Neurofibromatosis type – 1 (NF-1) presenting as intracerebral haemorrhage in a young adult- unveiling a rare culprit

Anamika Giri1, Sourya Acharya2, Amol Andhale3, Sunil Kumar4, Rohan Kumar Singh5, Abhijit Chandankhede6

ABSTRACT
Neurofibromatosis type I (NF-I) is an autosomal dominant disorder. Epidemiologic data suggests it affects 1 in 3000 individuals. Various vascular abnormalities are reported to be associated with NF-1. Amongst these cerebrovascular anomalies are common in form of vascular stenosis or aneurysms. Arteriovenous malformations of the brain are still rarely found.

We present a case of a 24 year old male who presented to this hospital with one episode of generalised tonic clonic seizure. After clinical examination and investigations the diagnosis of intracerebral haemorrhage due to rupture arteriovenous malformation and NF-1 was made. This report highlights the rare association of intracerebral vasculopathy with NF-1.

Keywords: Pectus Excavatum, Neurofibromatosis, Aneurysm

1. INTRODUCTION
Neurofibromatosis is a set of hereditary illnesses characterised by the formation of tumours on nerve tissue. Tumors are usually present in the neurological system; include the brain, spinal cord, and nerves. Neurofibromatosis is categorized into three types: neurofibromatosis 1 (NF1), neurofibromatosis 2 (NF2), and schwannomatosis. NF1 is frequently discovered in childhood, whereas NF2 and schwannomatosis are discovered in early adulthood (Oderich et al., 2007). The tumours in these illnesses are normally benign, but they can become cancerous at times. The signs and symptoms are usually not very severe. Hearing loss, learning disabilities, heart and cardiovascular complications, vision loss, and extreme pain are all possible effects of neurofibromatosis. Vascular abnormalities are quite common in NF-1 and seen in the renal, coronary and gastrointestinal vessels. There has been literature on vascular abnormalities in cerebral vessels in the form of occlusions, aneurysms, arteriovenous malformations and Av Fistulae.
2. CASE REPORT

A 24 year old male patient came to the casualty with chief complaints of one episode of generalised tonic clonic seizures. This episode was associated with up rolling of eyes, tongue bite and frothing at mouth. Patient had no history of similar complaints in the past. There was no history of loss of consciousness. Patient had one episode of vomiting along with this episode. On examination; Patient was conscious but confused GCS 13/15. Pulse was 104/ minute, regular, Blood pressure was 130/80 mmHg. Neurologic examination revealed terminal neck stiffness. There were no cranial nerve abnormalities; power in all four limbs was 5/5 as per MRC grade. There were no sensory deficits. Plantars were bilateral extensor. Multiple neurofibromas were palpable over body; (Figure-1) café-au-lait spots were present. Pectus excavatum deformity was seen on chest (Figure 2). Patient was started on injection Levitiracetam 500 mg IV twice a day. In view of his complaints an emergency CT brain Plain was done which revealed haemorrhage in dependent part of fourth ventricle, third ventricle, left thalamus, perimesencephalic cistern with moderate dilatation of bilateral lateral ventricle (Figures 3, 4, 5 and 6). MRA revealed focal arteriovenous malformation along the left perimesencephalic cistern with arterial feeder from left posterior cerebral artery and venous drainage in internal cerebral veins (Figure 7). Patient was started on tablet Levetiracetam 500 mg twice a day. Patient was referred to Neurosurgery for further management. The patient underwent flow directed selective onyx embolization of the feeding vessels and nidus. Post embolizations there were no complications. Currently after 2 months of discharge patient has no active complaints and there is no neurodeficit.

Figure 1 Showing multiple neurofibromas in forearm
Figure 2 Showing Pectus Excavatum

Figure 3 CT axial section showing haemorrhage in dependant part of fourth ventricle.

Figure 4 CT axial section showing haemorrhage in the third ventricle
3. DISCUSSION

Neurofibromatosis is usually a benign condition but it can sometimes have potentially life threatening squeale. One such sequelae is vasculopathy especially in the nervous system (Abbas et al., 2017; Singh et al., 2021). These vasculopathies range from stenosis, aneurysms, malformations, ruptures to even fistula formation. This doesn’t usually affect the small vessels, medium to large sized vessels are usually affected. The exact cause of these vasculopathies is not known. It is said to be related to the activity of neurofibromin, the NF-1 gene’s protein product (Evans, 2018). Neurofibromin has been demonstrated to limit cell proliferation by negatively regulating the RAS signalling pathway and positively controlling intracellular cAMP levels. The loss of gene neurofibromin expression in NF-1 enhances vascular smooth muscle cell proliferation via the RAS signalling system, resulting in proliferation of intima and arterial stenosis. It has also been discovered that neurofibromin is distributed differently in the smooth
muscle layers and endothelium of different arteries, which may reveal why cerebral and renal vessels are more typically damaged by vascular dysplasia in NF-1 than the aorta.

A patient with neurofibromatosis may develop an AV fistula through one of two ways. Aneurysm development, leakage, and eventually rupture could be caused by dysplastic smooth muscle or neurofibromatous proliferation in the artery wall. Surgical excision, embolization or radiosurgery, (or mixes of these, in some situations) are all possibilities for treating AV malformations (Uhlmann and Plotkin, 2012). Approaches including one or another or combination of are both possible, information on outcomes is few, and data on outcomes is primarily based on guesswork from a set of cases participation of a multidisciplinary team (Roos, 1992).

It is recommended to apply a multidisciplinary approach which includes neurosurgery, radiation therapy and endovascular intervention, and make available all therapeutic options available. The purpose of treatment is to completely obliterate the arteriovenous malformation (Lin et al., 2000). Because partial obliteration appears to provide little or no benefit protection against haemorrhage, and may even increase the danger.

4. CONCLUSION
More research and reporting of such unique cases is the need of the hour. It will ensure prompt initiation of treatment and will significantly reduce mortality and morbidity. We aim to educate fellow physicians in ruling out such rare causes in a case of seizures by thorough examination and looking for conditions like neurofibromatosis and their sequelae which will be live saving and prevent any further complications.

Acknowledgement: We thank all the contributors involved in the study

Author Contributions
AG, SA, AA- initiated the idea of publication and contributed the intellectual content for the development of the manuscript
RKS diagnosed the intraparenchymal bleed on CT and provided precise images of CT and MRA
SA, SK, AC reviewed, proof read and edited the manuscript

Informed Consent
Written & Oral informed consent was obtained from all individual participants included in the study.

Funding
The study did not receive any external funding.

Conflict of interests
The authors declare that there are no conflicts of interests.

Data and materials availability
All data associated with this study are present in the paper.

REFERENCES AND NOTES