and 0.3% of intraspinal tumours [3]. Intramedullary schwannoma was first described by James Watson Kernohan, an Irish American Pathologist, in 1931 [4]. Penfield described the second case in 1932 [5]. According to Navarro Fernández JO et al., the last literature review in 2018 revealed 70 cases of intramedullary schwannoma [6]. Liang X et al., searched the English literature up to 2019 and found only 19 cases of intramedullary brainstem schwannomas [Table/Fig-4] [7-22].

Due to the rare location seen in radiology, these tumours might be misdiagnosed preoperatively as gliomas, leading to inappropriate management [23]. A judicious and comprehensive clinicoradiological analysis with histomorphological and immunohistochemical correlation, including a high index of suspicion, is the best way to reach a definitive diagnosis. Total resection of the tumour is the most beneficial treatment. The role of adjuvant radiotherapy is still not clear. In the present study, authors report a rare case of cervical intramedullary brainstem schwannoma which was suspected as a case of high-grade glioma clinicoradiologically. Combined histopathology along with IHC helped in the diagnosis of ancient schwannoma.

S. No.	Study	Age (years)/ Gender	Site of tumour	Symptoms	Duration of symptoms (months)	Treatment	Follow-up
1	Prakash B 1980 [8]	14/F	Pons	Facial asymmetry, squint, tinnitus, vertigo, 6th and 7th cranial nerve palsies, ataxia	36	Decompression	Good
2	Aryanpur J and Long DM, 1988 [9]	50/F	Medulla oblongata	Nausea, emesis, left-side limb numbness, diplopia, slight slurring of speech, unsteadiness of gait	1.5	Excision	Excellent
3	Ladouceur D et al., 1989 [10]	46/F	Brainstem	Blurred vision, dysarthria, dysphagia, left-side weakness and gait unsteadiness evolving	6	Excision	Excellent
4	Sharma V and Newton G, 1993 [11]	18/M	Medulla oblongata	NA	24	NA	NA
5	Tanabe M et al., 1996 [12]	68/F	Midbrain and pons	Right hemiparesis, sensory disturbance, and diplopia	7	Excision	Excellent
6	Sharma MC et al., 1996 [13]	14/M	Brainstem	Unsteadiness of gait, decreased vision both eyes, abnormal behaviour	12	Excision	Be lost to follow-up
7	Sharma MC et al., 1996 [13]	14/M	Pons	Squint and facial asymmetry, Unsteadiness, 6th and 7th nerve paresis, left-side ataxia	3	Excision	Good
8	Lee SH et al., 1999 [14]	29/F	Brainstem, cerebellum, spinal cord	Facial hypoesthesia, insufficiency of cranial nerve VII, monoparesis	36	NA	NA
9	Lin J et al., 2003 [21]	48/M	Medulla oblongata	Right hemiparesis, ataxia and dysphagia	24	Excision	Excellent
10	Muzzafar S et al., 2010 [15]	68/M	Midbrain, pons, and medulla oblongata	Gait imbalance, coughing, and hiccups, nausea, vomiting, intermittent diplopia, and weakness in right arm	2	Excision	Excellent
11	Srivastav A et al., 2011 [16]	13/M	Midbrain and pons	Left hemiparesis, ataxia and slurring of speech, headache	4	Excision	Excellent
12	Ramos AA et al., 2013 [22]	17/F	Midbrain and pons	Dizziness, unsteadiness, and headache, left nystagmus, facial weakness, VI and VII nerves palsy, diplopia, and ataxia	3	Excision	Excellent
13	Konovalov AN et al., 2013 [17]	44/F	Midbrain	Left-sided numbness,	7	Excision	Excellent
14	Konovalov AN et al., 2013 [17]	22/F	Fourth ventricle brainstem	Intense headache, diplopia, unsteadiness in walking, weakness of facial muscles on the left-side, taste change, and left-sided hearing deterioration	3	Excision	Good
15	Konovalov AN et al., 2013 [17]	23/F	Medulla oblongata	Weakness and numbness of the right half of the body	2	Excision	Excellent

16	Sharma AK et al., 2016 [18]	26/F	Pons and medulla oblongata	Headache, progressive gait ataxia, right hemiparesis, left facial paresis, and slurring of speech	7	Excision	Excellent
17	Zhang Q et al., 2017 [19]	40/F	Medulla oblongata and cervical spinal cord	Cervical pain, weakness of the upper extremities and glove distribution numbness	12	Excision	Excellent
18	Gao Y et al., 2018 [20]	12/F	Medulla oblongata	Dizziness, headache, nausea, vomiting and require assistance with walking	12	Excision	Excellent
19	Liang X et al., 2020 [7]	51/M	Brainstem	Blurred vision, left lower limb weakness	1	Excision	Excellent
20	Present study, 2024	46/M	Right hemimedulla and cervicomedullary junction	Right shoulder pain, neck tightness and headache	4	Excision	Good

[Table/Fig-4]: Twenty reported cases of brainstem schwannoma with clinicoradiological features [7-22].

Schwannomas are benign, slow-growing tumours of myelin sheath origin. The common location is intradural and extramedullary. They are usually found in an extra-axial location in periventricular and cerebellar regions. The most common sites are the cervical region (58%) and thoracic region (32%), followed by the lumbar region (10%). An intra-axial location is extremely rare, particularly in the intramedullary brainstem [21,22]. The rarity of intramedullary schwannoma is due to the absence of Schwann cells in the brain parenchyma. Several hypotheses suggest the aetiopathogenesis of the intramedullary location of schwannoma. These include: a) Migration of schwann cells during embryogenesis; b) Transformation of multipotent stem cells of neuroectodermal origin into Schwann cells; c) schwann cell proliferation after injury; d) Ensheathment of schwann cells over aberrant intramedullary nerve fibers; e) Extension of schwann cells along the perivascular nerve plexus of the intramedullary region [2,3,24].

Schwannomas have several histomorphological variants, such as classical or conventional, cellular, plexiform, ancient, epithelioid, and melanotic [25]. The third most common variant is ancient schwannoma, comprising <1% of all schwannomas [26]. Ackerman and Taylor described the clear hypocellular areas in schwannomas as a degenerative change due to the long-standing duration of the tumour [27]. They coined these tumours as ancient schwannomas [27]. The histopathology of ancient schwannoma reveals mild patchy nuclear pleomorphism and hyperchromasia, along with degenerative changes like cystic areas and hyalinised blood vessels [25]. The atypical morphology of tumour cells mentioned above might raise suspicion of malignancy [25]. However, the absence of necrosis, diffuse atypia, capsular or vascular invasion, with no increase in mitotic figures, indicates the benign nature of the tumour [25]. The biological behaviour of these tumours is similar to the conventional variant [27]. These are slow-growing tumours with a low recurrence rate. Intramedullary schwannomas may be misdiagnosed as gliomas like ependymoma or astrocytoma because of their location and radiologically heterogeneous appearance [28,29]. Wu L et al., compared the clinical presentations of intramedullary tumours, comprising 173 cases of ependymomas, 70 cases of astrocytomas, and seven cases of schwannomas from 2003 to 2010, and reported somatic and neuralgic pain as one of the significant initial symptoms in schwannoma compared to astrocytoma and ependymoma [23].

A similar case report was published by Darwish BS et al., in May 2002 [30]. The case involved a 68-year-old female presenting with severe progressive cervical myelopathy, paraesthesia, weakness, and spasticity causing deteriorated gait. MRI findings suggested an intramedullary vascular malformation. Histopathology revealed features of ancient schwannoma. IHC showed S100 positivity and GFAP negativity. However, in present case, the histomorphology was not very clear as there were more cellular areas mimicking a tumour of glial origin. IHC confirmed the tumour as an ancient schwannoma.

The prognosis of these tumours is good. Total excision of the tumour is the best treatment for these cases, with drastic clinical improvement after surgery [23,28,29]. Recurrence is usually not observed after near-total excision of the tumour. Therefore, the role of the pathologist is crucial in these cases. Careful histopathological study, along with correlation with clinical features, radiological findings, and IHC, helps in making a definitive diagnosis and determining postoperative treatment. Informed consent was obtained from the patient before surgery and postoperative histopathological and immunohistochemical analysis.

CONCLUSION(S)

Schwannomas are slow-growing benign tumours with a rare intramedullary location and complete functional recovery post excision. They do not have pathognomonic clinical signs and symptoms to differentiate them from other intramedullary tumours; however, the possibility of intramedullary schwannoma should always be considered when a middle-aged patient presents with a history of chronic somatic and neuralgic pain and has a medullary lesion in the cervical or thoracic spine. Furthermore, a combined approach of clinical features with radiological findings, histopathological, and immunohistochemical evaluation can help in reaching a proper diagnosis.

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PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Pathology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India.
2. Postgraduate Student, Department of Pathology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India.
3. Professor, Department of Pathology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India.
4. Professor, Department of Pathology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India.
5. Professor, Department of Neurosurgery, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Prajna Das,
Plot No. 784/786, Lane 3, Jaydev Vihar, Bhubaneswar-751013, Odisha, India.
E-mail: prajnadas68@gmail.com

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