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Giant Plexiform Neurofibroma of the Thigh: A Case Report

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Abstract **Case Report**

Neurofibromas are known to manifest most frequently as localized lesions, less frequently as a diffuse form, and rarely as a plexiform variety We report the clinical and imaging features of a young male patient with biopsy proven plexiform neurofibroma (PNF). A 23 years old male, followed for neurofibromatosis type 1, plexiform lesions of the left lower limb progressively increasing in volume with scrotal extension. The MRI showed thickening of the cutaneous and subcutaneous soft tissues on the medial and posterior aspect of the left thigh, extending to the perineo-scrotal region. The role of imaging is important for a variety of reasons, including delineating the extent of involvement and effect on adjacent structures, exposing associated anomalies and last but not least, for predicting possible malignant transformation. MRI is the reference standard modality for evaluating neural tissues and also for delineating the parent nerve in cases of tumors of neural origin. Therapy of plexiform neurofibromas is usually surgical, aiming at resecting deforming masses and cancerous tissue when malignant transformation occurs.

Keywords: Plexiform neurofibroma, neurofibromatosis, imaging**.**

INTRODUCTION

Neurofibromas are known to manifest most frequently as localized lesions, less frequently as a diffuse form, and rarely as a plexiform variety [1, 2]. The plexiform variety is a least common form of neurofibromatosis which occurs in 5%, defined as one arising from multiple nerves and their branches and infiltrating the surrounding soft tissue and skin, has been less frequently described in radiology literature.

The clinical concern in a plexiform neurofibroma is not only towards the significant cosmetic disfigurement, and compression of the adjoining vital structures, but also due to its potential towards malignant transformation, which occurs in approximately 10% of cases [2].

The risk of malignancy increases with the duration of disease as well as according to size of lesion. The commonest malignancy in plexiform neurofibromatosis is Malignant Peripheral Nerve Sheath Tumors (MPNST) [3].

We report the clinical and imaging features of a young male patient with biopsy proven plexiform neurofibroma (PNF).

CASE REPORT

A 23 years old male, followed for neurofibromatosis type 1, plexiform lesions of the left lower limb progressively increasing in volume with scrotal extension.

On clinical examination we find a large left lower limb with obvious skin thickening extending to the scrotal region. Our patient had numerous café au lait spots and one plexiform neurofibroma. There was no significant personal or family history.

The MRI showed thickening of the cutaneous and subcutaneous soft tissues on the medial and posterior aspect of the left thigh, extending to the perineo-scrotal region, measuring 6.6 cm in maximum thickness at mid-thigh, extending over 37 cm, in T1 hyposignal, T2 hypersignal and STIR, diffusion hypersignal with high ADC, significantly enhanced after injection of Gadolinium.

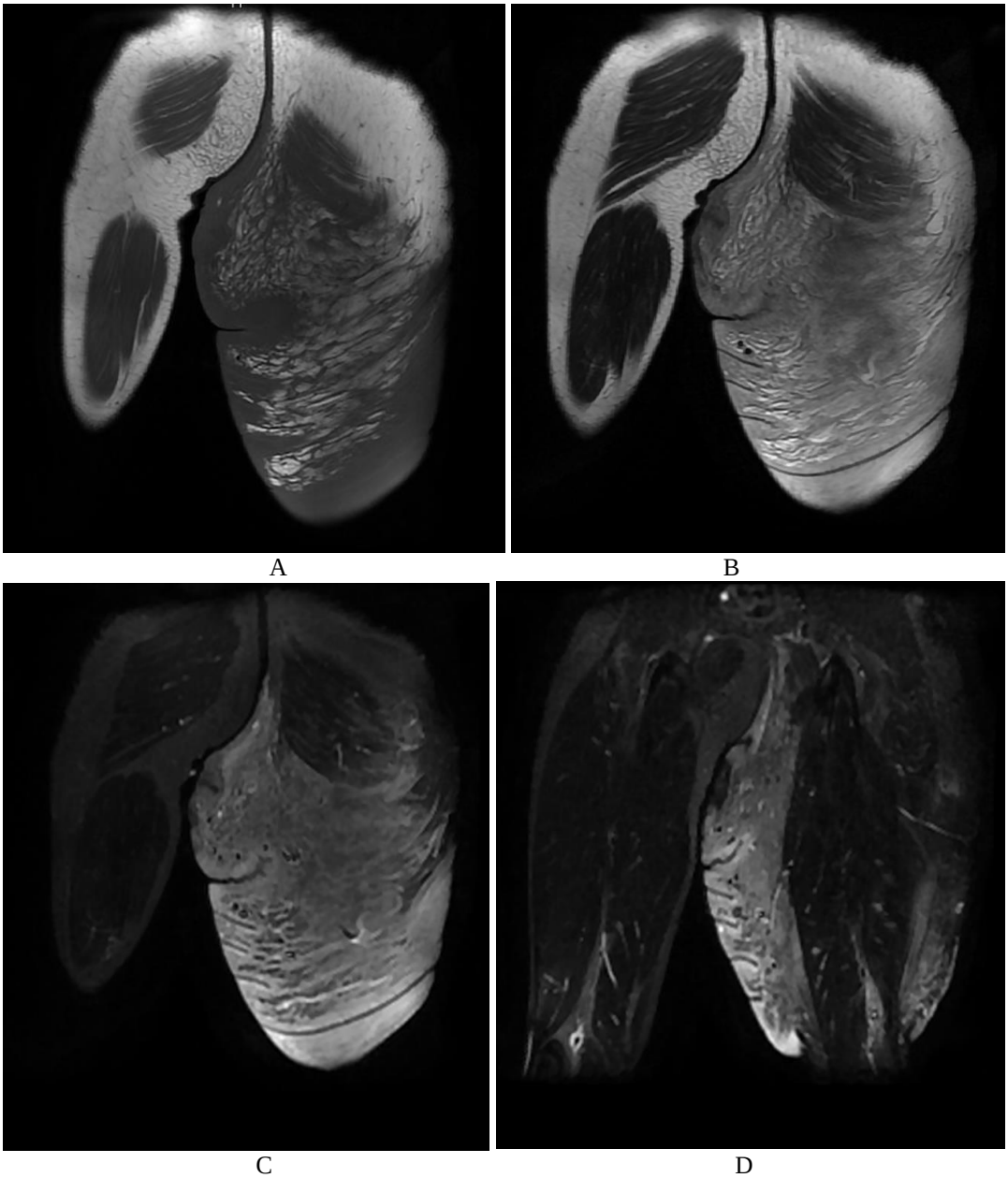
This thickening extends to the perineal region with invasion of the ischio-anal spaces more marked on the left ; it extends also to subperitoneally space without detectable intraperitoneal extension and to Left

intergluteal fold and also to The scrotal region without detectable testicular involvement.

This thickening reaches the popliteal region without detectable invasion of the popliteal fossa. And depply reaches the level of the muscular aponeurosis which is thickened and infiltrated, with no detectable extension to the muscle compartments (Figure 1 and 2).

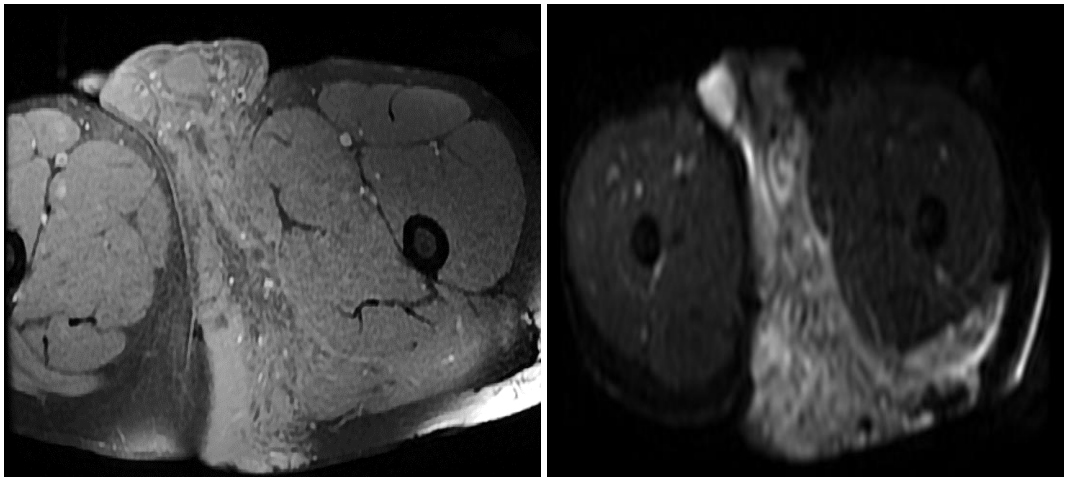
MRI appearance in favor of plexifroma neurofibroma of the left thigh with homolateral perineo-scrotal extension.

The patient underwent a Biopsy confirming the diagnosis of plexiform neurofibroma (PNF).



A B C D

Figure 1: Coronal view of T1 Sequence (A) T2 Sequence (B) and STIR sequence (C, D) demonstates: a thickening of the cutaneous and subcutaneous soft tissues on the medial and posterior aspect of the left thigh, extending to the perineo-scrotal region, with High signal changes on both STIR and T2W images



E F

Figure 2: Axial view of T1 post Contrast sequence (E) Axial view of Diffusion sequence demonstates a significantly enhanced of the cutaneous and subcutaneous soft tissues on the medial and posterior aspect of the left thigh, after injection of Gadolinium with high signal abnormalities in diffusion sequence

DISCUSSION

The term neurofibromatosis describes a group of genetic disorders that primarily affect the cell growth of neural tissues. At least eight forms of neurofibromatosis have been recognized, the most common form being neurofibromatosis type I (NF-I) [4].

Neurofibromas are the most common benign tumors of NF-I. These can develop at any point along a nerve and often form by late adolescence. Three subtypes of neurofibromas exist: cutaneous, subcutaneous and plexiform. The plexiform variety is specific for the disease [5].

Plexiform neurofibroma is an irregular, thick and non circumscribed tumor of peripheral nerve sheath which can involve multiple nerve fascicles. These are slow growing, painless and locally infiltrating tumors. The consistency of the lesion is compared to 'bag of worms' [6].

The disease is manifested by developmental changes in bone, skin and nervous system. Its incidence is estimated to be 1/2500 births per year and its penetrance is almost complete by 5 years of age. The NF1 gene responsible for the disease is located on chromosome 17 at locus 17q11.2 that codes for protein neurofibromin [7, 8]. The pattern of inheritance is autosomal dominant. The size of lesion can increase during pregnancy and puberty [2].

The term "plexus" refers to a combination of interlaced parts or a network. Plexiform neurofibromas are uncommon and occur almost exclusively in about 5-15% patients with neurofibromatosis-I. Two types of plexiform neurofibromas have been recognized: (a) a diffuse type/ elephantiasis neurofibromatosa and (b) a nodular type [9, 10].

The cranial nerves most commonly involved in plexiform neurofibromas are the fifth, ninth, and tenth. These masses can be quite disfiguring, and hemifacial hypertrophy can occur. These tumors are known to cause symptoms ranging from minor discomfort to extreme pain.

These lesions sometimes demonstrate a vascular nature, and they may cause dangerous bleeding and complicate surgical procedures. The size of these tumors may increase during puberty and pregnancy [11].

These lesions manifest early in life and tend to transform to malignant peripheral nerve sheath tumors (MPNST). Malignant progression is generally considered the main cause of mortality, occurring in 2% to 16% of cases [12].

The role of imaging is important for a variety of reasons, including delineating the extent of involvement and effect on adjacent structures, exposing associated anomalies and last but not least, for predicting possible malignant transformation.

The role of sonography as a primary modality remains to be recognized not only for the exclusion of simulating conditions at the earliest instance of imaging, but also because a radiation free technique is preferable in the younger population; The earliest description of the sonographic appearances of plexiform neurofibroma was perhaps by Reuter *et al.*, who described these tumors as comprising of hypoechoic nodules, which needed to be distinguished from an abscess and a vascular malformation [13]. However, a more definitive description was emphasized by Hong *et al.*, who described this entity as a poorly marginated tumor, comprising of multiple hypoechoic nodules on a hyperechoic background with significant vascularity [14].

The CT features of plexiform neurofibroma have been described as being typically low attenuation due to the myelinlipid content, fat entrapment and high-water content in endoneurial myxoid tissue [15, 16]. The role of CT is important to assess bony involvement.

MRI is the reference standard modality for evaluating neural tissues and also for delineating the parent nerve in cases of tumors of neural origin. In plexiform neurofibromas, the tumor has been described as being characteristically lobulated with a hyperintense signal on T2W imaging. A "target sign" has been described as being pathognomonic for plexiform neurofibroma and each "target" focus is believed to depict the individual involved nerve fascicle. The lesion has a central low intensity surrounded by a rim of high intensity, especially when oriented in the longitudinal direction of the nerve [15-17]. The central low intensity is due to the fibrous component and the surrounding myxoid elements lend the hyperintense signal. A "reverse target sign" has also been described in plexiform neurofibromas which is characteristically seen on contrast enhanced scans [1]. A similar appearance of a lobulated tumor with multiple foci showing target sign was seen in both our patients on T2W and on fat suppression sequences. The appearance reported on T1W sequences is that of a tumor hypointense to adjoining muscles, which was also seen in our patient. There is a distinct role for contrast enhanced MRI, to demonstrate peripheral enhancement, if the tumor is suspected to be undergoing malignant transformation [15]. The latter is indicated on non-contrast studies by perilesional edema, intratumoral cystic changes and heterogeneity on T1W images [15].

In cases with MRI signs suggestive of malignant transformation into a malignant peripheral nerve sheath tumor (MP NST), PET–CT is valuable in guiding the site for biopsy as well as for confirming malignancy [15]. Since the clinical stigmata of NF1 and the imaging features of plexiform neurofibroma are characteristic, a differential diagnosis may need to be considered only in those patients who lack overt clinical features. On ultrasound, the tumor may be mistaken for a vascular malformation and the distinguishing features include absence of a normal arborizing pattern and presence of a low resistance flow in the latter. The other entities which need to be excluded are infiltrative soft tissue sarcomas, such as a dermatofibrosarcoma protuberans, plexiform fibrohistiocytic tumor and desmoplastic melanoma [2].

Therapy of plexiform neurofibromas is usually surgical, aiming at resecting deforming masses and cancerous tissue when malignant transformation occurs. However, these masses tend to recur in 20% of cases despite an appropriate approach [2].

In unresectable, progressive and symptomatic lesions, good results have been reported recently after the administration of interferon-a. [19, 20]. However, the prognosis is still unpredictabledue to the high risk of progression of the disease and its variable expressivity [21].

CONCLUSION

Plexiform neurofibromas are a subset of neural tumors which occur characteristically in patients with NF1. The tumors which originate from nerve sheath, are large, lobulated masses and demonstrate characteristic imaging features of simultaneous involvement of subcutaneous and cutaneous tissues along with infiltrative invasion of deeper structures.

Imaging plays an important role in confirming the diagnosis, delineating involved structures, excluding simulating conditions and malignant transformation.

Patient Consent

The authors confirm that a written informed consent in the local language was obtained from the patient for publication of the case report, on the conditions of maintaining anonymity of identity.

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