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Case Report

Atypical presentation of neurofibromatosis type 1 in a 10-month-old girl: a case report

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ABSTRACT

Neurofibromatosis type 1 (NF1) is a neurocutaneous genetic disorder of heterogenic symptoms majorly affecting the nervous system, eye, skin and bone. This study was about a 10-month-old female child who developed a lump/mass on the left side of neck 3 months ago that rapidly increased in size along with ulceration and bleeding for one month with no associated symptoms. MRI of neck showed large heterogeneous and enhancing lesion with thick lobulated folds noted posteriorly, located in the left posterior cervical space deep to the sternocleidomastoid muscle. On histopathological examination nerve sheath tumor favoring NF1 was confirmed. Child underwent debulking/excision of the mass.

Keywords: NF1, Peripheral nerve sheath tumor, Neurofibroma, Neurofibromatosis 1, Neurofibromin, Optic pathway glioma, Lisch nodules, Acoustic neuroma

INTRODUCTION

NF1 is the most common hereditary multi tumor syndrome with an incidence at birth of approximately 1:3000 and it is caused by mutations in the NF1 gene. NF1 is localized on chromosome band 17q11.2 and it acts as a tumor suppressor gene.[2] The diagnosis of NF1 is based upon the presence of characteristic clinical features. According to NIH criteria, at least two of the following clinical features must be present to make the diagnosis of NF1: six or more café au lait macules (0.5 cm in children or >1.5 cm in adults), two or more cutaneous/ subcutaneous neurofibromas or one plexiform neurofibroma, axillary or groin freckling, optic pathway glioma, two or more Lisch nodules (iris hamartomas seen on slit lamp examination) and bony dysplasia (sphenoid wing dysplasia, bowing of long bone±pseudoarthrosis), first degree relative with NF1. Genetic testing is not required, but can it be a useful tool in confirming the diagnoses of children who do not meet diagnostic criteria or only exhibit café-au-lait macules and axillary freckling.[1] It has multimodal therapeutic approach.[2]

CASE REPORT

The patient, a 10-month-old child, presented through the OPD with complaints of mass on the left side of the neck for 3 months. This left-sided neck mass rapidly increased in size with associated ulceration and bleeding from the surface of the mass for one month. There was no history of fever, weight loss, pain, dysphagia, dyspnea, syncopal episodes associated with the mass. On general examination an ulcerated mass (12×14 cm) was evident on the left side of neck that did not move on deglutition and there were no matted lymph nodes along the length of the sternocleidomastoid (Figure 1 A and B). The mass was causing distortion of the left ear lobule. It was firm in consistency, fixed to the overlying skin and the

underlying structures (immobile), with no active bleeding from the ulcerated surface. The inferior limit was palpable hence, there was no retrosternal extension. There were no café-au-lait spots on the body. Slit lamp examination was conclusive of Lisch nodules. MRI of neck showed a large heterogeneous and enhancing lesion with thick lobulated folds noted posteriorly, located in the left posterior cervical space deep to the sternocleidomastoid muscle splaying the carotid vessel, however, the fat planes remained intact (Figures 2 A and B). Differential diagnoses were cervical teratoma and lymphomatous node. Histopathological examination following the Tru-cut biopsy showed nerve sheath tumor favoring neurofibromatosis type-I (Figure 4). A tumor composed of proliferating nerve fibers comprising Schwann cells, fibroblasts and perineural cells with elongated nuclei having wavy, serpentine configuration in extra myxoid background of thin collagenous stroma. No verocay bodies or palisading of nuclei was observed. No evidence of granuloma or malignancy was obtained. Ultrasound of abdomen and pelvis showed multiple sub-centimetric mesenteric lymph nodes. Based on these findings, diagnosis of nerve sheath tumor (NF1) was established. The patient underwent surgical debulking/excision of mass (benign tumor).

Per-operative findings were those of a large, highly vascular, and firm fungating mass on the left side of the neck having the following features: presence of the mass in the anterior triangle of the neck extending to the posterior triangle and attached to the mastoid process and the occipital bone; the mass was external to the carotid sheath and had a necrotic center (Figure 3).

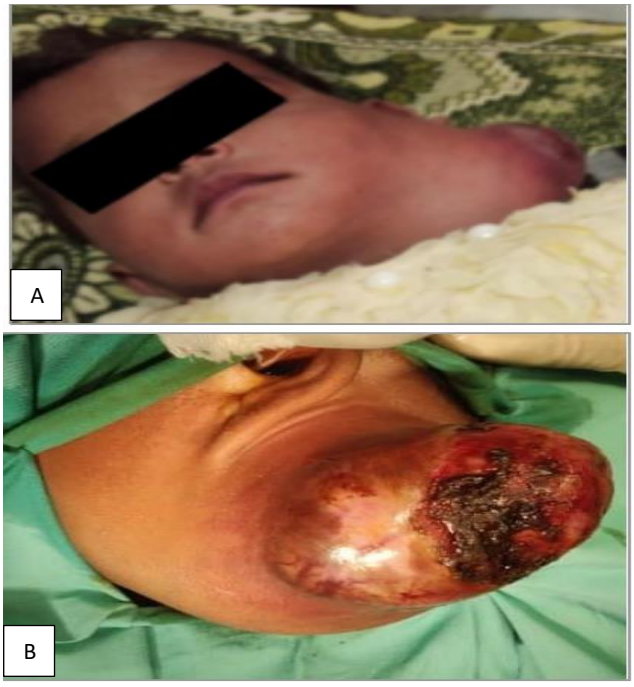

Figure 1 (A and B): Ulcerated and fungating left sided neck mass.

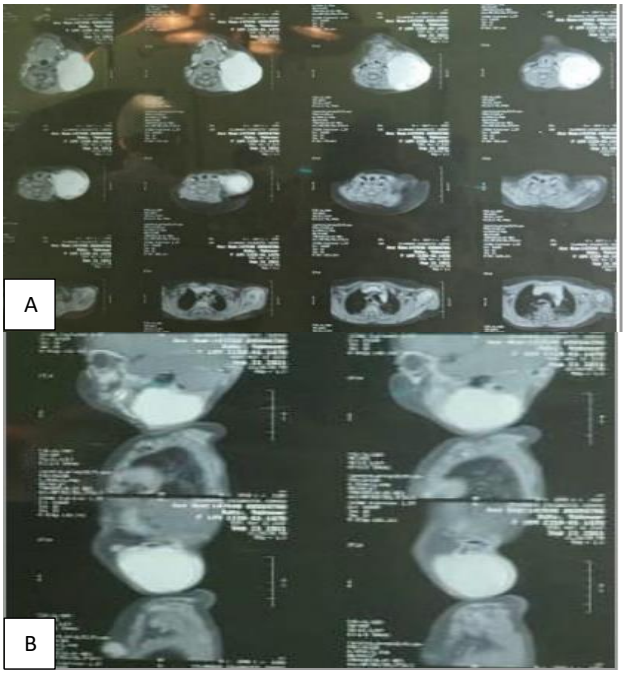

Figure 2 (A and B): MRI of the neck with splaying of the carotid sheath, however, deep to the sternocleidomastoid.

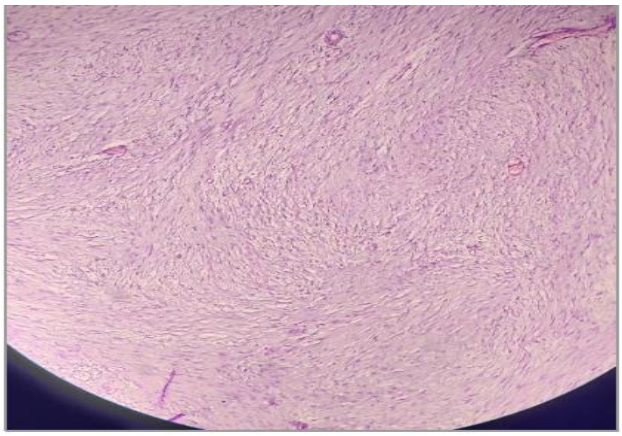

Figure 3: Spindle cells with hyperchromatic nuclei with shredded carrot collagen.

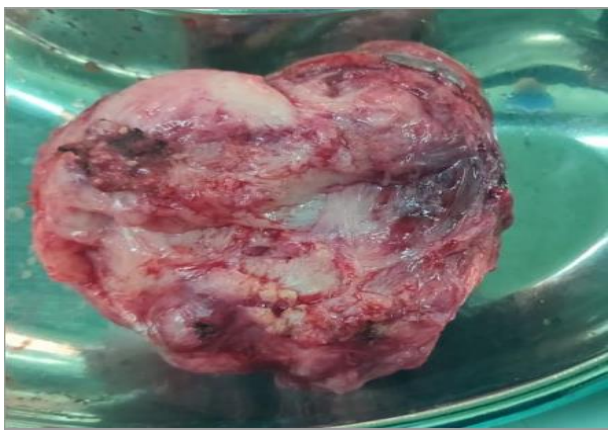

Figure 4: Post resection tumor.

DISCUSSION

The neurofibromatoses are a group of heterogeneous disorders that include NF1, neurofibromatosis type 2 (NF2) and schwannomatosis. NF1, formerly known as von Recklinghausen disease, is the most common of these three conditions and represents one of the most frequently diagnosed cancer predisposition disorders involving the nervous system.[3] While NF1 primarily affected the central and peripheral nervous system, multisystem involvement was the rule, with dermatologic, cardiovascular, gastrointestinal and orthopedic affectation often reported. Importantly, NF1 is a disorder of heterogeneity such that affected individuals can be variably affected, even within the same family.[4] Individuals with NF1 have a predisposition to benign and malignant tumor formation and the hallmark lesion is the neurofibroma, a benign peripheral nerve sheath tumor. The gene for NF1 was cloned on chromosome 17q11.2 and neurofibromin, the NF1 protein, controls cell growth and proliferation by regulating the proto-oncogene Ras and cyclic adenosine monophosphate (AMP).[5] Neurofibromin is necessary for embryonic development and involved mainly in the differentiation of neural crest derived cells, mesenchymal cells, neural cells, melanocytes and bone cells. Over 1485 different mutations have been identified in the NF1 gene so far, most of which led to a synthesis of truncated, non-functional protein. It is estimated that the point mutations are responsible for approximately 90% of cases of NF1. The remaining 5-7% of NF1 cases are associated with the presence of a single exon or whole NF1 gene deletion (17q11.2 microdeletion syndrome).[6] Nearly all individuals with neurofibromatosis type 1 develop pigmentary lesions (café-au-lait macules, skinfold freckling and Lisch nodules) and dermal neurofibromas. Some individuals develop skeletal abnormalities (scoliosis, tibial pseudarthrosis and orbital dysplasia), brain tumors (optic pathway gliomas and glioblastoma), peripheral nerve tumors (spinal neurofibromas, plexiform neurofibromas and malignant peripheral nerve sheath tumors), learning disabilities, attention deficits, and social and behavioral problems, which can negatively affect quality of life. In 50% of NF1 patients, the clinical symptoms become apparent below 1st year and in 97%, before the age of 8 years.[6] All these manifestations (except the malignant peripheral nerve sheath tumors) were stable or slowly progressive. Treatment was symptomatic in all cases except for the patient with malignant peripheral nerve sheath tumors, who needed extensive surgery and radiotherapy. With the identification of NF1 and the generation of accurate preclinical mouse strains that model some of these clinical features, therapies that target the underlying molecular and cellular pathophysiology for neurofibromatosis type glioblastoma), peripheral nerve tumors (spinal neurofibromas, plexiform neurofibromas and malignant peripheral nerve sheath tumors), learning disabilities, attention deficits and social and behavioral problems, which can negatively affect quality of life. In 50% of NF1 patients, the clinical symptoms become apparent below 1st year and in 97%, before the age of 8 years.[6] All these manifestations (except the malignant peripheral nerve sheath tumors) were stable or slowly progressive. Treatment was symptomatic in all cases except for the patient with malignant peripheral nerve sheath tumors, who needed extensive surgery and radiotherapy. With the identification of NF1 and the generation of accurate preclinical mouse strains that model some of these clinical features, therapies that targeted the underlying molecular and cellular pathophysiology for NF1 were becoming available. Although no single treatment existed, current clinical management strategies included early detection of disease phenotypes (risk assessment) and biologically targeted therapies. Similarly, new medical and behavioral interventions were emerging to improve the quality of life of patients.[7]

CONCLUSION

The prevalence of NF1 is about 1:3000. There are no known ethnic groups in which NF1 does not occur or is unusually common. The prevalence is higher in children than in adults, a difference that results at least in part from the early death of some NF1 patients. The classic manifestations of NF1 include café-au-lait macules, skinfold freckling, neurofibromas, brain tumors, iris hamartomas and characteristic bony lesions. In addition, patients with NF1 are at increased risk for learning and intellectual disabilities, aqueduct stenosis, pheochromocytoma, vascular dysplasia, scoliosis and cancer. High-intensity signals on brain magnetic resonance imaging are a frequent finding without known clinical significance. Most brain tumors are benign and asymptomatic, but malignant brain tumors occur. The major cause of death is malignancy, including brain tumors and malignant peripheral nerve sheath tumors. Management includes genetic counselling, regular eye examinations and careful physical exams.

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REFERENCES

1. Martin S, Fica S, Parfeni O. Somatostatinoma and Neurofibromatosis type 1-a case report and review of the literature. Diagnostics. 2020;10(9):620.
2. Kieffer S. Treatment for Neurofibromatosis (NF) Type 1. Johns Hopkins comprehensive neurofibromatosis (NF) center. Available at: https://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/neurofibromatosis/nf1/treatment-nf1.html. Accessed October 24, 2021.
3. Theos A, Korf BR. Pathophysiology of neurofibromatosis type 1. Ann Intern Med. 2006;144(11):842-849.

4. Cimino PJ, Gutmann DH. Neurofibromatosis type 1 ld. Handb Clin Neurol. 2018;148:799-811.
5. Ferner RE, Gutmann DH. Neurofibromatosis type 1 (NF1): diagnosis and management. Handb Clin Neurol. 2013;115:939-55.
6. Abramowicz A. Neurofibromin in neurofibromatosis type 1-mutations in NF1gene as a cause of disease. Dev Period Med. 2014;18(3):297-306.
7. Gutmann DH, Ferner RE, Listernick RH, Korf BR, Wolters PL, Johnson KJ. Neurofibromatosis type 1. Nat Rev Dis Primer. 2017;3(1):1-17.
8. Friedman JM. Epidemiology of neurofibromatosis type 1. Am J Med Genet. 1999;89(1):1-6.
9. Anderson JL, Gutmann DH. Chapter 4-Neurofibromatosis type 1. In: Islam MP, Roach ES, eds. Handbook of Clinical Neurology. Vol 132. Neurocutaneous Syndromes. Elsevier. 2015:75-86.
10. Tonsgard JH. Clinical Manifestations and Management of Neurofibromatosis Type 1. Semin Pediatr Neurol. 2006;13(1):2-7.

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