Archives of Neurosurgery in Africa
Vol. 2 No. 2 July - December, 2021 29-34

Spinal Schwannomatosis Unassociated with Phakomatosis: A Case Report

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ABSTRACT

Schwannomas are slow-growing encapsulated benign tumours of the peripheral nerves. The multiplicity of these tumours have been linked with genetic anomalies associated with neurofibromatosis. Schwannomatosis is a rare autosomal-dominant tumour syndrome characterized by the concurrence of multiple schwannomas of the peripheral nervous system, with no involvement of the vestibular nerve. This contrasts with neurofibromatosis 2 in which the existence of bilateral vestibular schwannomas is pathognomonic. Spinal schwannomatosis without features of neurofibromatosis is a very rare occurrence, previously unreported in Nigerian neurosurgical literature. We present a Nigerian patient with cervical intradural-extramedullary and thoracic intramedullary spinal schwannomas. His treatment outcome and a brief literature review were also discussed.

Keywords:

Schwannomas, Clongenital neurilemmomatosis, Intradural tumours, Neurofibromatosis type 3

Introduction

Schwannomas are well-encapsulated benign nerve sheath tumours of Schwann cell origin which constitute approximately 33% of all benign primary spinal tumours.[1,2] About 90% of these tumours are solitary and sporadic.[2,3] However, the synchronicity of multiple schwannomas in the same individual is usually associated with an underlying genetic predisposition to tumourigenesis as seen in phakomatoses such as neurofibromatosis and schwannomatosis.[1,2,4] Schwannomatosis is a remarkably rare disease entity characterised by multiple extracranial schwannomas occurring in the absence of the genetic mutations of neurofibromatosis.[1,2,4] In this paper, we present a case of spinal schwannomatosis in a middle-aged Nigerian patient.

Case Report

A 43-year-old man who presented to our surgical out-patient clinic with a 2-year history of low back pain and progressive paraparesis which culminated in paraplegia about 7 months from the onset of symptoms. He had an associated history of paraesthesia/numbness of the lower extremities.

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There were no features of autonomic dysfunction, neck pain or sensorimotor deficits involving his upper limbs. He had no cutaneous anomaly, family history of neurocutaneous disorder or neoplasm. Examination revealed a middle-aged man with satisfactory general examination findings. He was fully conscious, had normal mental status/ pupils and no cranial nerve deficits. He had reduced muscle bulk in his lower limbs, spastic paraplegia, brisk knee/ ankle jerks/ sustained ankle clonus/extensor plantar response bilaterally. Power was grade 5 in the upper extremity muscle groups. His sensory level was T10 with sacral sparing. Ocular and cutaneous examination revealed no feature of neurofibromatosis. The rest of his systemic examination findings were normal. He was thus diagnosed with T10 non-traumatic myelopathy.

Magnetic resonance imaging (MRI) showed a right-sided C2-C3 intradural/ extramedullary tumour with significant cord compression (Figure 1a/b). There was a synchronous, ill-defined T10/T11 intramedullary tumour (Figure 1c/d). The brain MRI showed no intracranial lesion and his abdominopelvic ultrasound scan revealed normal findings. He had C2-C3 laminectomies with complete excision of the cervical tumour. The intraoperative findings were those of a right anterolateral fibrous pinkish tumour, with significant cord compression (Figure 2a). His postoperative course was satisfactory and he remained free of neurological deficits referrable to the cervical spine as he did preoperatively. He had T10/T11 laminectomies with gross total excision of the thoracic intramedullary tumour ten days after his initial surgery. Intraoperatively, we noted a mixed consistency pinkish intramedullary tumour (Figure 2b). Both tumours were diagnosed histologically as schwannomas (Figures 3/4). The patient made no neurologic gains following the second surgery and also developed new-onset bisphincteric incontinence which persists at the time of this report.

Figure 1 (a-d): Spinal magnetic resonance imaging

1a: Pre-contrast sagittal reconstructed T 1 - weighted image (T1WI) of the cervical spine showing a C2-C3 intradural/extramedullary isointense tumour (black arrow). Curiously, the patient was asymptomatic for this lesion despite the extent of cord compression shown here.

1b: Contrast-enhanced T1WI of the cervical spine. Note the bilobed nature of the tumour and the avid contrast enhancement of the tumour (white arrow)

1c: Pre-contrast sagittal reconstructed T1WI of the thoracic spine showing an ill-defined intramedullary tumour (black arrow) at the level of the T10/11 intervertebral disc space

1d: The lesion demonstrates a moderate degree of enhancement on contrast administration (white arrow)

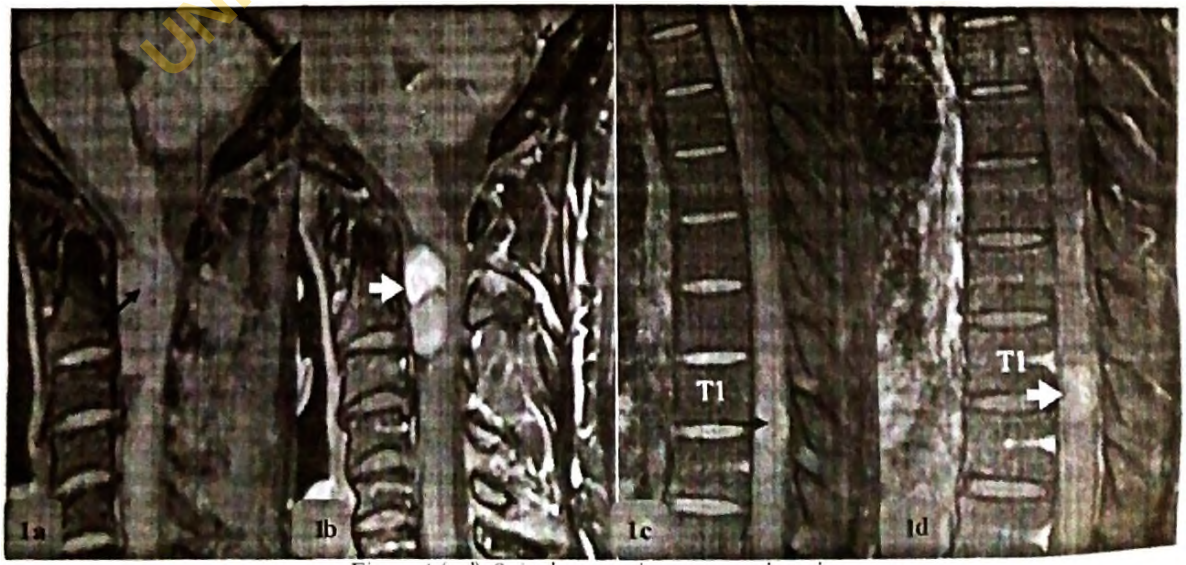

Figure 1 (a-d): Spinal magnetic resonance imaging

Figure 2 a and b: Intraoperative images
a: Note the right-sided intradural/ extramedullary location (thick white arrow) of the cervical tumour. The thin black arrows show the edges of the retracted dura (following durotomy), while the grey arrow depicts the spinal cord. The lesion was approached via a posterior approach
b: Note the intramedullary location (instrument) of the thoracic tumour.

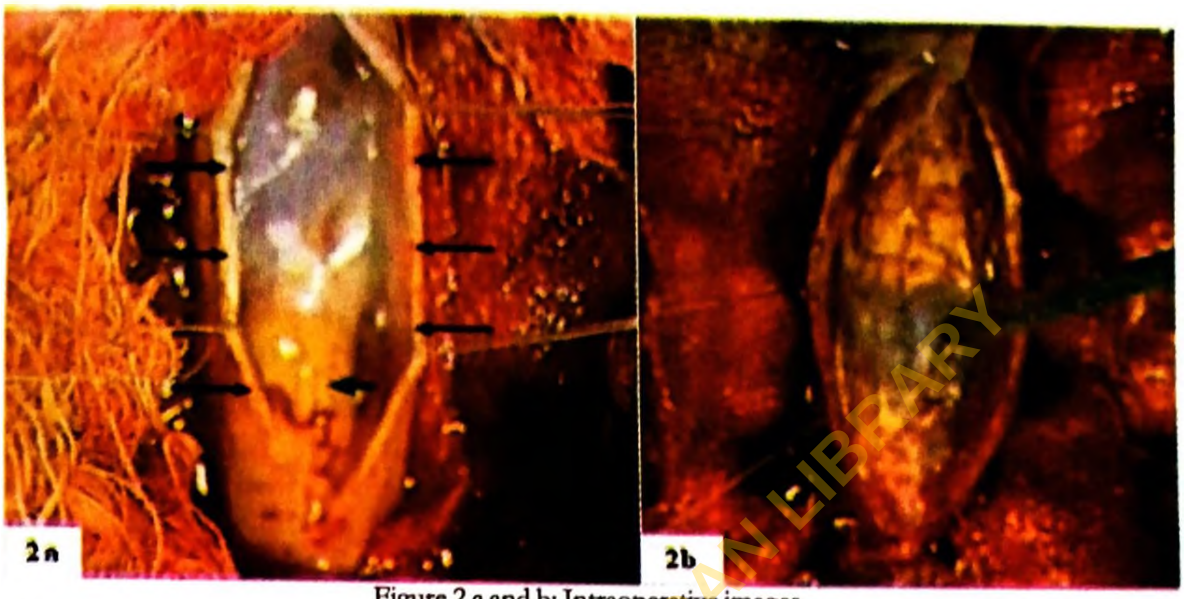

Figure 2 a and b: Intraoperative images

Figure 3a and b: Photomicrographs of the hematoxylin and eosin staining of the cervical lesion showing the histological features of a schwannoma
a: Low power view showing multiple Verocay bodies (black arrows)
b: Verocay body depicting palisading spindle cells with intervening acellular areas (circled)

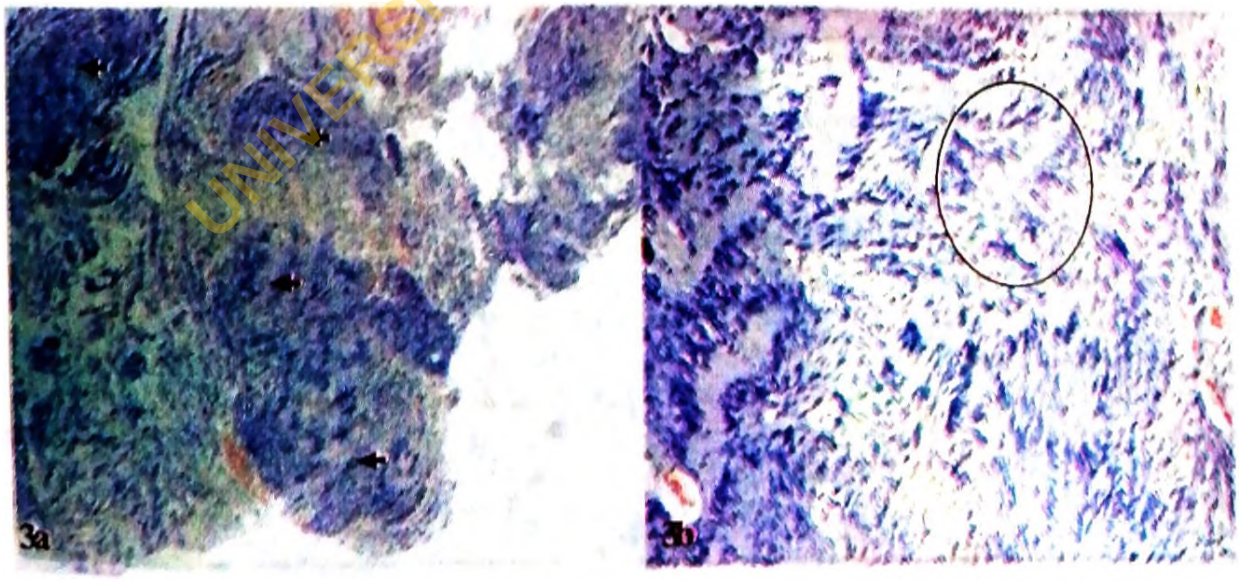

Figure 3a and b: Photomicrographs of the hematoxylin and eosin staining of the cervical lesion showing the pathognomonic histological features of a schwannoma

Figure 4a and b: Photomicrographs of the thoracic lesion
a: Shows focal residual Verocay bodies (black arrows) with extensive degeneration and fibrosis (red arrow) indicative of an 'ancient' schwannoma **b:** Other aspects of the tumour show thick-walled blood vessels (blue arrow) and multiple spindle-shaped cells (yellow arrows)

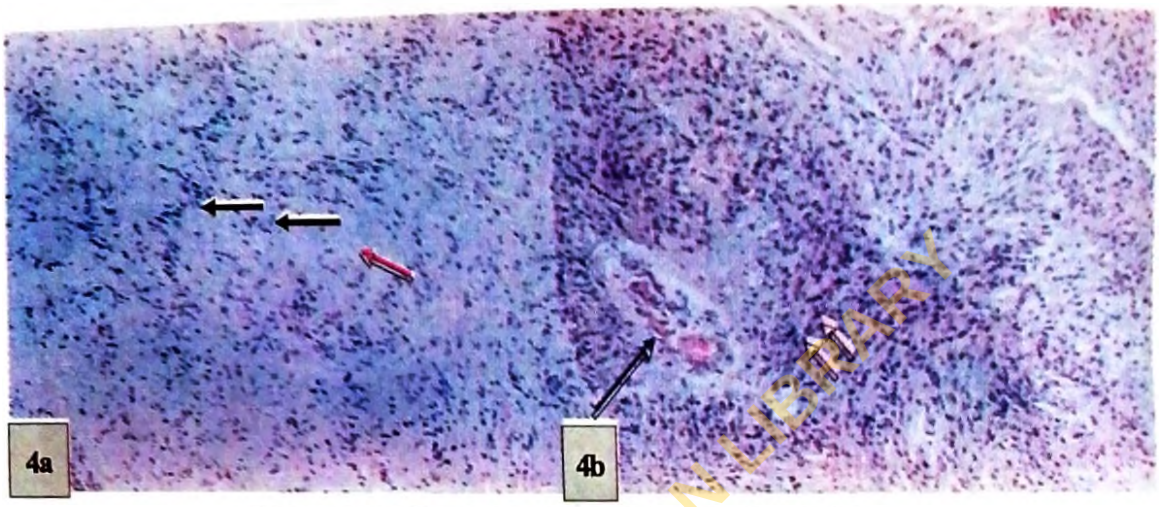

Figure 4a and b: Photomicrographs of the thoracic lesion

Discussion

We have reported a middle-aged Nigerian man with cervical and thoracic spinal schwannomatosis without the classical clinical features of neurofibromatosis. This patient was asymptomatic for the higher lesion which was intradural/extramedullary but symptomatic for the intramedullary thoracic lesion. His brain magnetic resonance imaging revealed no intracranial neoplasm and both tumours were histologically confirmed as schwannomas. This represents the first report of spinal schwannomatosis in the absence of a phakomatosis in Nigerian neurosurgical literature.

Schwannomatosis, also known as congenital neurilemmomatosis, is an autosomal-dominant disease defined by the development of multiple schwannomas of the peripheral nervous system without concurrent involvement of the vestibular nerve. [1,2,4-6] This incredibly rare condition, described by some authors as a third form of neurofibromatosis, differs from neurofibromatosis 1 and 2 (NF1/2) in the remarkable absence of cutaneous lesions and NF 2 in particular due to the absence of bilateral vestibular schwannomas. [5-7] In a retrospective analysis of 87 patients with schwannomatosis by Merker *et al,* 89%, 74%, and 9% of the subjects had peripheral tumours, spinal tumours, and intracranial non-vestibular tumours respectively. [8] Majority of these patients presented between 30 and 60 years, with pain as the most common presenting symptom as seen in the index patient. [8]

While the incidence rate of this condition is largely unknown in the Nigerian population, the annual incidence of schwannomatosis has been reported to be approximately 0.55-0.58 in 1,000,000 individuals, with life expectancy reported to be near-normal and significantly longer than for patients with neurofibromatosis 2. [2,5,6,8] Although schwannomatosis and NF2 are phenotypically similar, they are genetically different and show differences in the anatomic distribution of the lesions, clinico-radiological profile, and treatment outcomes. [3,9] While the presence of bilateral vestibular schwannomas is pathognomonic of NF 2, schwannomatosis is characterised by the presence of multiple non-vestibular extracutaneous schwannomas. Following a study on 14 patients with multiple pathologically defined schwannomas without vestibular localisation, MacCollin *et al* in 1996

developed the first criteria for diagnosis of schwannomatosis.[10] They went further to propose the diagnostic criteria for the clinical diagnosis of schwannomatosis 9 years later, which were modified in 2006 by Baser *et al* to further refine their specificities.[11,12] These criteria affirmed that patients with schwannomatosis must have no vestibular schwannoma, NF 2 mutation or first-degree relative with NF2.[13] In 2013, Plotkin *et al* proposed the consideration of the diagnosis of schwannomatosis in patients who had a unilateral vestibular schwannoma and also in patients with intracranial meningioma.[14]

Schwannomatosis has been classified into three with the following diagnostic criteria:

(A) *Definite schwannomatosis:*

(i) Presence of two or more extracutaneous schwannomas,

(ii) Age < 30 years,

(iii) Absence of vestibular schwannomas and,

(iv) Lack of NF2 mutations.

(B) *Possible schwannomatosis:*

(i) No symptom(s) of eighth nerve dysfunction,

(ii) Age < 45 years,

(iii) Presence of $\geq$ 2 extracutaneous schwannomas and,

(iv) Absence of NF mutation.

C) *Segmental schwannomatosis:* Defined by MacCollin as multiple schwannomas located on one limb or $\leq$ 5 contiguous segments of the spine.[6,8,11,13]

Although, the diagnostic criteria for schwannomatosis proposed by earlier authors excluded patients with vestibular schwannomas, other authors have posited that schwannomatosis patients may still develop unilateral vestibular schwannomas in later years[15,16] Molecular studies of NF2 patients have revealed an autosomal germline mutation in the NF2 gene at 22q12, whereas schwannomatosis has a non-germline genetic linkage to chromosome 22.[6,17] Our patient had "definite Schwannomatosis" because he had two histologically diagnosed spinal schwannomas, was < 30 years of age at the time of diagnosis and did not have any clinico-radiological evidence of a vestibular schwannoma.

However, we were unable to screen for constitutional NF2 mutation, a significant limitation in our low socio-economic region. Surgical resection is the treatment modality of choice for schwannomatosis and is indicated for symptomatic lesions. In the case presented, we opted to excise the cervical tumour first because of its substantial mass effect on the spinal cord and the potential for clinically debilitating/ life-threatening sequelae associated with its high location. The intramedullary location of the tumour could explain the patient's poor neurologic status (paraplegia) pre-operatively and the neurologic deterioration (autonomic dysfunction) post-operatively. Both intradural tumour location and poor pre-operative neurologic grade are established poor prognostic indicators for functional recovery in patients with spinal tumours.[18]

Conclusion

In conclusion, multiple spinal schwannomas could occur even in the absence of underlying genetic mutations associated with a phakomatosis. Therefore, screening of the entire spine with high-resolution MRI is mandatory in individuals diagnosed with schwannoma at any spinal level to rule out asymptomatic lesions elsewhere along the spine or neuraxis.

Conflict of Interest: None declared

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