An Interesting Case of MISME Syndrome

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Abstract

Multiple inherited schwannomas, meningiomas, and ependymomas (MISME) syndrome or neurofibromatosis type 2 is an autosomal dominant condition characterized by multiple schwannomas, meningiomas, and ependymomas. Bilateral vestibular schwannomas are the hallmark of this condition, which is seen in the majority of patients. Presence of multiple cranial and spinal tumors of different types should alert the radiologist to this possibility so that a timely diagnosis can be made.

Keywords
- meningioma
- schwannoma
- ependymoma
- neurofibromatosis
- MRI

Introduction

Multiple inherited schwannomas, meningiomas, and ependymomas (MISME) syndrome is in fact another name for neurofibromatosis type 2 (NF2), which is considered by some as a misnomer because neurofibromas are uncommon in this condition.[1] This is an autosomal dominant condition with a pathogenic mutation in the *NF2* gene but some cases are also sporadic.[2] It is a less common condition occurring in approximately 1 in 50,000 individuals as compared with neurofibromatosis type 1 (NF1), which is seen in 1 of 3,000 to 5,000 individuals. The latter is caused by a mutation in the *NF1* gene. NF1 is characterized by cutaneous neurofibromas, plexiform neurofibromas, optic gliomas, Lisch nodules, and café-au-lait macules.[3] Here, we report an interesting case of MISME syndrome where the entire spectrum of findings was noted radiologically.

Case Report

An 18-year-old young man presented to the neurosurgery outpatient department of our hospital with complaints of seizures for the past 1 year, hearing loss in both ears, tinnitus, dizziness for 2 months, and paraparesis for previous 15 days. He had a few scattered skin nodules since birth. He had been treated in the village by some local doctor and carried no treatment records. There was no similar family history. After the onset of paraparesis, he was brought to our hospital and advised a magnetic resonance imaging (MRI) of the dorsolumbar spine and brain.

Contrast-enhanced MRI of dorsolumbar spine revealed multiple small enhancing intradural mass lesions along the nerve roots of cauda equina and in the neural foramina, likely schwannomas. There were multiple other intradural extramedullary enhancing mass lesions in the spinal canal which were compressing the adjacent spinal cord, likely schwannomas and meningiomas (►**Fig. 1**). The largest of these mass lesions was seen at D10 and D11 levels which were causing cord compression with edema, suggestive of compressive myelopathy. There were additional multiple small mass lesions in the cervical and dorsal spinal cord as well as cervicomedullary junction, which were hyperintense in T2W images and enhanced with contrast (►**Fig. 2**). These could be ependymomas or astrocytomas. The brain MR study revealed heterogeneously enhancing bilateral vestibular (acoustic) schwannomas, trigeminal schwannomas as well as left frontal, right parafalcine and suprasellar meningiomas (►**Fig. 3** and ►**Fig. 4**). With these findings, we diagnosed the patient with MISME syndrome/NF2.

Discussion

MISME syndrome or NF2 occurs due to mutation of the *NF2* gene on chromosome 22q12. A protein called Merlin which plays a role in growth inhibition and tumor suppression is encoded by this gene. Hence, this mutation results in the development of multiple benign neoplasms such as schwannomas, meningiomas, and ependymomas.[4]

Bilateral vestibular or acoustic schwannomas (VS) are considered the hallmark of NF2. These occur in up to 95% of the patients. Schwannomas occur in other cranial, spinal, and peripheral nerves, especially third and fifth cranial nerves. Cranial and spinal meningiomas are noted in approximately 50 to 60% patients. Patients can also develop low grade

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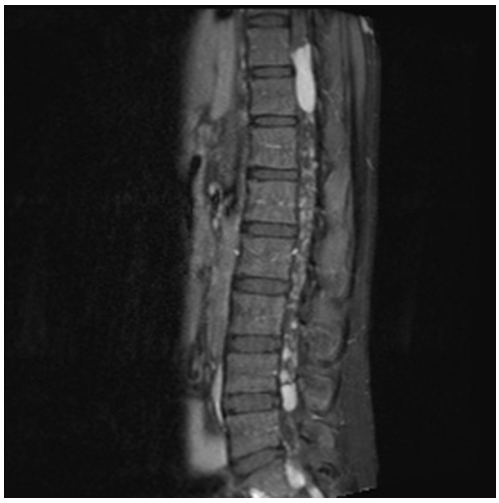

Fig. 1 Sagittal contrast-enhanced magnetic resonance image of dorsolumbar spine showing multiple small enhancing intradural mass lesions along the nerve roots of cauda equina and a larger homogeneously enhancing intradural extramedullary mass at D10 and D11 levels.

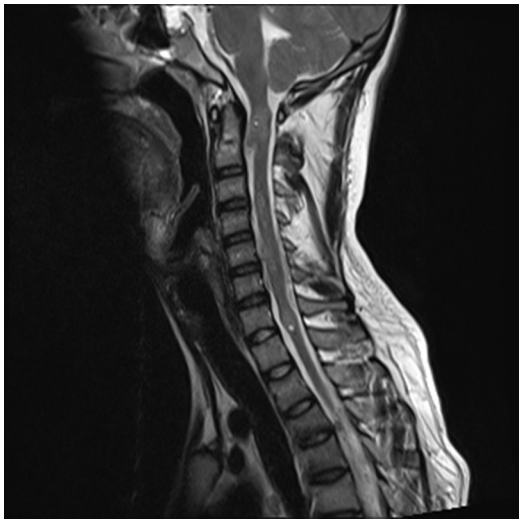

Fig. 2 Sagittal T2-weighted magnetic resonance image of cervical spine showing multiple hyperintense intramedullary mass lesions.

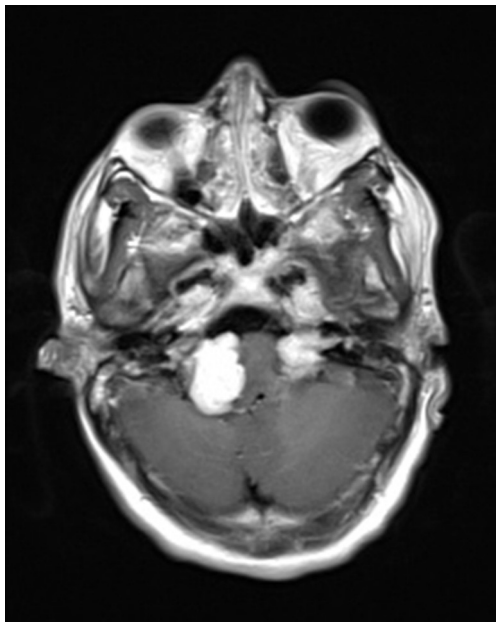

Fig. 3 Axial contrast-enhanced magnetic resonance image of brain showing bilateral vestibular and trigeminal schwannomas.

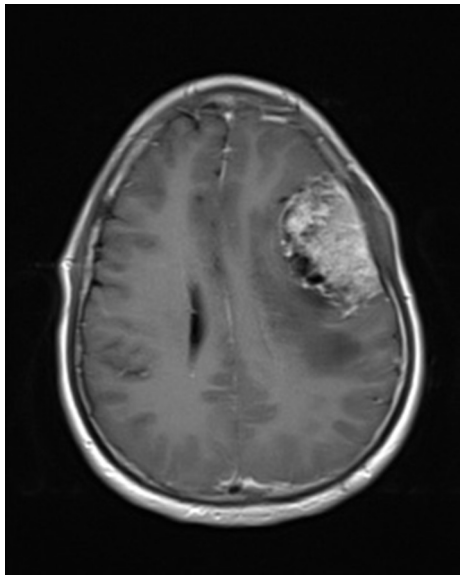

Fig. 4 Axial contrast-enhanced magnetic resonance image showing a left frontal meningioma with interspersed small cystic areas.

malignant lesions such as ependymomas which are seen in approximately 90% patients as well as gliomas. It is possible that the initial presentation may not be due to the VS and may be due to other cranial or spinal tumors.[3,5]

The Manchester criteria with subsequent revision is used to establish the diagnosis of NF2 (►**Table 1**).[6,7] Our patient had bilateral VS, other cranial nonvestibular schwannomas and meningiomas along with a large number of spinal intradural extramedullary and intramedullary tumors. These findings were consistent with the diagnosis.

In a large series by Patronas et al, 63% patients of NF2 had spinal tumors. 53% of these had multiple enhancing intramedullary tumors which had a central location in the cord and measured 4 to 44 mm in diameter. These were located mostly in the cervical cord (56%), followed by the thoracic cord (36%) and cervicomedullary junction (7%). Histology revealed that most of these were ependymomas and astrocytomas. A total of 55% of the patients had intradural extramedullary tumors and in 44% of these, there was evidence of cord compression. Most of these tumors were schwannomas followed by meningiomas and even few neurofibromas. Due to the cord compression, patients underwent surgery more often for intradural extramedullary tumors rather than intramedullary tumors.[8] Patients with spinal tumors present with NF2 symptoms at a younger age.[9]

Table 1 The Manchester criteria for the diagnosis of NF2. The diagnosis can be made if any one of the following are present

1	Bilateral vestibular schwannomas before 70 y of age.
2	Unilateral vestibular schwannoma before 70 y of age AND first degree relative with NF2.
3	Any two of following: meningioma, nonvestibular schwannoma, neurofibroma, glioma, cerebral calcification, cataract AND First degree relative with NF2 OR unilateral vestibular schwannoma and negative LZTR1 testing (if two or more nonintradermal schwannomas).
4	Multiple meningiomas AND Unilateral vestibular schwannoma OR any two of these: nonvestibular schwannoma, neurofibroma, glioma, cerebral calcification, cataract.
5	Identification of NF2 gene mutation from blood or an identical mutation from two different tumors in the same person.

Abbreviations: LZTR1, leucine-zipper-like transcription regulator 1; NF2, neurofibromatosis type 2.

Conclusion

This case showed the entire spectrum of radiological findings in MISME syndrome/NF2. NF2 is considered by some as a misnomer due to the paucity of neurofibromas. It is important for radiologists to be aware of this spectrum as often patients present with paraparesis. The finding of multiple different types of spinal tumors should alert the radiologist to this possibility and scanning of the brain should be the next step to reach the diagnosis.

Source of Support
None.

Conflicts of Interest
None declared.

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