Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/mjafi

Images in Medicine

A case of neurofibromatosis type 2 (NF2) with classic imaging and skin findings

Lt Col Saikat Bhattacharjee [a], *Lt Col Preema Sinha* [b,*], *Surg Cmde Arti Sarin* [c], *Col B.K. Prasad* [d]

[a] *Classified Specialist (Radiodiagnosis), Military Hospital Kirkee, Pune 411020, India*
[b] *Assistant Professor, Department of Dermatology, Armed Forces Medical College, Pune 411040, India*
[c] *Consultant (Radiodiagnosis), Command Hospital (Southern Command), Pune 411040, India*
[d] *Classified Specialist (ENT), Command Hospital (Central Command), Lucknow, India*

ARTICLE INFO

Article history:
Received 18 October 2016
Accepted 24 July 2017
Available online 5 October 2017

Keywords:
Neurofibromatosis type 2
Vestibular schwannomas
Meningiomas
Ependymomas
Café au lait macules

ABSTRACT

Neurofibromatosis is a neurocutaneous, tumor predisposing, inheritable disorder characterized by tumors of the brain and spine and the presence of skin lesions. The most important tumors associated with neurofibromatosis are vestibular nerve schwannomas, with others being meningiomas and ependymomas. The cord is also affected by tumors, ependymoma being the commonest, besides meningiomas and schwannomas. We present a case with café au lait macules, neurofibromas in the skin, bilateral VIII cranial nerve schwannomas, multiple meningiomas in the brain and spine, ependymomas in the brain and spine, and schwannomas in the cauda equina nerve roots.

Introduction

Neurofibromatosis is a hereditary neurocutaneous disorder characterized by skin abnormalities and disposition to multiple neurological tumors that affect the brain and the spinal cord. Schwannomas of the cranial nerves, meningiomas and ependymomas are the most common tumors associated with the disease. The hallmark dermatological abnormalities associated with the condition are café au lait macules and neurofibromas of the skin.

Clinical and imaging findings

A 23-year-old male patient presented with progressive hearing loss in the right ear that was noticed since 10 days. There was no history of otalgia, otorrhea, or trauma to the ears. There was no contributory past or family history. There was no history of seizures or any other sensory or motor symptoms in the individual.

General examination revealed a café-au-lait macule on the skin of the anterior abdominal wall (Fig. 1a). Also noted were

* *Corresponding author.*
E-mail address: sinhapreema@gmail.com (P. Sinha).
http://dx.doi.org/10.1016/j.mjafi.2017.07.007

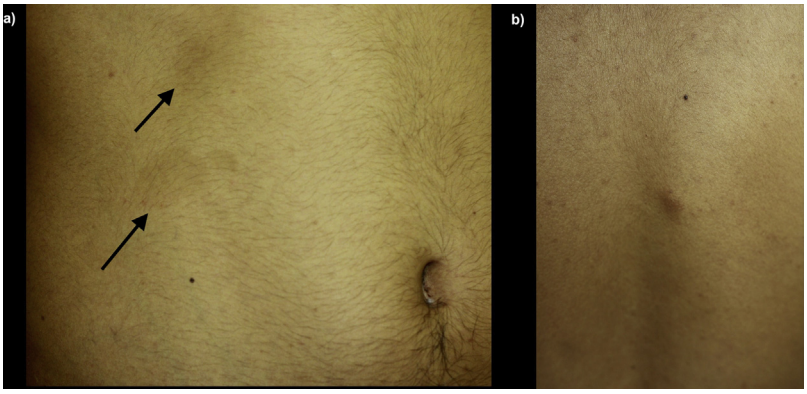

Fig. 1 – (a) Café au lait macule (black arrows) on the right side of the trunk. (b) Neurofibromas on the back.

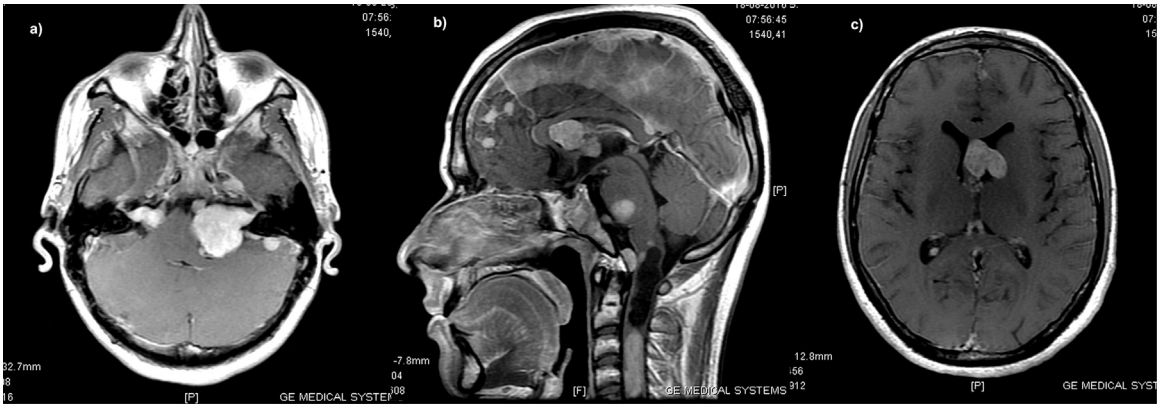

Fig. 2 – (a) Axial contrast-enhanced T1WI MRI showing bilateral VIII nerve schwannomas with ''ice cream cone'' appearance. (b) Sagittal contrast-enhanced T1WI MRI showing multiple enhancing meningiomas arising from the falx cerebri. (c) Axial contrast-enhanced T1WI MRI showing ependymoma in the left lateral ventricle.

multiple, soft, nodular cutaneous swellings involving the trunk and the limbs (Fig. 1b). Local ear examination revealed normal external auditory canals and tympanic membranes bilaterally. Audiometric testing proved right-sided sensorineural hearing loss. An magnetic resonance imaging (MRI) of the brain revealed bilateral lesions arising from the vestibulocochlear nerves of either side extending out of the porus acousticus and into the cerebellopontine angle of the respective side depicting a typical 'ice-cream' cone appearance of vestibular schwannoma (Fig. 2a).

Multiple, avidly enhancing, extra-axial nodular lesions were seen arising from the falx cerebri, the tentorium cerebelli, and the meninges overlying the convexities; these lesions were likely to be meningiomas (Fig. 2b). An optic nerve meningioma was also present on the right. There was nodular thickening of the falx and the tentorium cerebelli at places. An avidly enhancing, extra-axial nodular lesion was seen with a broad base toward the septum pellucidum and projecting into the frontal horn of the left lateral ventricle; this was likely to be an ependymoma (Fig. 2c).

In the contrast-enhanced MRI of the spine, intramedullary tumors with variegated signal intensity were noted at multiple places along the spinal cord with hydromyelia involving almost the entire cord (Fig. 3a–c). Multiple enhancing meningeal tumorlets were also observed.

Multiple neurofibromas were seen extending through the neural foramina of the spine. The cauda equina nerve roots showed enhancing nodular lesions suggestive of schwannomas (Fig. 3d).

Histopathology of one of the nodular lesions on the trunk revealed it to be a neurofibroma.

He was diagnosed as a case of neurofibromatosis type 2 (NF2) and referred for neurosurgeon's opinion. Surgery to address the vestibular schwannomas and the cervical ependymoma was offered to the patient.

Discussion

Neurofibromatosis type 2 (NF2) is a neurocutaneous disease that predisposes to multiple tumors of the central and peripheral nervous systems.[1] It is rare, with an incidence of 1 in 60,000. NF2 is associated with deletion of the NF2 gene/Merlin/Schwanomin gene, located on the long (q) arm of chromosome 22, at band 12.2 (22q12.2).[2] The Schwanomin gene encodes for the cytoskeletal protein neurofibromin 2, which is similar to some members of the ERM (ezrin, radixin, and moesin) family of proteins, known for their role in linking cytoskeletal components with cell membrane proteins. Neurofibromin 2 regulates ion transport, modulates cytoskeletal

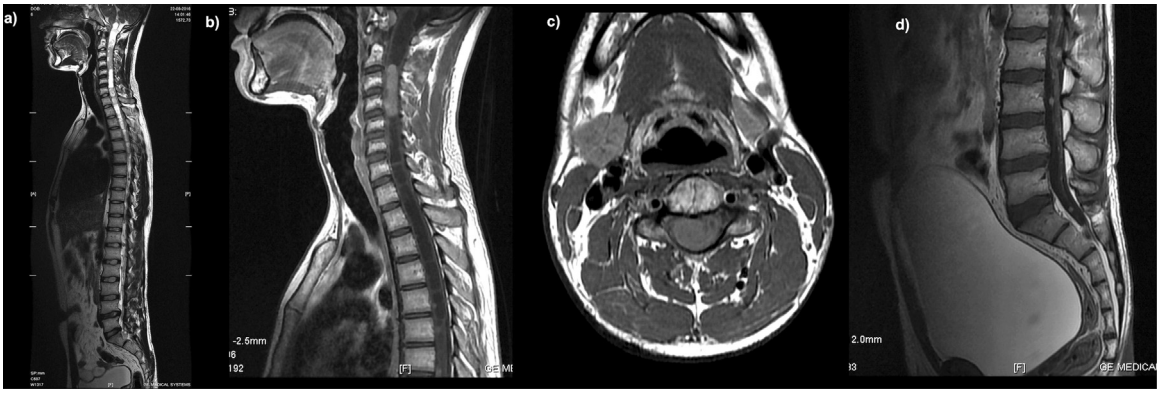

Fig. 3 – (a) Sagittal T2WI of the spine showing hydromyelia, as well as multiple intramedullary and multiple intradural-extramedullary tumors. (b) Sagittal contrast-enhanced T1W1. (c) Axial contrast-enhanced T1WI showing intramedullary cervical cord ependymoma. (d) Sagittal contrast-enhanced T1WI showing enhancing schwannomas arising from the cauda equina nerve roots.

dynamics, and interacts with proteins on the cell surface. Schwann cells, meningeal cells, nerve cells, and cells of the lens express this gene fundamentally.

Neurofibromin helps in growth suppression of these cells by various intercellular signaling pathways. Uncontrolled multiplication of cells ensues when Merlin is deleted through mutation. The deletion is inherited in 50% of the cases, with the other half resulting due to de novo mutations.

First proposed in 1988, the diagnostic criteria for NF2 require either the presence of bilateral vestibular schwannomas or a family history with unilateral vestibular schwannoma and any one of the following: meningioma, glioma, neurofibroma, schwannoma, or posterior subcapsular opacities.

These criteria have undergone several revisions and modifications and alternative diagnostic criteria such as the Manchester criteria or the National Neurofibromatosis foundation criteria have been proposed.[3]

The most distinctive feature of the disease is bilateral schwannomas of the superior vestibular branch of the eighth cranial nerves. Besides these, the disease is characterized by the presence of schwannomas of the other cranial nerves, meningiomas, and tumors of the spinal canal.[1,4] Also referred to as MISME, the acronym stands for Multiple Intracranial Schwannomas, Meningiomas, and Ependymomas.

Although the clinical presentation varies, a large proportion of patients present due to the involvement of the CN VIII by schwannomas.[4] Progressive hearing loss is the most commonly reported symptom, with the others being tinnitus, impaired balance, and paresthesias around the temporal region. Schwannomas are also seen affecting the third and the fifth cranial nerves. In a study of 48 patients with NF2 by Mautner et al., vestibular schwannomas were found in 96% of the patients, spinal tumors in 43 (90%), eye involvement in 30 (63%), meningiomas in 28 (58%), and trigeminal schwannomas in 14 (29%).[5]

Reduced visual acuity due to the involvement of the optic nerves by intracranial tumors or due to posterior subcapsular cataracts, cortical wedge opacities, and epiretinal membrane is fairly common in NF2.[4,6]

The skin manifestations associated with this entity are café au lait macules, schwannomas, and neurofibromas.[4]

Tumors of the spinal cord include ependymomas, which form the majority, with the others being meningiomas, schwannomas, and neurofibromas. Evaluation of spinal MRI by Patronas et al. in 49 patients with NF2 revealed 26 patients with intramedullary lesions and 27 having intradural-extramedullary tumors.

The management of NF2 primarily involves the surgical removal of symptomatic intracranial and intraspinal tumors.[6] Stereotactic radiosurgery, radiation therapy, and microsurgery are resorted to in patients with aggressive tumors or with patients having surgical risks. Cochlear implants and brainstem implants are offered as part of auditory rehabilitation to patients with loss of hearing in specialized centers.

Other therapies targeting the various implicated protein-signaling cascades by drugs such as elotinib and orafenib are being evaluated for the treatment of NF2 and may offer hope to patients suffering from this often-debilitating disease.

Conflicts of interest

The authors have none to declare.

REFERENCES

1. Evans DG. Neurofibromatosis type 2 (NF2): a clinical and molecular review. *Orphanet J Rare Dis*. 2009;4:16.
2. Tsukita S, Yonemura S. ERM (ezrin/radixin/moesin) family: from cytoskeleton to signal transduction. *Curr Opin Cell Biol*. 1997;9(1):70–75.
3. Baser ME, Friedman JM, Wallace AJ, Ramsden RT, Joe H, Evans DG. Evaluation of clinical diagnostic criteria for neurofibromatosis 2. *Neurology*. 2002;59:1759–1765.
4. Evans DG, Huson SM, Donnai D, et al. A clinical study of type 2 neurofibromatosis. *Q J Med*. 1992;84:603–618.
5. Mautner VF, Tatagiba M, Lindenau M, et al. Spinal tumors in patients with neurofibromatosis type 2: MR imaging study of frequency, multiplicity, and variety. *AJR Am J Roentgenol*. 1995;165:951–955.
6. Evans DGR, Baser ME, O'Reilly B, et al. Management of the patient and family with neurofibromatosis 2: a consensus conference statement. *Br J Neurosurg*. 2005;19:5–12.