Original Research Paper

Volume-9 | Issue-3 | March-2019 | PRINT ISSN - 2249-555X

General Medicine

A RARE PRESENTATION OF NEUROFIBROMATOSIS TYPE 1 VASCULOPATHY

Dr. P. Raja Sekhar M.D, Professor, Department Of General Medicine Kurnool Medical College Kurnool.

Dr. S . Noorzia Sulthana* Junior Resident, Department Of General Medicine, Kurnool Medical College, Kurnool. *Corresponding Author

Dr. G. Indraja Himavardhini Junior Resident, Department Of General Medicine, Kurnool Medical College, Kurnool.

ABSTRACT A 35 year female presented with radicular neck pains of 4 months duration ,with quadriparesis , stiffening and paresthesias in all limbs since 10days. Past history of multiple pigmented swellings all over the body since 20 years. O/E she is fitting under NF TYPE 1 criteria with confirmation of complaints on systemic examination. MRI & CECT SPINE showed left vertebral artery Dural AV malformation extending from C2 to C6 segments passing through intervertebral foramen causing cord compression. NF1 Vasculopathy affecting extracranial vertebral artery presenting as spastic quadriparesis, radicular neck pains and paresthesias is discussed here,pointing out varied presentations of NEUROFIBROMATOSIS.

KEYWORDS : NEUROFIBROMATOSIS TYPE 1, Vasculopathy, Quadriparesis, Extracranial vertebral artery

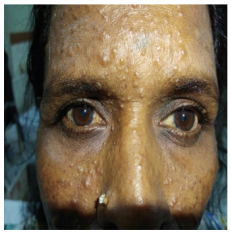
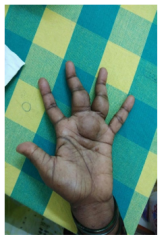
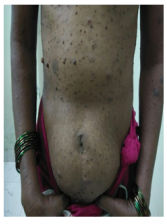
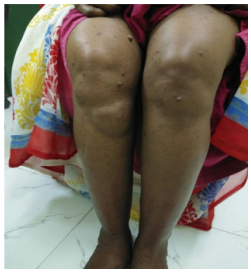
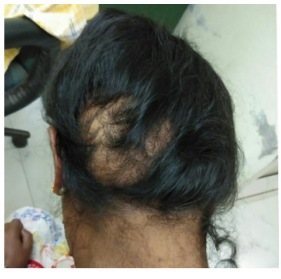
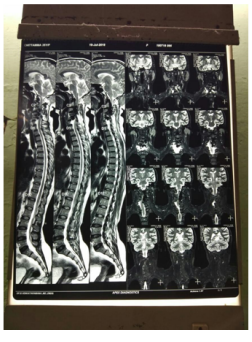
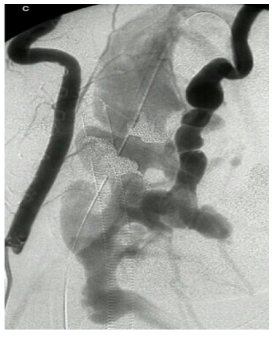
INTRODUCTION:

NEUROFIBROMATOSIS TYPE 1 is one of the most common inherited autosomal dominant disorder resulting from NF1 gene mutation with 100% penetration and wide phenotypic variability.This disorder primarily affects neural crest but also involve non-neural crest tissues like bone,blood vessels.Vasculopathies are the least publicized but most important manifestation.NF1 can have three patterns of vascular lesions: Arterial stenosis or occlusion,dysplastic changes with aneurysm formation and ruptured arteries causing arteriovenous fistula. Of these three, stenosis of the renal artery is the most frequent, but occlusion of the cerebral arteries can also occur and may result in "moyamoya like" disease. Aneurysmal formations and Fistulae in the head and neck region typically affect the vertebral arteries rather than the carotid arteries, these parachordal or vertebra-vertebral fistulas being the consequence of an arterial rupture.

CASE REPORT:

A 35 year female presented with radicular neck pains of 4 months duration, with weakness of both upper limbs & lower limbs for 10 days and paresthesias in all limbs since 10days. H/O multiple pigmented swellings all over the body since 20 years of age. Family H/O similar swellings in father,brother & sister present.On general examination she has cafe-au-lait spots,multiple neurofibromata,plexiform lesions over scalp,left 3rd & 4th fingers and right knee,axillary freckling with features s/o NEUROFIBROMATOSIS type 1 (The requisites for diagnosis are the presence of two or more of the following criteria: six or more "café-au-lait" spots, two or more neurofibromas of any type, or one plexiform neurofibroma; axillary or inguinal freckling; two or more Lisch nodules; optic pathway gliomas; distinctive bone lesions such as sphenoid dysplasia or thinning of the long bone cortex, with or without pseudoarthrosis and, finally, a firstdegree relative diagnosed with NF-1).

On systemic examination higher mental functions, cranial nerve examination is normal. Motor system examination revealed hypertonia with a power of 4+/5 in both upper & lower limbs. Superficial abdominal reflexes are absent & plantars are extensors. Deep tendon reflexes are 3+ (exaggerated) with ankle clonus. Paresthesias involving dermatomes C2 to C6.No signs of cerebellar Involvement and Meningeal irritation. MRI Cervical spine showed large hyposignal T1/hyposignal T2 epidural lesions compatible with flow void structures at the left side of C2-6 levels . MRI cervical spine with contrast showed dilated tortuous non-thrombosed left vertebral artery (V2&V3) extending from C2-C6 causing compression of cord & nerve roots with spinal cord pushed to right side s/o epidural vertebral AV fistula. angiography disclosed a vertebrovertebral arteriovenous fistula (VVAVF) fed by a dysplastic left vertebral artery at C4 level draining into a complex network of venous channels including the epidural and vertebral venous plexus, internal and external jugular veins. Patient was referred to Neurosurgery for further management

DISCUSSION:

Neurofibromatosis type 1 (NF-1) is a common genetic disorder with a prevalence of about one patient in 3 – 4000. It is an autosomal dominant genetic disorder results from NF-1 gene mutation. The NF-1 gene was isolated in the proximal portion of the long arm of chromosome 17. It encodes a protein, neurofibromin that is expressed in all tissues during organogenesis, but is found just in a few specific cells in adult individuals, it seems to be involved in the control of cellular growth and differentiation.

Neurofibromin expression has been recognized in endothelial and smooth muscle cells of blood vessels in renal and cerebral arteries and in the aorta.Its function in vascular cells is not known but

neurofibromin expression is related to a down-regulating of cellular growth and its loss is therefore associated with cell proliferation (tumoral mechanism). A defect in neurofibromin may therefore be linked to vasculogenesis in NF-1 by stimulation of the proliferation of endothelial and smooth muscle cells. By the same mechanism, the integrity of the endothelial layer can be compromised following a breakdown function promoting the spread of cells and stenosis or increase the fragility of the vessel wall. Other hypotheses for vascular abnormalities in NF-1 include the presence of a dysplastic process due to abnormal function of neurofibromin altering the vascular histogenesis or the modification of the normal process of vascular maintenance and repair.

The vascular disease in NF-1 does not affect all arteries globally in an NF-1 patient, a 'second hit' mutation of the normal NF-1 allele may be needed to promote vascular changes or a somatic mutation at another locus may be necessary for development of NF-1 vascular lesions. Environmental factors probably contribute, such as local hemodynamic injury, diet, smoking, exercise, stress and other recognized factors of vascular lesions.

In 1974, Greenepostulated two basic groups of vascular lesions associated with NF-1: dysplasia of the vessel wall with smooth muscle cell proliferation and a perivascular involvement, either causing retraction or infiltration of the vessel wall by neurofibromatous tissues. Both processes may lead to stenosis and occlusive symptoms or arterial dysplasia, aneurysmal formation or arterial rupture.

In cases of parachordal fistulas in NF-1 the suggested two pathological mechanisms: the first theory stated that dysplastic smooth muscle or neurofibromatous proliferation in the arterial wall leads to an aneurysm that may subsequently rupture into adjacent veins, while the second postulation is related to mesodermal dysplasia that may lead to congenital fistula.Since the cervical part of the vertebral artery is the only craniocervical vessel to be derived from the mesoderm while all other vessels are derived from neural crest cells, one may presume mesodermal dysplasia as the cause for the parachordal fistulae which is further underlined by the fact that the (neural crest derived) intracranial portion of the vertebral artery is never involved in the vascular diseases present in NF-1.

Among 33 cases collected from literature and one case added in this report, the mean age of onset of symptoms was 50 years.These fistulas frequently occurred in women (72%), on the left side (60%), unilaterally (93%) and principally involving the vertebral artery (91% are truly VVAVF). The parachordal fistulas are arteriovenous shunts located in different areas along the neuroaxis following the notochord and fed by metameric arteries of the craniocervical junction or segmental arteries in the paraspinal region at different levels from the basisphenoid from thoracic, lumbar and sacral regions. In NF-1, there is a clear predominance of occurrence in neck region. The symptoms of lesions at cervical level are mainly caused by compression by epidural engorged venous dilatation. Bruit and tinnitus are most commonly reported but cervical myelopathy and radicular pain have more clinical impact.

Considering the pathologic changes in the arterial wall in NF-1 patients, the optimal treatment for aneurysmal or arteriovenous fistula is sacrifice of the affected artery. The endovascular technique can deal properly with VVAVFs. In the cases reviewed managed endovascularly , the embolism materials were diverse (balloons, glue, bare and gianturco coils) but no matter what was used the goal was common: to occlude the fistulous site with or without the parent vessel.

CONCLUSION: NF1 has extremely variable expression from simple skin macules and neurofibromas to aggressive multiple tumour presentations or complex vascular lesions. In the future it will be very important to identify the role of the NF gene and neurofibromin in vascular phenotypic expression and vessel wall proliferation, as well as to recognize and propose a gene therapy method, feasible and efficient, applicable in NF-1 patients before the onset of vascular disorders. Attention should be paid to the management of lesions in the cervical region in NF-1 and further to suspected aneurysms or arteriovenous fistulas, an appropriate radiological approach has to be iplemented regarding the essential role of MRI, MR angiography and angiography in these diseases.

REFERENCES :

1. Extracranial Vertebral Artery Involvement in Neurofibromatosis Type I Report of Four Cases and Literature Review; V.M. PEREIRA, S. GEIPRASERT, Interventional Neuroradiology 13: 315-328, 2007.
2). Riccardi VM:The vasculopathy of NF-1 and histogenesis control genes. Clin Genet 58: 345-347, 2000.
3) Saylor: The vascular lesions of neurofibromatosis. Angiology (25): 510-519, 1974.
4) www.NCBI.nih .gov articles.