DOI: 10.7860/JCDR/2024/69601.19254

Case Report

Radiology Section

Multiple Cranial Nerve Involvement in a Complex Case of MISME Syndrome in a Paediatric Patient: A Case Report

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ABSTRACT

Neurofibromatosis 2 (NF2) is characterised by numerous tumours in the central and peripheral nervous systems due to NF2 gene abnormalities that cause the tumour suppressor protein, Merlin, to disappear. Often referred to as Multiple Inherited Schwannomas, Meningiomas, and Ependymomas (MISME), a distinctive characteristic of NF2 is bilateral vestibular schwannomas manifesting in late adolescence with symptoms such as sensorineural hearing loss, tinnitus, and balance issues. Two distinct phenotypes, Wishart and Feiling-Gardner, characterise NF2. This case report discusses the case of a paediatric patient who presented with bilateral hearing loss, giddiness, and blurring of vision and sought a Magnetic Resonance Imaging (MRI) examination which revealed bilateral vestibular schwannomas, non vestibular schwannomas, left sphenoid wing meningiomas, multidirectional spinal schwannomas, spinal nerve sheath tumours, and lesions in the retroperitoneal region. Despite an absent family history, significant involvement of cranial nerves strongly indicates classical NF2. Management focuses on preserving function, and surgery is contemplated for symptomatic lesions and tumours causing cord compression. Gamma Knife radiosurgery and targeted therapies have been investigated.

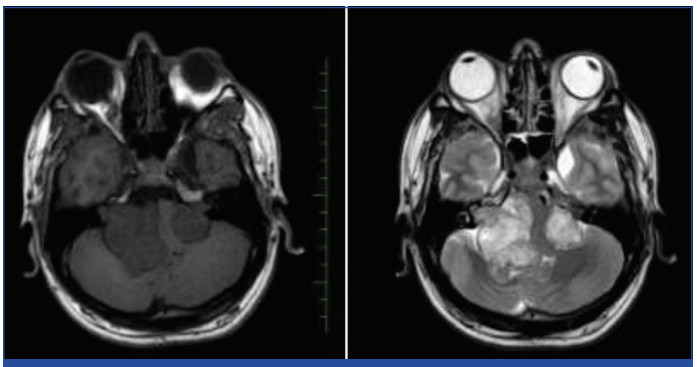
Keywords: Computed tomography, Magnetic resonance imaging, Multiple inherited schwannomas, Meningiomas and ependymomas, Vestibular schwannoma

CASE REPORT

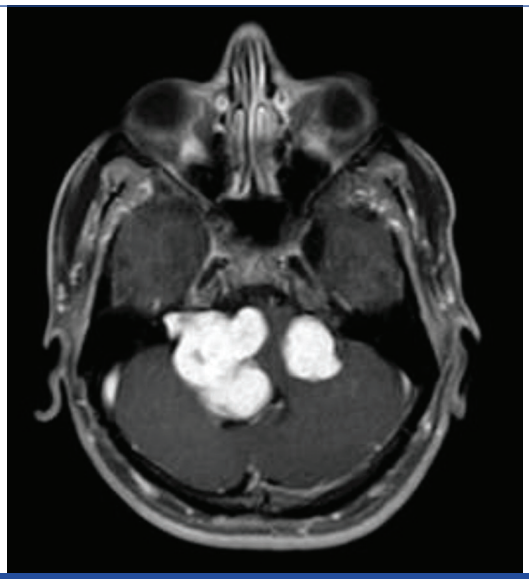
A 15-year-old paediatric male patient presented with bilateral hearing loss and giddiness for four months and blurring of vision in the right eye. The patient had a history of drooping of the left eyelid since childhood. There was no known family history, particularly regarding meningiomas and NF2. Physical examination yielded normal results with no presence of neurocutaneous markers and demonstrated a Glasgow Coma Scale score of 15/15. Audiogram findings revealed sensorineural hearing loss. The patient underwent a comprehensive MRI examination of the brain with the whole spine (plain and contrast study) using a 1.5 Tesla Philips MRI machine.

The imaging of the brain revealed infratentorial heterogeneous bilateral cerebellopontine angle lesions [Table/Fig-1] with intense postcontrast enhancement and multiple non enhancing necrotic areas within, suggestive of vestibular schwannomas [Table/Fig-2]. There was ipsilateral intracanalicular extension and widening of the porus acousticus. Multifocal areas of Susceptibility Weighted Imaging (SWI) hypointensities suggestive of micro-haemorrhages were observed [Table/Fig-3]. MR spectroscopy showed a choline peak [Table/Fig-4]. The lesion was observed compressing the fourth ventricle, causing mild supratentorial hydrocephalus.

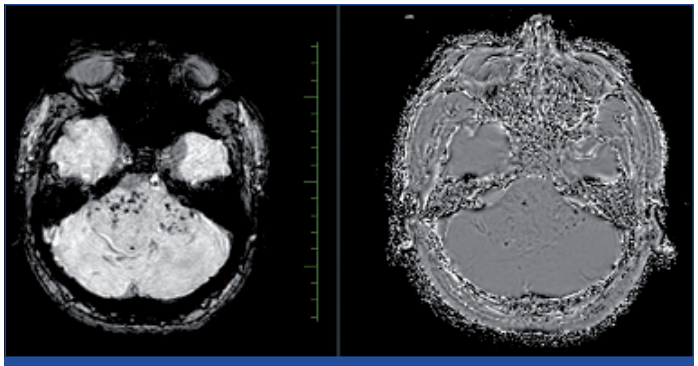
Two supratentorial dural-based lesions suggestive of meningiomas [Table/Fig-5] were observed, each along the posterior and medial aspect of the greater and lesser wings of the left sphenoid bone, and another along the posterior and lateral aspect of the greater wing of the left sphenoid bone, showing intense enhancement, thickening, and enhancement of the adjacent dura, giving a positive dural tail sign [Table/Fig-6]. The terminal segment of the left internal carotid artery, along with its branches, was observed traversing through the lesion. Multifocal areas of SWI hypointensities, which on CT were confirmed to be calcifications, were observed [Table/Fig-7]. The lesion also caused hyperostosis of the adjacent bony framework. There was a marked deviation of the left eye towards the left lateral aspect caused by ipsilateral medial rectus palsy due to the mass effect of the aforementioned sphenoid meningioma [Table/Fig-8].



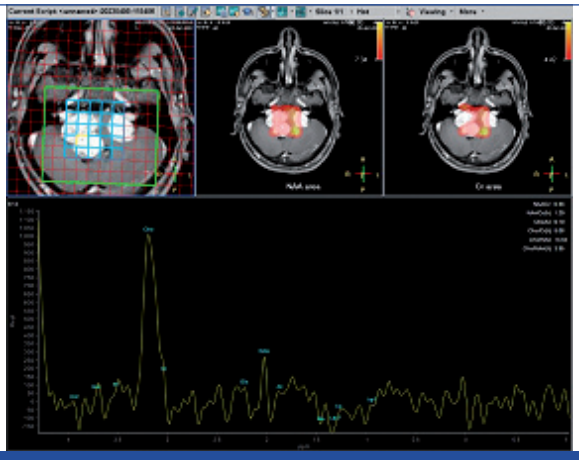
[Table/Fig-1]: MRI Brain axial T1WI and T2WI showing infratentorial, extra-axial fairly defined multilobulated bilateral cerebellopontine angle heterogenous lesions which on T1 appears hypointense and T2 hyperintense.



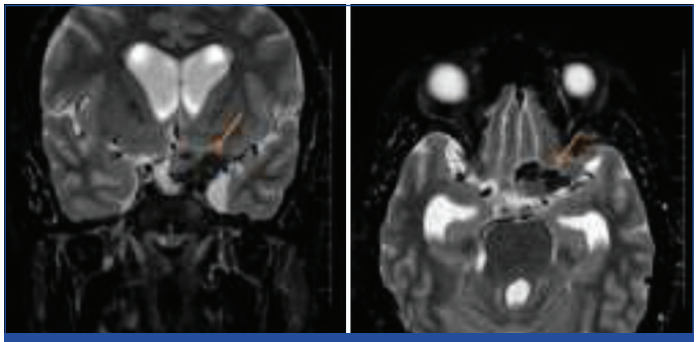
[Table/Fig-2]: MRI Brain Axial T1 postcontrast sequence showing infratentorial, extra-axial multilobulated bilateral cerebellopontine angle lesions with intense heterogenous enhancement and multiple non enhancing areas within (likely necrotic areas).



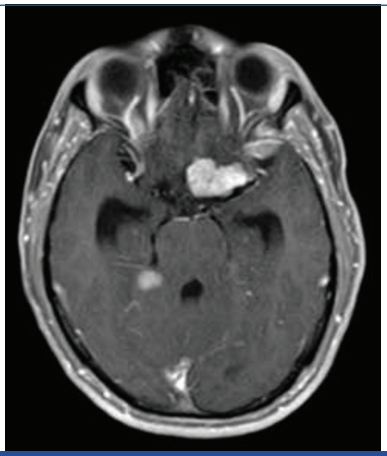
[Table/Fig-3]: MRI Brain axial SWI showing multiple specks of hypointensities with corresponding phase low signal intensity-suggestive of micro-haemorrhages.



[Table/Fig-4]: MR Spectroscopy of right cerebellopontine angle lesion showing choline peak.

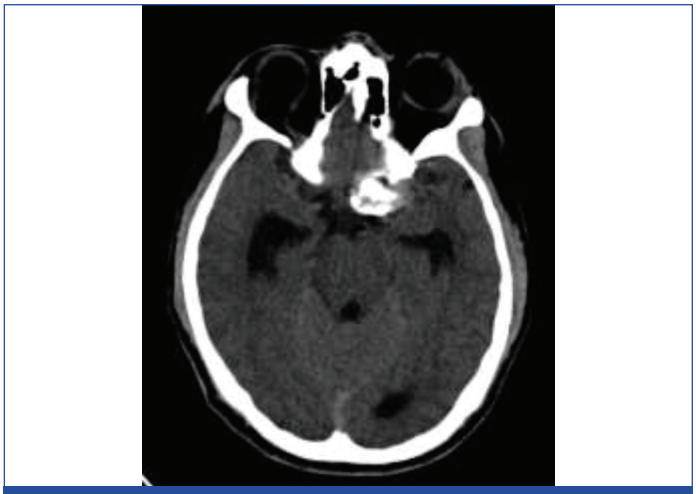


[Table/Fig-5]: MRI Brain coronal and axial T2WI showing heterointense lesion along posteromedial aspect of greater and lesser wing of left sphenoid bone (orange arrows) extending into suprasellar cistern causing cortical buckling of adjacent left temporal lobe, uncus and left basifrontal lobe.

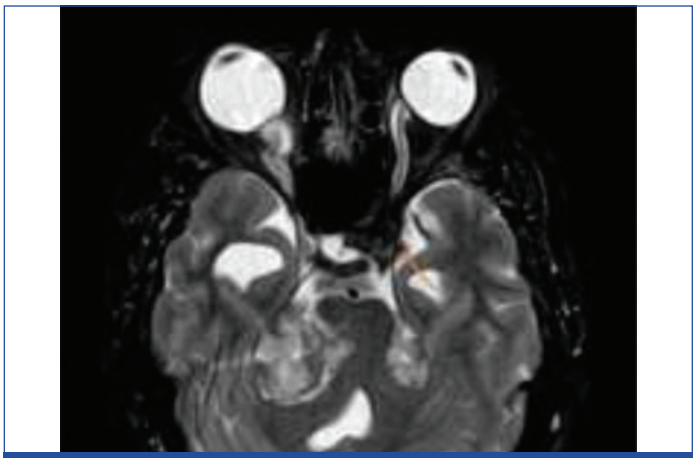


[Table/Fig-6]: MRI Brain axial T1 postcontrast sequence showing intensely enhancing lesion along the posterior and medial aspect of the greater and lesser wing of left sphenoid bone suggestive of meningioma.

Tiny, fairly defined, lobulated, heterogeneous lesions involving the cisternal segment of the right oculomotor nerve and bilateral trigeminal nerves, showing intense enhancement postcontrast,



[Table/Fig-7]: CT Brain axial showing an hyperdense and near completely calcified lesion along the posterior and medial aspect of the greater and lesser wing of left sphenoid bone.



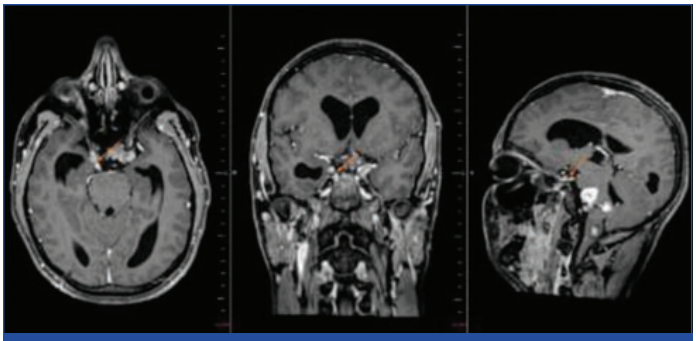
[Table/Fig-8]: MRI Brain axial T2WI showing heterointense lesion along posteromedial aspect of greater and lesser wing of left sphenoid bone (orange arrow) causing deviation of left eye towards the left due to ipsilateral medial rectus palsy by the aforementioned sphenoid meningioma.

implying non vestibular schwannomas, were also observed [Table/Fig-9,10]. Severe tortuosity of the bilateral optic nerves, suggestive of intracranial hypertension, was noted.

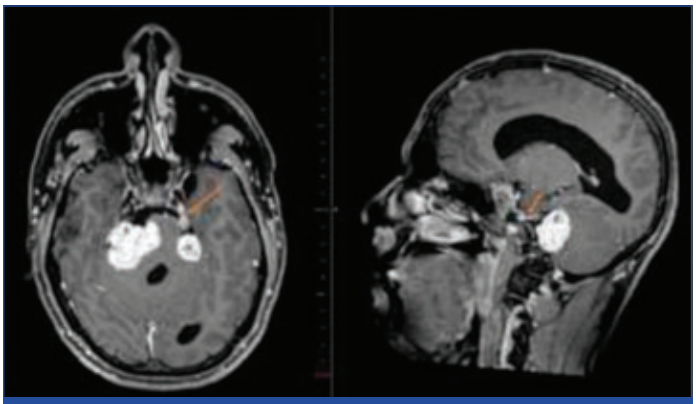
Imaging of the spine revealed an intensely enhancing intramedullary lesion in the cervicomedullary junction at the level of the C1 vertebra, suggestive of ependymoma, causing perilesional oedema and mild expansion of the spinal cord [Table/Fig-11,12]. Another well-defined, intensely enhancing, intradural extramedullary lesion was observed within the anterior and left lateral aspect of the spinal canal [Table/Fig-13], extending through multiple neural foramina as a multilobulated, multidirectional "dumbbell" shaped mass into the extraspinal space, representing a spinal schwannoma [Table/Fig-14]. On CT, the lesions were causing negative bone remodeling in the form of erosions [Table/Fig-15]. Mass effect of the lesions was noted in the form of compression of the bilateral D11-L2 traversing nerve roots and encasement of the left D12-L1 exiting nerve roots, extending into the left psoas major and abutting the inter and lower pole medial cortices of the left kidney [Table/Fig-16].

Multiple fairly defined, similar but smaller enhancing lesions, likely spinal nerve sheath tumours, were also observed along the proximal aspect of the right D11-L2 spinal nerves [Table/Fig-17], and a few homogeneously enhancing, lobulated lesions were seen involving the retroperitoneal region (para-aortic region) [Table/Fig-18].

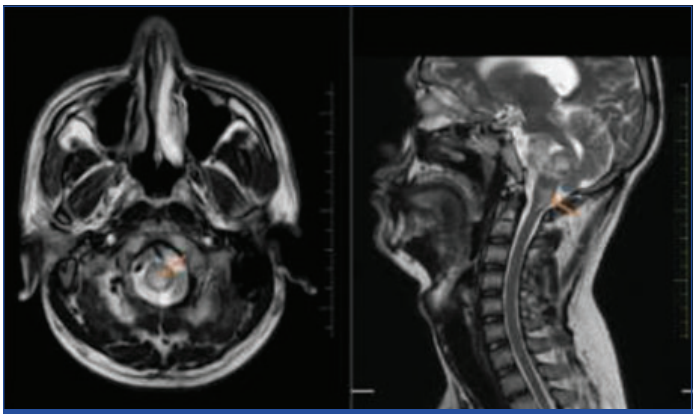
The clinical diagnosis in this case was NF2, evident from the presentation of multiple tumours involving the central and peripheral nervous systems. The patient's symptoms of bilateral hearing loss, giddiness, blurring of vision, and left eyelid drooping further support the diagnosis of NF2. Differential diagnosis considered include other



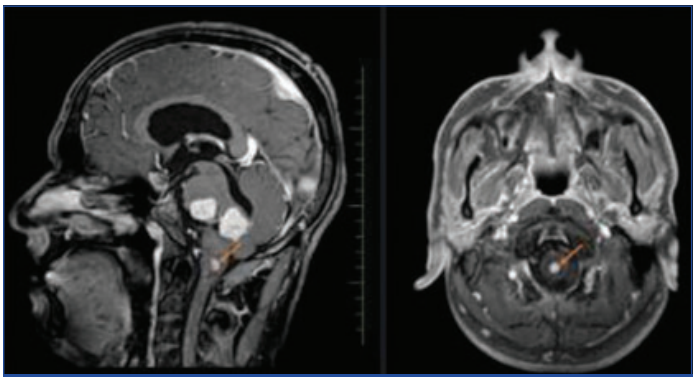
[Table/Fig-9]: MRI Brain axial, coronal and sagittal T1 postcontrast sequence showing intensely enhancing lobulated lesion in the cisternal segment of right oculomotor nerve (orange arrow).



[Table/Fig-10]: MRI Brain axial and sagittal T1 postcontrast sequence showing intensely enhancing lobulated lesion in the cisternal segment of left trigeminal nerve (orange arrow).

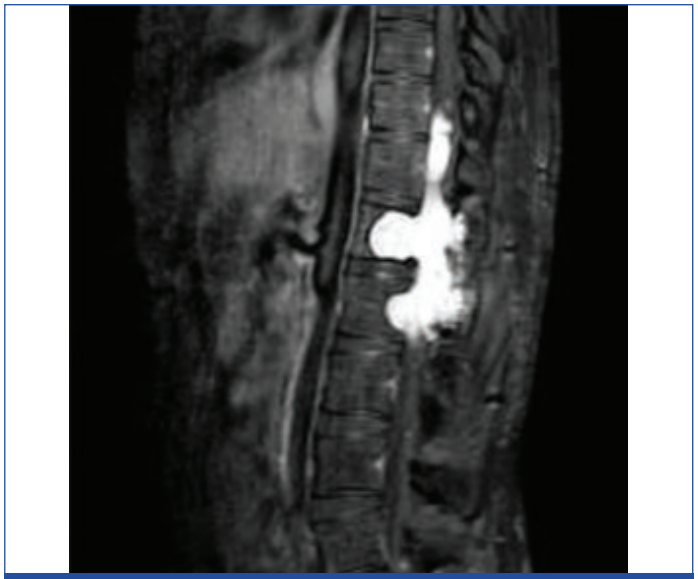


[Table/Fig-11]: MRI Brain axial and sagittal T2WI showing an hyperintense lesion in the cervico-medullary junction at the level of C1 vertebra (orange arrow) causing mild expansion of the spinal cord.

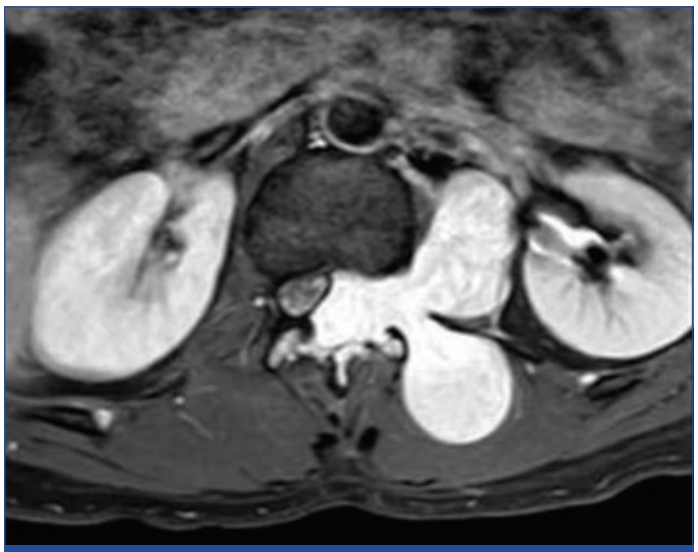


[Table/Fig-12]: MRI Brain sagittal and axial T1 postcontrast sequence showing an intensely enhancing lesion in the cervico-medullary junction at the level of C1 vertebra (orange arrow) suggestive of ependymoma.

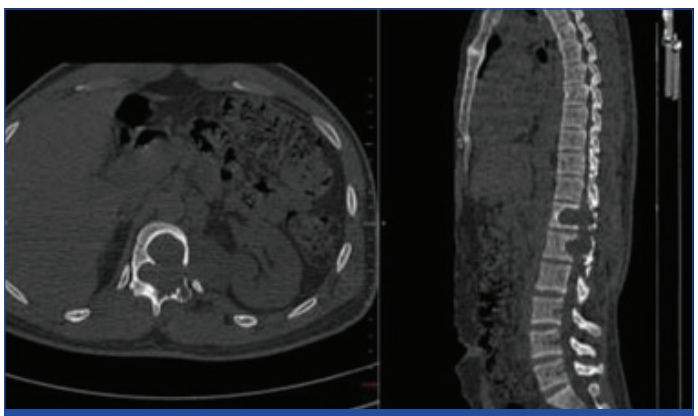
conditions presenting with similar symptoms or imaging findings, such as NF1, schwannomatosis, and multiple meningiomas syndrome. However, the comprehensive clinical presentation, along with imaging findings consistent with NF2, strongly supports the diagnosis of this condition in this paediatric patient.



[Table/Fig-13]: MRI dorsolumbar spine sagittal T1 postcontrast sequence showing an intensely enhancing multilobulated intradural extramedullary lesion within the anterior aspect of spinal canal at the level of inferior endplate of D10 to superior endplate of L2 vertebra.



[Table/Fig-14]: MRI dorsolumbar spine axial T1 postcontrast sequence showing an intensely enhancing lobulated intradural extramedullary lesion extending through multiple neural foramina as a multidirectional "dumbbell" shaped mass into extraspinal space.

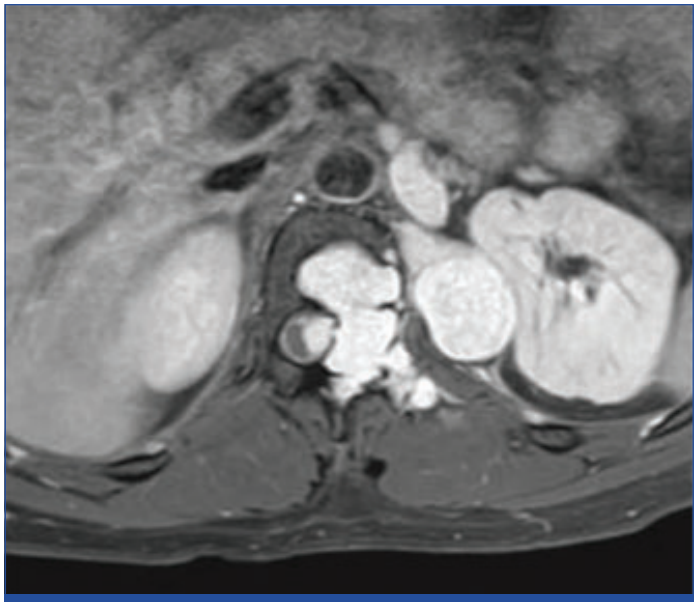


[Table/Fig-15]: CT dorsolumbar spine axial and sagittal images showing negative bone remodeling in the form of erosive changes of the involved vertebrae.

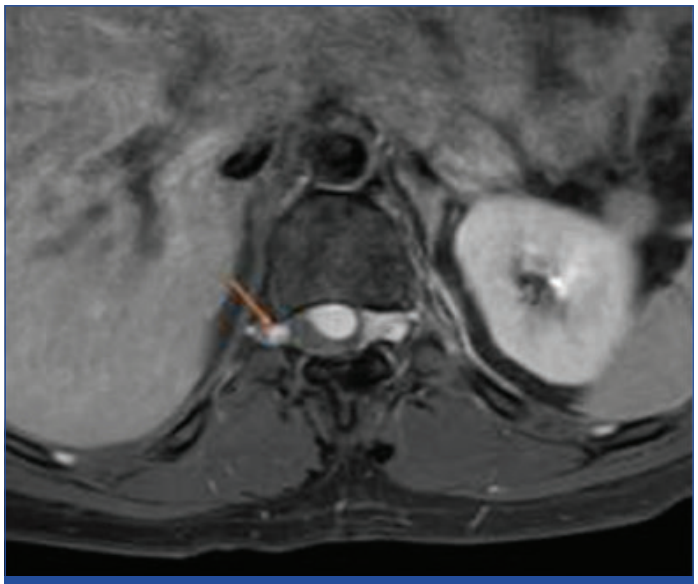
The patient was directed to an advanced medical facility for additional care, and subsequent attempts to contact the patient were unsuccessful.

DISCUSSION

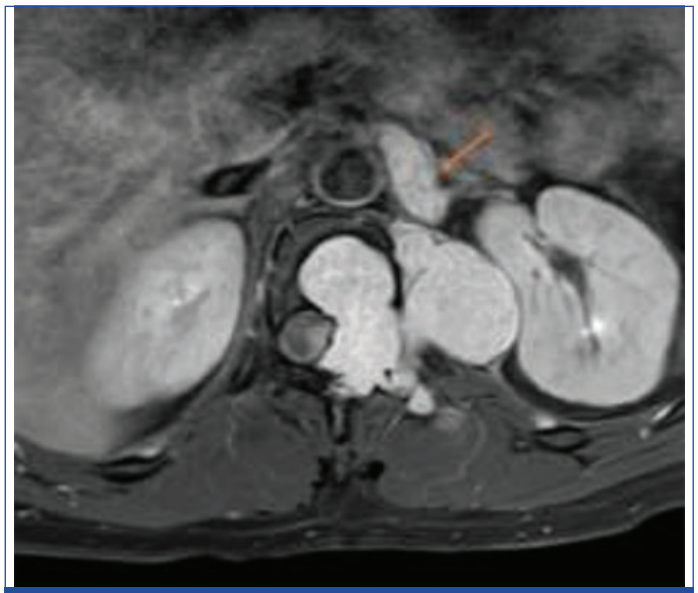
NF2 is a rare autosomal dominant condition distinguished by the formation of multiple tumours in both the central and peripheral



[Table/Fig-16]: MRI dorsolumbar spine axial T1 postcontrast sequence showing an intensely enhancing multilobulated intradural extramedullary lesion causing mass effect and extending into the left psoas major and abutting the inter and lower pole medial cortices of left kidney.



[Table/Fig-17]: MRI dorsolumbar spine axial T1 postcontrast sequence showing a similar but smaller enhancing lesion seen along the proximal aspect of right spinal nerve (orange arrow).



[Table/Fig-18]: MRI dorsolumbar spine axial T1 postcontrast sequence showing fairly defined homogenously enhancing lobulated lesion involving the retroperitoneal region (para-aortic region) at the level of D12 vertebra (orange arrow).

nervous systems [1]. It is considered a misnomer due to the lack of presentation of neurofibromas in this disorder. NF2 is closely associated with mutations in the NF2 gene on chromosome 22q12, which lead to the disappearance of the tumour suppressor protein known as Merlin [2]. Merlin plays a critical role in maintaining the structural integrity of cells by connecting the cytoskeleton to the plasma membrane [3].

The spectrum of tumours associated with NF2 includes schwannomas, meningiomas, and ependymomas, making NF2 alternatively referred to as MISME. NF2 is commonly diagnosed during the second and third decades of life [4]. Individuals who have a family history of NF2 need to be screened as early as age 10 or 12. The Manchester Criteria have been widely regarded for the diagnosis of NF2, encompassing several key indicators. These include the presence of bilateral vestibular schwannomas, other tumours associated with NF2 such as meningiomas and schwannomas outside the vestibular nerves, onset of tumours before a certain age, and consideration of molecular testing for NF2 mutations [5-7].

The Feiling-Gardner and Wishart phenotypes are two different NF2 presentations. When numerous tumours occur in the brain and spine of patients under 20 years, it is indicative of a more aggressive Wishart phenotype. Patients older than 20 years old who have the Feiling phenotype experience less aggressive tumour growth [8].

NF2 usually presents itself during late adolescence/early adulthood and is mainly attributed to schwannomas, with symptoms presenting in the form of sensorineural hearing loss, tinnitus, and lack of balance. Schwannomas are benign tumours that originate from peripheral nerve sheaths and are the most common type of spinal tumour in NF2 [9]. A characteristic hallmark of NF2 is the occurrence of bilateral vestibular schwannomas, and it's worth noting that approximately 10% of individuals diagnosed with this type of tumour also have NF2 [10]. Jugular foramen schwannomas and hypoglossal schwannomas are the next most common cranial nerve schwannomas, with trigeminal schwannoma coming in second behind vestibular nerve tumours [11]. Pure motor nerves are less commonly affected by schwannomas than sensory or mixed sensory and motor nerves. Schwannomas most commonly occur in the cervicothoracic area, where they begin at the dorsal root. Numerous small schwannomas, often called tumourlets, are commonly seen throughout the cauda equina in many patients [12].

Meningiomas represent the second most common tumours in NF2, identified in over 50% of NF2 patients, with adult NF2 patients typically having an average of three meningiomas, predominantly occurring in the supratentorial region along the falx cerebri; however, they can also occur anywhere throughout the central nervous system. In the spinal cord, meningiomas are primarily observed in the thoracic region [13].

Ependymomas are low-grade tumours that are typically located in the cervical part of the spinal cord or the intramedullary region of the conus medullaris. Roughly, 90% of NF2 patients have ocular abnormalities, with posterior subcapsular lenticular cataracts being the most frequent ocular symptom [14].

Very few cases of MISME syndrome have been chronicled. One such case report described a unique case of MISME syndrome in a patient with NF2, showcasing multiple tumours involving different regions of the nervous system. The report underscored the challenges of managing extensive tumour burden in NF2 patients and highlighted the significance of early diagnosis and multidisciplinary management in improving patient outcomes [15].

A study focusing on the outcomes of Gamma Knife Stereotactic radiosurgery (GKS) in treating NF2-associated meningiomas highlighted favourable tumour control rates and minimal adverse effects of GKS, suggesting it as an effective treatment option for NF2-associated meningiomas [16].

Another case report discussed a rare constellation of findings in a patient with NF2, presenting with extensive cranial nerve involvement leading to various neurological symptoms. This case emphasised the importance of comprehensive neurological evaluation and individualised treatment planning in managing NF2 patients with cranial nerve tumours [12]. In this case report, all the features of this syndrome extensively involving the brain and spinal cord can be seen in the same patient.

CONCLUSION(S)

This case highlights the comprehensive manifestation of NF2 in a paediatric patient, characterised by bilateral sensorineural hearing loss, cranial nerve involvement, and multiple tumours throughout the central and peripheral nervous systems. Even if there isn't any pertinent family history, the case's several observations-particularly the widespread involvement of the cranial nerves-strongly imply a classical presentation of NF2. Neurological examination and central nervous system imaging are the main diagnostic tools. Because individuals with NF2 have a lifetime tendency to grow new tumours or experience the recurrence of existing ones, it is vital to stress that the condition is incurable and that the primary goal of care is to preserve function. Symptomatic lesions are usually removed as part of treatment plans, and further lesions are routinely checked for. When there are indicators of spinal cord compression, surgical intervention for spinal tumours is typically explored. The key inference drawn from this case underscores the importance of recognising NF2's varied clinical presentation, emphasising the need for early diagnosis and intervention to preserve function and improve patient outcomes.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Jan 15, 2024
- Manual Googling: Feb 19, 2024
- iThenticate Software: Feb 21, 2024 (6%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jan 15, 2024**
Date of Peer Review: **Feb 17, 2024**
Date of Acceptance: **Feb 23, 2024**
Date of Publishing: **Apr 01, 2024**