A case of elephantiasis neuromatosa

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ABSTRACT

Elephantiasis neuromatosa (EN) is a rare and unique complication of plexiform neurofibroma, a type of neurofibromatosis type 1, and manifests as hypertrophy of an extremity (either lower limb or upper limb). EN can be seen in individuals of any age group including children and young adults where males and females are affected equally. Diagnosis is done primarily by magnetic resonance imaging of the affected region along with a history and clinical examination. EN may lead to severe functional impairment of the involved limb with cosmetic disfigurement. Treatment is mainly surgical with less satisfactory results. Here, we present a 6-year-old child with EN.

Key words: *Elephantiasis neuromatosa, Limb hypertrophy, Neurofibromatosis type 1, Plexiform neurofibroma*

Elephantiasis neuromatosa (EN) is a rare and unique complication of plexiform neurofibroma, generally manifests as hypertrophy of an extremity [1,2]. Common sites of involvement, in the order of frequency, are the lower limb and upper limb, followed by the trunk and head and neck [3]. The disease can be seen in individuals of any age group irrespective of their sex. The possible pathogenetic mechanism proposed in EN is early and excessive growth in the width and length of the affected limb due to a neoplastic proliferation of the perineural connective tissue, along with the congenital lymphatic insufficiency and chronic hyperemia [4].

Plexiform neurofibroma, an uncommon skin tumor, is found in up to 26% of patients with neurofibromatosis type 1 (NF-1) [1]. NF-1 or Von Recklinghausen disease is a neurocutaneous disorder, with autosomal dominant inheritance, occurs due to the genetic defect localized in the long arm of chromosome 17q11.2 with a frequency of approximately 1 in 3000 births [5]. Plexiform neurofibroma, pathognomonic of NF-1, usually presents at birth or during the first several years of life. They are unencapsulated and poorly circumscribed tumors [4]. They may involve the long segment of a major nerve trunk and its branches and characteristically show diffuse irregular infiltration into adjacent muscle and fat [6]. This tumor has a locally aggressive behavior, but the infiltrative pattern is not indicative of malignancy and has no histologic evidence of anaplastic or mitotic features [7]. Here, we describe a child with EN.

CASE REPORT

A 6-year-old female child was brought to our neurology department with complaints of enlarged right lower limb with difficulty in walking from 2 years of age. Her birth and developmental history were normal. At 2 years of age, her parents noticed minimally enlarged right lower limb compared to the left, which was slowly and progressively increasing in size. This made her to find difficulty in walking, sitting, and getting up. Her father was a neurofibromatosis patient; he had multiple cutaneous neurofibromas over face, chest, and both upper and lower limbs and café-au-lait macules over trunk, without any deformities or restricted movements of limbs. Examination of the child revealed few café-au-lait spots over chest and back. Otherwise, no external markers of NF were found. Her right lower limb was enlarged and bulky from the gluteal region to foot (Figs. 1 and 2). Engorged veins and hyperpigmentation were seen over her right thigh. Sensation was appreciated normally in the affected limb and other limbs. Otherwise, examination was unremarkable.

With these features of focal gigantism, evaluation was initiated and the basic blood and urine investigations were noncontributory. Magnetic resonance imaging (MRI) of lumbosacral spine showed plexiform neurofibroma involving all right lumbosacral nerve roots extending from the level of the right neural foramen to the formation of sciatic nerve (Fig. 3). A lobulated intraspinal and extradural tumor component of the right L4 nerve root were seen, which was indenting on underlying thecal sac and nerve roots. The intraspinal tumor component was causing widening of the right L4/L5 neural foramen. MRI of the abdomen and pelvis revealed the plexiform thickening of entire right lumbosacral neural plexuses with abnormally thickened sciatic and femoral nerves causing mass effect on pelvic colon and bladder neck (Fig. 4). MRI of the right lower limb showed extensive and conglomerate soft tissue masses of NF infiltrating the subcutaneous fat and muscles with resultant atrophy and poor differentiation of

Figure 1: Patient's photographs showing gigantism of the right lower limb

Figure 2: Patient's photographs showing gigantism of the right lower limb

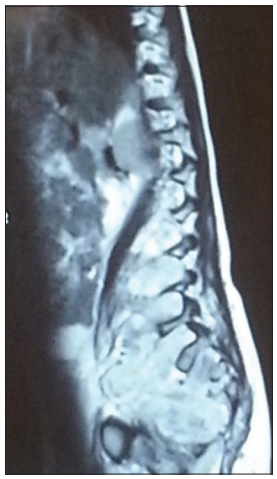

Figure 3: Magnetic resonance imaging lumbosacral spine sagittal view showing plexiform neurofibromatosis of all right lumbosacral nerve roots extending from the level of the right neural foramen to the formation of sciatic nerve

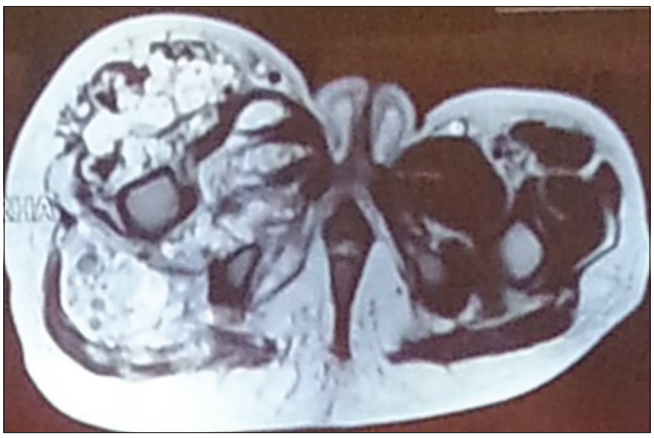

Figure 4: Magnetic resonance imaging lower limb (axial view) showing neurofibromatosis in the right thigh with atrophy and poor differentiation of muscles of all the compartments

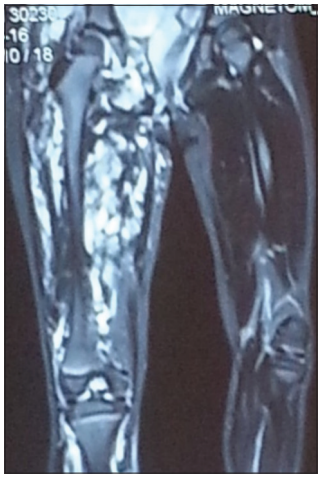

Figure 5: Magnetic resonance imaging lower limbs (coronal view) showing neurofibromatosis with soft tissue hypertrophy along with atrophy and poor differentiation of lower limb muscles of all the compartments in the right side

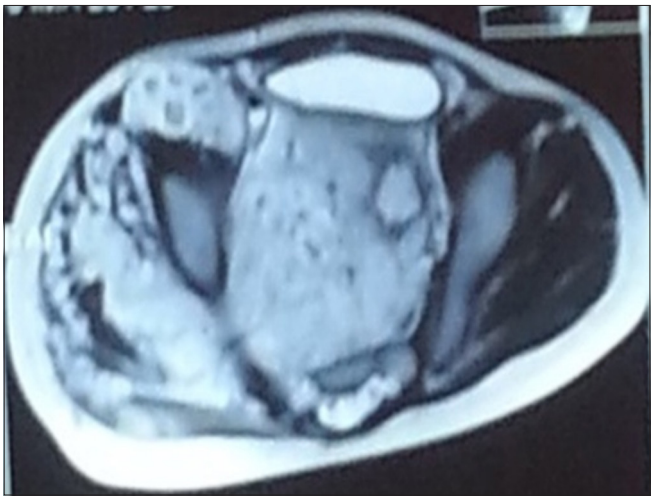

Figure 6: Magnetic resonance imaging abdomen and pelvis showing the plexiform thickening of entire right lumbosacral neural plexuses causing mass effect

muscles of all the compartments from gluteal region to the foot (Figs. 5 and 6). Histopathological examination of tumor mass was not done. These clinical features and neuroimaging findings suggested the diagnosis of EN although we could not confirm it by genetic studies due to non-availability at our center.

DISCUSSION

EN is a rare complication of plexiform neurofibroma which manifests as hypertrophy of an extremity [1,2]. Plexiform neurofibroma, in its most extreme form, may involve an entire extremity, with severe hypertrophy of the skin, soft tissues, and the underlying bony structures which results in focal gigantism [8]. The affected limb may become very large and deformed, and is, therefore, termed as "EN" [5]. The tumor masses of plexiform NF may be extensive and produce the appearance of "bag of worms" [6]. Plexiform neurofibromas are often hypervascular and can lead to massive spontaneous hemorrhage or severe bleeding during surgery. Apart from neurofibroma, patients with EN may have other features of NF such as café-au-lait macules, axillary or inguinal freckles, skeletal abnormalities, optic glioma, and Lisch hamartomas in iris. Among the seven diagnostic criteria prescribed, at least two are needed to make the diagnosis of NF. Our patient had three of the diagnostic features such as plexiform neurofibroma, strong family history (father was a neurofibromatosis patient), and café-au-lait spots, which confirmed the diagnosis.

The radiological modalities, most often used in analyzing neurofibroma, are computed tomography (CT) and MRI. CT is inferior to MRI in making specific diagnosis though it may be useful to provide a precise evaluation of the bone lesion and the extent of the soft tissue lesion [9]. MRI is better in soft tissue contrast resolution and the visualization of tissue planes. Furthermore, MRI study of involved limb may demonstrate the target sign, fascicular sign, and split-fat sign, typical features of neurofibromatosis [1]. In addition, MRI and magnetic resonance angiography are useful in imaging the vasculature of a plexiform neurofibroma which is essential for proper surgical planning [9]. Apart from the radiological evaluation, tissue biopsy and histopathological study, sequencing of the NF-1 gene through molecular testing, are useful in confirming the diagnosis [4].

The common differential diagnoses are other soft tissue lesions and tumors causing elephantiasis such as filariasis, macrodystrophia lipomatosa, lymphangiomatosis, and vascular malformation such as hemangioma and massive subperiosteal hematoma [10]. In addition, other dysplastic, hamartomatous disorders such as Proteus syndrome and Klippel-Trenaunay-Weber syndrome should also be considered.

The symptoms characteristic of Klippel-Trenaunay-Weber syndrome is venous varicosities, extensive nevus flammeus or cutaneous hemangiomas, and hypertrophy of soft tissue and bones [11]. In our patient, Klippel-Trenaunay-Weber syndrome was ruled out by the absence of cutaneous hemangioma and the presence of diagnostic features of NF I. Another important differential diagnosis is the Proteus syndrome, a rare complex hamartomatous postnatal overgrowth syndrome [9]. It is characterized by partial gigantism of the hands, feet, or both, plantar hyperplasia, and hemangiomas of the spleen, lipomas, lymphangiomas, varicosities, verrucous epidermal nevi, macrocephaly, and cranial exostosis. Essentially, any tissue or organ can manifest overgrowth including the spleen, kidneys, thymus, gut, and the brain. The history, clinical examination, and MRI scan of lumbosacral spine and lower limb were helpful to make the diagnosis of EN in our patient as well as to rule out the other conditions.

EN may produce severe functional impairment of the involved limb with affected quality of life, along with cosmetic disfigurement and psychological stress. Treatment for diffused and progressive plexiform neurofibroma is primarily surgical [12], as massive soft tissue neurofibroma does not respond to chemotherapy or radiotherapy [13]. However, complete resection of the tumor is not possible because of marked entanglement of the tumor with the nerves. Also there is a potential for regrowth from the residual tumor. Hence multiple surgeries may be needed. In addition, there is high risk of bleeding at surgery [13].

The prognosis of EN depends on various factors including the site of involvement, the severity of the signs and symptoms, and the surgical management. In many patients, it is difficult to completely restore the affected limb to normal quality and surgical resection and restoration is often challenging. In our patient, hypertrophied right lower limb had resulted in minimal functional impairment as well as cosmetic disfigurement. Hence, pediatric and plastic surgeons consultations were advised, but parents did not turn up for follow-up treatment.

CONCLUSION

As a preventive measure, in people with family history of neurofibromatosis, genetic testing of the expecting parents and prenatal diagnosis with molecular testing of the fetus during pregnancy may help in understanding the risks better during pregnancy. In addition, genetic counseling will help assess the risks before planning for a child.

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