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Giant plexiform neurofibroma of lower limb: Importance of radiology in diagnosis, complications and management

Udeagu G. C[1], *Njeze N. R*[2], *Ukwuaku C. C*[1]

[1]*Department of Radiology, Imo State University Teaching Hospital Orlu, Nigeria.*
[2]*Department of Radiation Medicine, Faculty of Medical Sciences, University of Nigerian, Enugu, Nigeria.*

Abstract

Plexiform neurofibromatosis is reported to occur in 26.7% of patients with type I neurofibromatosis. Plexiform neurofibromas present at, or soon after, birth as areas of hyperpigmentation, thickening of the skin and excess hair. In 50 percent of cases, it results from autosomal dominant transmission and in the remaining 50 percent of cases it arises as a spontaneous genetic mutation with no known cause. It affects all three germ layers and it is capable of involving any organ system. Plexiform neurofibroma pathognomonic of von Recklinghausen disease (neurofibromatosis type 1) and the gene responsible for the disorder is located in the chromosome region 17q11.2. The aim of this article is to report a rare case of giant plexiform neurofibromatosis in 15 year old Nigerian boy, its complications, its association with birth mark and hyperpigmentation, and its management.

Keywords: Left lower limb, giant plexiform neurofibromatosis.

Introduction

Neurofibromatosis is an inherited disease caused by one of two genetic processes. In 50 percent of cases, it results from autosomal dominant transmission and in 50 percent of cases it is a spontaneous genetic mutation with no known cause.[1] Rarely, neurofibromatosis is caused by deletion of the NF1 or NF2 gene.[1] Plexiform neurofibromatosis is reported to occur in 26.7% of patients with type I neurofibromatosis.[2] Plexiform neurofibromas present at, or soon after, birth as areas of hyperpigmentation, thickening of the skin and excess hair.[3,4] It is autosomal dominant inherited disorder probably of neural crest origin. It affects all three germ layers and it is capable of involving any organ system. Plexiform neurofibroma (pathognomonic of (NF1) von Recklinghausen disease and the gene responsible for the disorder is located in the chromosome region 17q11.2.[5,6]

The prevalence of NF1 has been estimated to be about 1/3500 in the USA and the United Kingdom and its birth incidence has been reported to vary from 1/2558 to 1/4292, the mutation rate being 3.1×10^{-5} to 6.5×10^{-5}. Its peak age prevalence is 20-29 years.[4] The incidence of NF2 is 1/50,000 birth.[6] Sex incidence-F: M=1:1.[6]

This case was presented because plexiform neurofibromatosis is a rare pathology in our environment. Its prevalent rate is 1 in 2558 to 4292 births.

Corresponding Author: Dr. Godwin Chukwuemeka Udeagu

Department of Radiology,
Imo State University Teaching Hospital,
Orlu, Nigeria.
E-mail: udeagugg@gmail.com

Case report

Patient was a 15 year old boy who presented at the hospital with inability to walk following abnormal swelling in the left leg. This patient was born with a large birth mark on the posterior aspect of the left leg. At the age of 7 years he noticed a swelling on the dorsum of the left foot. This swelling ascended to the whole left lower limb and to the trunk. His 52 year old father had a similar condition but no history

of same illness on both fathers' and sons' siblings. On examination, patient looked ill, wasted and in obvious distress. He was afebrile, pale and well oriented in time place or person. Examination of musculoskeletal system revealed grossly enlarged left lower limb. The swelling extends from the left foot to left lower back (trunk) with associated multiple hyper pigmentation on the body (cafe au-lait spot). Muscle power on the left lower limb was grade 1 and grade 5 on the right lower limb. The cardiovascular system, respiratory system and central nervous systems examination appear normal. Plain radiograph of the left lower limb revealed excessive soft tissue growth involving the whole left lower limb with defective modeling, over growth and under growth of the left femur and bones of the foot. The distal tibia and fibula also appear incomplete with significant callus formation suggestive of pseudoarthrosis. A diagnosis of plexiform neurofibromatosis was made.

Fig 1: Gross image of 15 year old boy with abnormal soft tissue swelling of the left lower limb (X) due to plexiform neurofibromatosis.

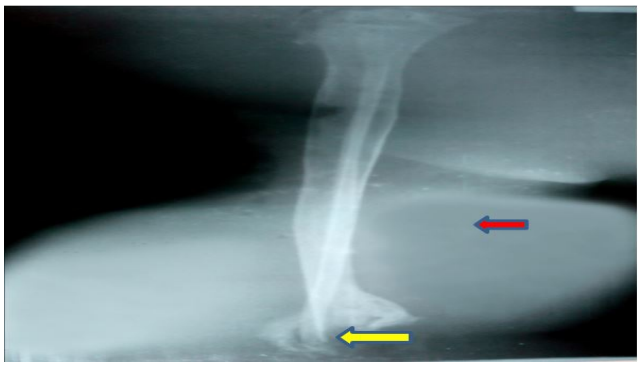

Fig 2: Antero-posterior radiograph of the left leg showing huge soft tissue swelling (red arrow) with associated bone destruction and pseudoarthrosis of the distal left tibia and left fibula (yellow arrow).

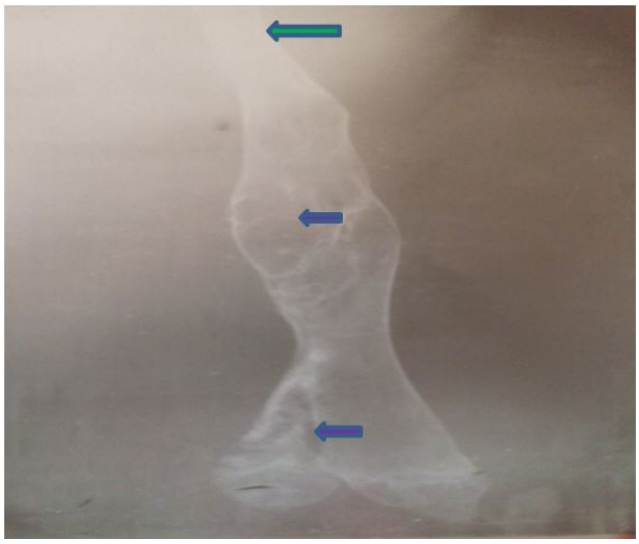

Fig 3: Antero-posterior radiograph of left thigh showing thinning of the superior aspect of the left femur (green arrow) and multiple lytic destructive lesions in the middle and distal aspect of left femur (purple arrows) due to plexiform neurofibromatosis.

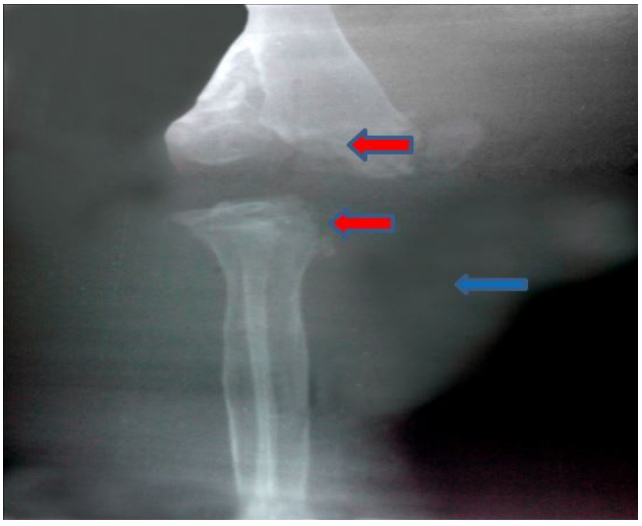

Fig 4: Antero-posterior radiograph of the left knee joint showing huge soft tissue swelling of the left lower limb (blue arrow) and lytic destruction of the articular bones of the left knee joint (red arrows).

Discussion

Type 1 or peripheral neurofibromatosis (NF1) is characterized by peripheral lesions and bone disorders while type 2 or central neurofibromatosis is characterized by multiple acoustic schwannomas, meningiomas, etc.[6] Cutaneous findings in NF1 include café-au-lait spots, axillary freckling, skeletal dysplasia and growth of both benign and malignant nervous system tumours especially

benign neurofibroma.[7] NF1 occurs more commonly, in approximately 1 in 3000 births, whereas NF2 affects roughly 1 in 25,000-50,000 individuals.[6,8] In index case cutaneous findings like multiple cafe'au lait sports and axillary freckling are noted which is in agreement with the study of David T Hsieh and Amy Kao.[7]

Neurofibromatosis is caused by one of two genetic processes like autosomal dominant transmission and spontaneous genetic mutation but rarely, neurofibromatosis is caused by deletion of the NF1 or NF2 gene.[1] In the present case patient inherited the disease from his father as an autosomal dominant transmission of NF1 gene as in the studied literature.[1] Predisposing factors include advance paternal age > 35 years. In this case patient father was 37 years and he had cutaneous neurofibromatosis as evidenced by multiple cafe au lait spots. The father bore this child at the age of 37 years.

Children with NF1 frequently develop orthopaedic problems like spine deformities, particularly scoliosis/ kyphoscoliosis and tibia dysplasia. Others may develop overgrowth of a limb without any underlying bony abnormalities. Tibia dysplasia may lead to fracture; pseudoarthrosis and limb length discrepancy. In index case patient had multiple cafe–au-lait spots, multiple cutaneous tumours. He also had excessive exuberant soft tissue overgrowth in the affected lower limb, lower limb length disparity and orthopaedic complications like pseudoarthrosis of distal left femur and tibia and lytic expansile lesions on the femur, these features are in support with the literature of Sutton D.[3]

Diagnosis can be made clinically but radiological investigations like plain radiograph, computed tomography and magnetic resonance imaging can be used to establish complications of the disease on bones and soft tissues. In this case plain radiograph of the lower limb in antero-posterior and lateral projections are used to establish both soft tissue and bone complications of neurofibromatosis in the affected left lower limb.

Massive plexiform neurofibromatosis results in functional disability and severe disfigurement. Resection and debunking of invasive plexiform neurofibromas is associated with a high rate of recurrence. Complete resection developed recurrence in 20% and incomplete resection had a recurrence of up to 45%. It would appear that timely intervention could limit the disfigurement and morbidity associated with large lesion.[9] In the present case there is severe disfigurement of the left lower limb which extends to the left lower back due to delay presentation; this is in support to the study of Power et al.[9]

Plexiform neurofibromas may be difficult to treat surgically, often recurring after resection because of residual tumor cell collections deep in soft tissues. Surgeons must realize that removing some of these lesions can result in substantial blood loss and must be planed accordingly.[10] Giant neurofibromas are very difficult to manage surgically as they are extensively infiltrative and highly vascularized. These types of lesions require complex preoperative and postoperative management strategies.[11] In the index case surgeons declare the lesion inoperable because it extends from the left foot to the left lower back without any zone of transition; this is in support to the studies of David et al,[12] Roberto et al,[11] and Alvin et al,[10] who reported that surgical removal of large plexiform neurofibromatosis is very difficult and is associated with poor prognosis. Malignant peripheral nerve sheath tumors (MPNSTs) are highly aggressive soft tissue sarcomas managed better with radiotherapy.[13]

Malignant progression occurs in 2–16% of patients and is the major cause of morbidity and mortality in NF1.[14] Also Malignant Peripheral Nerve Sheath Tumors comprise approximately 5-10% of all soft tissue sarcomas. They can occur either spontaneously (TP53 mutation) or in association with neurofibromatosis-1 (NF1).[15] It appears to be only increased in NF2 amongst those that have been irradiated and lifetime risk of MPNST in NF1 is between 9–13%.[15,16,17,18] In this case biopsy and histology of the lesion confirmed benign soft tissue tumour from NF1.

Prognosis

NF1 may reduce life expectancy by up to 15 years, usually due to malignant tumors.[19] In index case morbidity is very high and patient was managed conservatively and he died few years after presentation, which is in support of the studied literature.[19]

Summary

The report is on a 'rare' case of left lower limb 'giant' plexiformneurofibroma in a 15-year old

male who presented late; had radiologic investigations showing evidence of bony complications; and whose tumour was deemed 'inoperable.' No form of intervention was done, and tumour followed natural course, with death of the patient a few years after presentation.

Conclusion

A case of left lower limb giant plexiform neurofibromatosis in a 15 year old boy has been presented. This case was presented to show the importance of radiology in the diagnosis, management and complications of this very rare type of neurofibromatosis.

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