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Case Report

Bilateral trigeminal neurofibromas-keep an eye out

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ABSTRACT

Neurofibromatosis type 1 (NF1) and type 2 (NF2) are inherited phakomatoses which occur due to mutations in tumor suppressor genes NF1 and NF2, and present with protean manifestations. One of the important manifestations of these neurocutaneous conditions is multiple benign and malignant nerve sheath tumors which can occur anywhere in the body. Multidisciplinary team involvement and timely imaging plays a vital role to precisely identify the culprit tumors and treat promptly. Our patient is a 35 years-old female presented with proptosis, bilateral upper limb and lower limb weakness. MRI performed on an urgent basis showed multiple neurogenic tumors involving trigeminal nerves bilaterally and multiple peripheral nerves. Later, the patient was diagnosed as NF1 based on national institute of health (NIH) clinical diagnostic criteria. Bilateral plexiform trigeminal neurofibromas, as seen in our patient, are uncommon tumors of NF1 and are not described in the imaging literature. The tumors on both the sides were seen extending along the branches of the trigeminal nerve including maxillary and mandibular branches expanding the pterygo-maxillary fissure and foramen ovale respectively. Radiologist plays an important role in recognizing these tumors and also delineating the extent of the tumors helping in the patient management. In view of multiple tumors with extensive involvement and patient preference, our patient was managed conservatively and appropriate monitoring strategy was planned by the multidisciplinary team to follow up.

Keywords: Neurofibroma, Trigeminal, NIH

INTRODUCTION

Neurofibromatosis type 1 (NF1) and type 2 (NF2) are inherited rare phakomatoses occurring due to mutations in tumor suppressor genes NF1 and NF2 respectively.[1] NF1 presents with protean clinical manifestations and usually is diagnosed early in childhood when NIH diagnostic criteria is satisfied. Diagnostic criteria as defined by NIH criteria consensus conference in 1987 includes six or more café au lait spots, two or more lisch nodules, axillary/ inguinal freckling, 2/more neurofibromas/ 1 plexiform neurofibromas, optic pathway gliomas, characteristic bone lesions like sphenoid wing dysplasia/ pseudoarthrosis of tibia and first degree relative with NF1.[2] The patient should satisfy at least 2 criteria to have a clinical diagnosis of NF1. Other manifestations of NF1 include focal abnormal signal intensity (FASI) lesions in brain, vasculopathy, scoliosis, vertebral scalloping, low grade gliomas, and abdominal tumors including neurofibromas, neuro-endocrine tumors and Cajal cell neoplasms.

The most common tumors in patients with NF 1 neurofibromas either cutaneous/ in deeper tissues including periorbital, GI tract, mediastinal and retroperitoneal.[3,4] Plexiform neurofibromas present in approximately 30% of NF1 patients.[5] Plexiform neurofibromas are neurofibromas that grow to involve multiple fascicles/ branches of a nerve/ plexus. Characteristic "bag of worms" description given on palpation of these tumors can be attributed to the growth pattern of these tumors. These tumors have a high incidence of transformation to malignant nerve sheath tumors and hence of concern.[5,6] Our patient is a 35 years

female presented with proptosis secondary to plexiform neurofibroma involving bilateral trigeminal nerves and its branches. It is uncommon to have bilateral trigeminal plexiform neurofibroma which makes the presentation unique. We also discuss varied manifestations of NF1, role of imaging, various imaging findings of NF1 and also reiterate the importance of multidisciplinary team involvement in managing these patients especially the plexiform neurofibromas.

CASE REPORT

A 35 years old female presented with proptosis and weakness of both upper and lower limbs. The patient developed these symptoms over a period of one week. There were no other systemic symptoms including fever, loss of appetite, night sweats or weight loss. Clinical examination revealed power of around 4/5 in all four limbs and axial proptosis of both eyes. No features were suggestive of upper motor neuronal involvement. With the provisional clinical diagnosis of demyelinating polyneuropathy, the patient was referred for emergency MRI brain and spine. Brain MR imaging showed lobulated heterogenous signal intensity lesions (predominantly hyperintense on T2W sequence and hypointense on T1W sequence) involving both the trigeminal nerves (Figure 1).

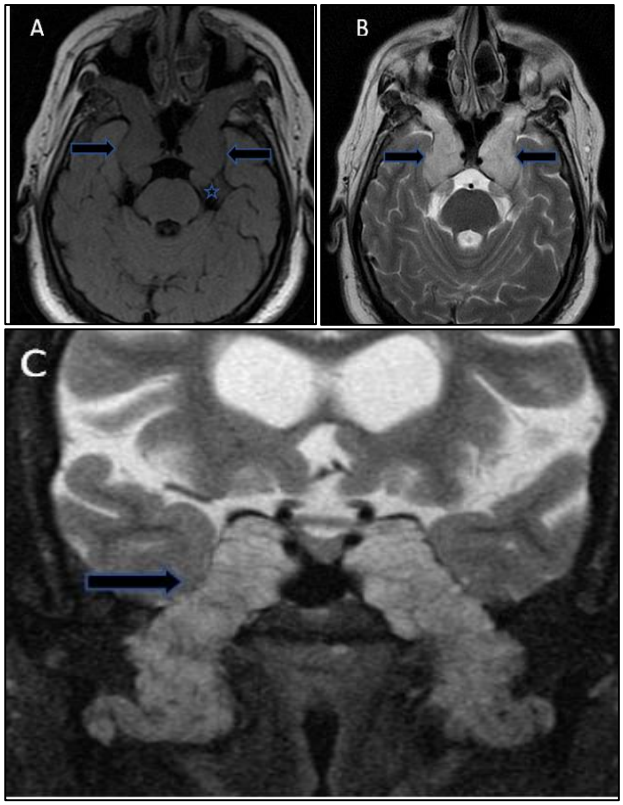

Figure 1 (A-C): Axial T1W, T2W and coronal T2W images of bilateral trigeminal plexiform neurofibromas (arrows, cavernous sinus component). The cisternal component of the tumor is appreciated on the axial images (*).

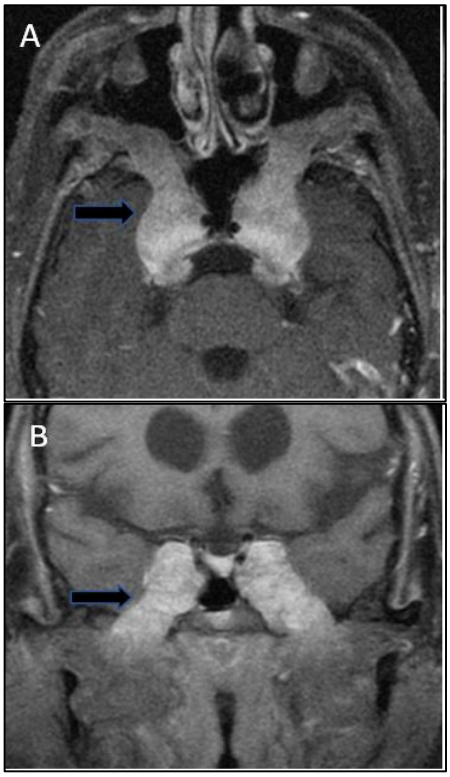

Figure 2 (A and B): Post contrast axial and coronal images of homogenously enhancing bilateral trigeminal plexiform neurofibromas.

The lesions show homogenous enhancement on post contrast imaging (Figure 2). The lesions were seen extending along the branches of the trigeminal nerve bilaterally namely maxillary and mandibular divisions widening the pterygopalatine fissure and foramen ovale. On spine imaging, diffuse peripheral nerve sheath tumors were seen involving almost all the peripheral nerves including intercostal nerves, brachial plexus, lumbar and sacral plexuses.

The patient was later diagnosed with NF 1 based on the NIH clinical diagnostic criteria. She had axillary freckling and few subcutaneous neurofibromas. Our patient is unique because the presentation is unusual and delayed in contrast to the usual age of NF 1 presentation. In view of multiple tumors with extensive involvement and patient preference, the symptoms were managed conservatively and appropriate monitoring strategy was planned by the multidisciplinary team to follow up. In addition, genetic counseling was also offered.

Uncommon NF tumors including plexiform neurofibromas of bilateral cavernous sinuses, bilateral Cranio orbital parasellar neurofibromas extending through superior orbital fissure and unilateral parasellar plexiform neurofibroma have been described in the literature. However, bilateral trigeminal plexiform neurofibromas with extension along its branches are also uncommon tumors to occur and have not been published in the imaging literature to our knowledge.

DISCUSSION

Neurofibromatosis type 1 (NF1) is an autosomal dominant inherited neurocutaneous syndrome with approximate incidence of 1 in 3000 births. This is the most common form of neurofibromatosis accounting for almost 96% followed by NF2 in 3%. The recently identified entity Schwannomatosis is a much less known variant.[3] NF1 is diagnosed when two or more of the NIH diagnostic criteria is satisfied which includes café au lait spots, axillary or inguinal freckling, lisch nodules, neurofibromas or plexiform neurofibroma, optic pathway glioma, bone lesions likely sphenoid wing dysplasia and first degree relative with neurofibromatosis type 1.[2,3] Other cranial manifestations of NF1 include FASI lesions in brain and low-grade gliomas. FASI lesions in brain, previously described as unidentified bright objects or unidentified neurofibromatosis objects occur commonly in basal ganglia, cerebellum, medial temporal lobes and brainstem.[4] Abdominal and pelvic manifestations include neurofibromas, neuroendocrine tumors, gastrointestinal stromal tumors, adenocarcinoma of gastrointestinal tract, paraganglioma, and renal artery stenosis.[7] Musculoskeletal manifestations of neurofibromatosis type 1 include elephantiasis neuromatosa resulting from massive enlargement of soft tissue secondary to neurofibroma, scoliosis, posterior vertebral scalloping, other dystrophic changes like thinning of posterior elements of the vertebrae secondary to mesodermal dysplasia, penciling of ribs, bowing and pseudoarthrosis mainly in tibia and lucent lesion representing Non Ossifying fibroma.[8] Role of advanced imaging techniques including diffusion MR imaging, MR spectroscopy and positron emission tomography in the evaluation of the neurofibromas have been described in the literature.[9]

Plexiform neurofibroma, pathognomonic of NF1, presents in 30% of these patients and involve multiple fasciles or branches of the nerve. Congenital plexiform bilateral neurofibromas of cavernous sinuses have been described in the literature in a two-month-old child.[10] There are reports available on bilateral and unilateral parasellar plexiform neurofibromas extending through the superior orbital fissures.[11,12] To the best of our knowledge, bilateral plexiform trigeminal neurofibromas in an adult has not been described in the literature. Plexiform neurofibromas tend to manifest early in life and are associated with higher risk of malignant transformation. The average rate of malignant transformation is around 2 to 16 % and considered as the main cause of mortality in these patients.[5] Two markers were recently identified as early risk predictors of developing malignant transformation-IGFBP1 (insulin-like growth factor binding protein 1) and RANTES (regulated upon activation, normal T cell expressed and secreted).[13] The authors found high concentration of these markers in malignant nerve sheath tumors as compared to patient without and hence these markers may be useful screening method to identify malignant transformation.[13] We would like to reiterate the importance of identifying these tumors and delineating the extent of involvement which helps in decision making. MR imaging is the modality of choice to monitor the progression and extent of these tumors. It is crucial to judiciously utilize MRI to monitor these tumors especially when there is an unusual new symptom.

The mainstay of management of NF1 is age specific monitoring for development of new lesions or vascular complications. Ideally, annual assessment in NF clinic is the best option for adults but if the patient elects not to attend, they should be fully aware of the disease process. Annual blood pressure measurements and being aware of unusual symptoms, particularly the features of malignant transformation of neurofibromas and of spinal cord compression is the minimum requirement for an asymptomatic adult NF1 patient.[14] Our patient was appropriately counselled and suggested an annual monitoring strategy by the multidisciplinary team. She was also detailed about the warning signs as well as encouraged to recognize any unusual symptom as early as possible.

Surgery is the mainstay of treatment for the culprit lesion especially if there is a malignant transformation, but it might be limited because of the disease extent. There is always a chance of recurrence which is up to 20% in plexiform neurofibromas.[5] Newer US FDA approved agents are available for inoperable progressive extensive plexiform neurofibromas and good results have been reported.[15] We opted conservative management to surgery in our patient due to the extensive tumor involvement and patient preference to avoid surgery. We also planned to monitor the patient clinically and by imaging these plexiform neurofibromas for any evidence of malignant transformation.

CONCLUSION

It is important to keep neurogenic tumors (neurofibroma/ schwannoma) as one of the differentials of any acute or chronic neurological presentation, with or without NF1. Radiologist plays a vital role to look for the presence and extent of these tumors on imaging carefully. The prognosis of these tumors is always better if diagnosed early but unfortunately these tumors may be asymptomatic for years, only to present late with extensive involvement. Management of neurofibromatosis type 1 patients is undoubtedly a multidisciplinary team approach and it is important to have a coordinated effort for close monitoring of these patients. Though surgery remains the mainstay of therapy for plexiform neurofibromas especially with malignant transformation, newer drugs are available with promising initial results.

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REFERENCES

1. Wang MX, Dillman JR, Guccione J. Neurofibromatosis from Head to Toe: What Radiologist Needs to Know. Radiographics. 2022;42(4).
2. National Institutes of Health Consensus Development Conference Statement: neurofibromatosis. Bethesda. Md USA 1987. Neurofibromatosis. 1988;1:172-8.
3. Kresak JL, Walsh M. Neurofibromatosis: A Review of NF1, NF2, and Schwannomatosis. J Pediatr Genet. 2016;5(2):98-104.
4. Bekiesinska-Figatowska M. A mini review on Neurofibromatosis type 1 from the radiological point of view. J Rare Dis Res Treat. 2017;2(6);45-9.
5. Tchernev G, Chokoeva AA, Patterson JW, Bakardzhiev I, Wollina U, Tana C. Plexiform Neurofibroma: A Case Report. Medicine (Baltimore). 2016;95(6):e2663.
6. Mautner VF, Hartmann M, Kluwe L. MRI growth patterns of plexiform neurofibromas in patients with neurofibromatosis type 1. Neuroradiology. 2006;48:160-5.
7. Zulfiqar M, Lin M, Ratkowski K, Gagnon MH, Menias C, Siegel CL. Imaging Features of Neurofibromatosis Type 1 in the Abdomen and Pelvis. AJR Am J Roentgenol. 2021;216(1):241-51.
8. Patel NB, Stacy GS. Musculoskeletal manifestations of neurofibromatosis type 1. AJR Am J Roentgenol. 2012;199(1):W99-106.
9. Ahlawat S, Blakeley JO, Langmead S, Belzberg AJ, Fayad LM. Current status and recommendations for imaging in neurofibromatosis type 1, neurofibromatosis type 2, and schwannomatosis. Skeletal Radiol. 2020;49(2):199-219.
10. Meersschaut VA, Kros JM, Catsman-Berrevoets CE, Lequin MH. Congenital bilateral plexiform neurofibromas of the cavernous sinuses. Pediatric Radiol. 2003;33;272-4.
11. Li P, Yang Z, Wang Z, Liu P. Bilateral Cranio-Orbital Neurofibromas in a 16-year-old child with neurofibromatosis 1. Neurol India. 2016; 64: 835-6.
12. Khan SN, Sepahdari AR. Orbital masses: CT and MRI of common vascular lesions, benign tumors, and malignancies. Saudi J Ophthalmol. 2012;26(4):373-83.
13. Park SJ, Sawitzki B, Kluwe L. Serum biomarkers for neurofibromatosis type 1 and early detection of malignant peripheral nerve-sheath tumors. BMC Med. 2013;11:109
14. Ferner RE, Huson SM, Thomas N, Moss C, Willshaw H, Evans DG et al. Guidelines for the diagnosis and management of individuals with neurofibromatosis 1. J Med Genet. 2007;44(2):81-8.
15. Mukhopadhyay S, Maitra A, Choudhury S. Selumetinib: the first ever approved drug for neurofibromatosis-1 related inoperable plexiform neurofibroma. Curr Med Res Opin. 2021;37(5):789-94.

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