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Bilateral extensive linear nodules on upper extremities in a child - a rare presentation of neurofibromatosis type 1 (Recklinghausen disease)

Vijay Zawar[1], *Antonio Chuh*[2]

1. Skin Disease Centre, Nashik, India
2. The University of Hong Kong and Queen Mary Hospital, Pokfulam, Hong Kong

Corresponding author:

Dr Vijay Zawar

Shreeram Sankul Opp. Hotel Panchavati

Vakilwadi, Nashik-422002

Maharashtra State

India

E-mail: *vijayzawar@yahoo.com*

Tel.: 0253-2571820

Fax: 0253-2312056

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Abstract

Background: Type 1 neurofibromatosis is a common neurocutaneous disease characterised by café-au-lait macules, neurofibromas, plexiform neurofibromas, axillary freckling, optic glioma, and Lisch nodules.

Main observations: We report a 10-year old boy with a rare presentation of type 1 neurofibromatosis, presenting with bilateral, multiple linear asymptomatic nodules extending from the axillae to the wrists, bilateral thickening of ulnar and supraorbital nerves, and 16 cafe café-au-lait macules over 0.5 cm in diameter on trunk and extremities, and bilateral axillary freckles. We diagnosed neurofibromatosis 1 clinically on the basis of NIH diagnostic criteria.

Conclusion: As the clinical criteria were fulfilled, we believe that excisional biopsy as an invasive procedure was not clinically indicated for a 10-year-old child in this scenario. The patient has to be followed-up for possible malignant transformation of tumors.

Introduction

Most patients with neurofibromatosis 1 (NF-1) exhibit diffuse neurofibromas and café-au-lait macules. For patients with segmental NF-1, neurofibromas and café-au-lait lesions are localised in one body segment. We describe a 10-year-old boy with multiple linear nodules in both upper extremities, absence of subcutaneous masses on his trunk, but with café-au-lait macules over his trunk and extremities.

Case report

A 10-year old boy had a two year history of slowly progressive, multiple non-painful and non-pruritic slowly progressive nodules on his arms and forearms. He enjoyed good past health, and had no visual disturbance, tinnitus, vertigo or convulsions. His scholarly progress was satisfactory. Physical activities were unaffected. His family members were unaffected except for his grandfather, who had café-au-lait macules on his trunk.

Examination revealed well developed pre-pubertal boy with normal growth parameters. His blood pressure was 120/84 mmHg in supine position in right upper limb. Multiple linear nodules were noted on his both upper extremities, extending from the axillae to the wrists (Fig. 1). All nodules were subcutaneous and measured approximately 0.5-1 cm in diameter and were round to oval in shape (Fig 2-3). The mobility of nodules was higher along transverse direction than such along longitudinal direction. He also had bilateral thickening of ulnar and supraorbital nerves with no neurological deficit. We noted total 16 café-au-lait macules on his body (Fig. 4). All café-au-lait lesions were about 0.5-2.0 cm in diameter. Bilateral axillary freckles were evident (Fig 2). There was mild scoliosis but no tibial bowing, no kyphosis. He also had an irregular, soft, non-indurated movable mass around his right medial malleolus but with no bony abnormality on X-ray. No facial or orbital deformity and no exophthalmos were noted. Pelvis was symmetrical. Gait was normal. Developmental, endocrinal and neurological examinations

revealed no abnormality. No other skin lesion was noted.

We referred the patient to an ophthalmologist, who reported no abnormality on slit-lamp examination. His CT scan of head and pure-tone audiometry reports were normal.

We diagnosed NF-1 based on clinical appearance. We examined all his first-degree relatives, finding no evidence of NF-1. We counselled the family on the diagnostic implications and potential complications of NF-1 for the patient, his family, and his future descendents. His father declined excisional biopsy for one of the lesions for histopathological confirmation. We arranged for regular follow-up for the patient. We advised the family that any pain or increase in size of the nodules might implicate malignant transformation, and that excisional biopsy might be indicated then.

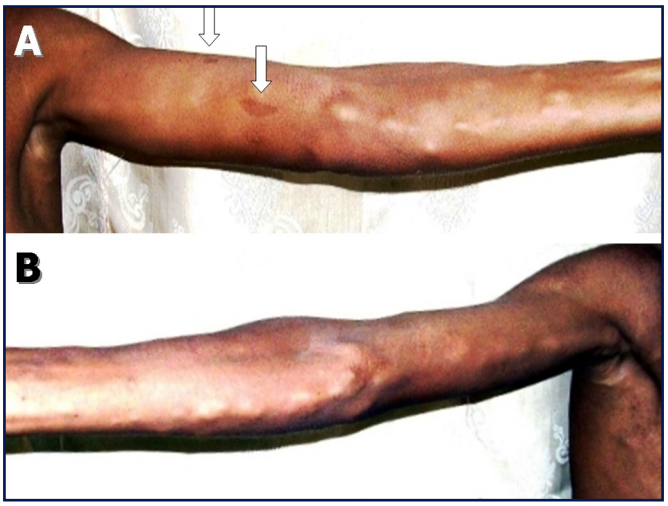

Figure 1

Multiple linear nodules extending from the axilla to the wrists on left (A) and right (B) side. Arrows point to two café-au-lait macules.

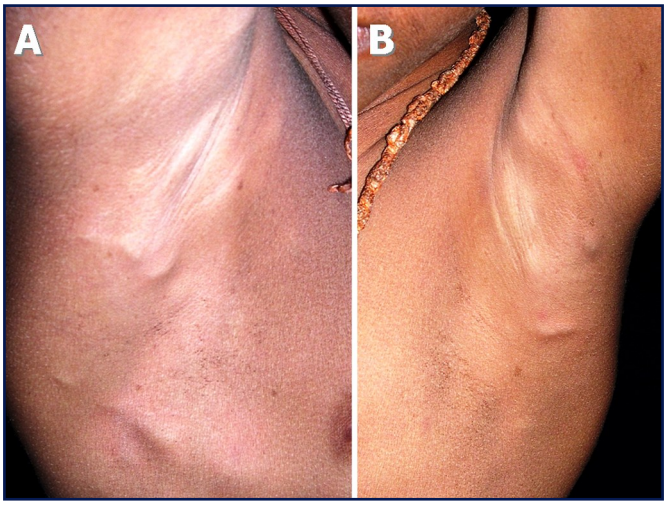

Figure 2

Axillary freckles in right (A) and left (B) axillae.

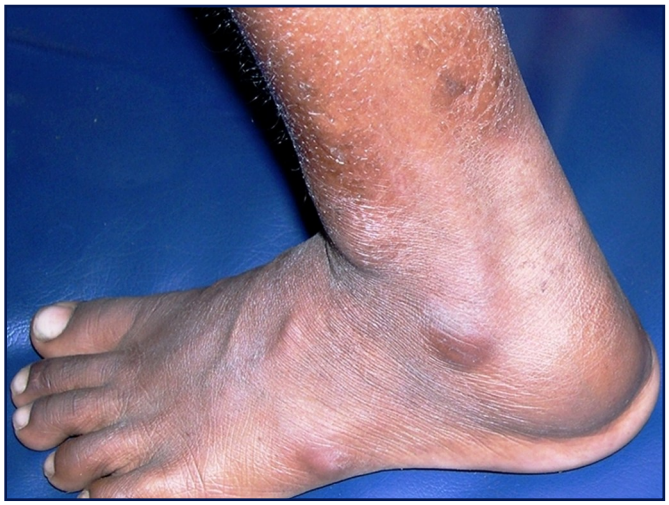

Figure 3

A soft subcutaneous mass around left ankle with no radiological evidence of pseudoarthrosis.

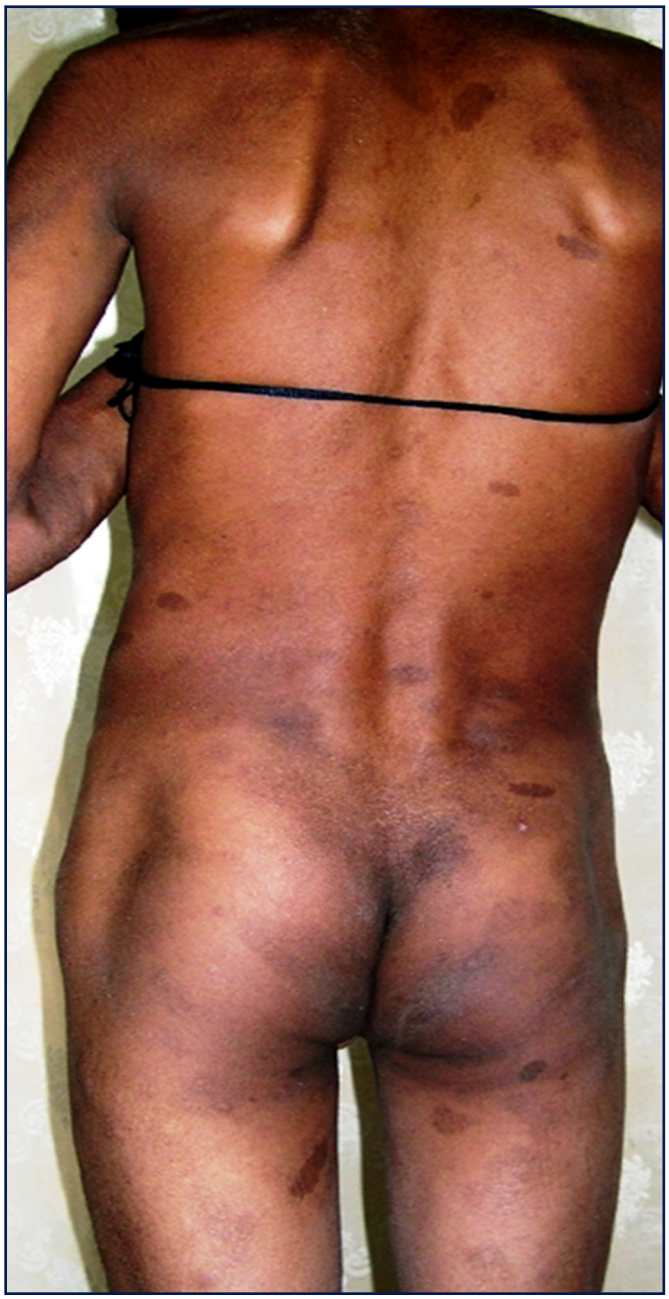

Figure 4

Mild scoliosis in thoracic spine and multiple café-au-lait macules on the trunk.

Discussion

NF-1, also known as von Recklinghausen's disease or peripheral neurofibromatosis, is a common neurocutaneous disease. The diagnostic criteria are at least two of the seven cardinal clinical features: (1) six or more café-au-lait macules over 5 mm in greatest diameter in pre-pubertal individuals and over 15 mm in greatest diameter in post-pubertal individuals, (2) two or more neurofibromas of any type or one plexiform neurofibroma, (3) freckling in the axillary or inguinal regions, (4) optic glioma, (5) two or more Lisch nodules, (6) any distinctive osseous lesion such as sphenoid dysplasia or thinning of the long bone cortex with or without pseudarthrosis, and (7) a first degree relative with NF-1.[1,2]

Table 1
NIH Diagnostic criteria for neurofibromatosis type 1[1]

At least two of the seven criteria need to be fulfilled to establish the diagnosis.

- Six or more café-au-lait macules larger than 5 mm in the greatest diameter in prepubertal children and larger than 1.5 cm in postpubertal individuals
- Two or more neurofibromas of any type or 1 plexiform neurofibroma
- Multiple freckles in the axillary or inguinal region
- A distinctive osseous lesion, such as sphenoid dysplasia or thinning of long bone cortex, with or without pseudoarthrosis
- Optic glioma
- Two or more iris hamartomas (Lisch nodules) seen on slitlamp or biomicroscopy examination
- A first-degree relative (parent, sibling, offspring) with NF1, as diagnosed by using the above criteria.

These criteria might not be sensitive enough for the diagnosis of NF-1 in young children.[3] However, the criteria should incur high sensitivity and specificity to be applicable to our patient aged 10.[3] Exhibiting criteria (1) and (3), our patient fulfiled the diagnostic criteria of NF-1. Although NF-1 is transmitted with an autosomal dominant fashion for many patients, in about 30-50% of all patients with NF-1 arises from spontaneous mutation.[4] The absence of family history for our patient is thus not unusual.

The limitation of this report is that lesional histopathological confirmation is not available. However, parents of our patient declined excisional biopsy for one of the nodules, and we therefore duly respect their decision. As the clinical criteria of NF-1 are already fulfilled, we believe that excisional biopsy as an invasive procedure is not clinically indicated for a 10-year-old child in this scenario.

Widespread, bilateral linear nodules along the ulnar nerves in a child without truncal lesions as a presenting manifestation is an extremely unusual and highly striking feature in our patient. The term "segmental neurofibromatosis" is sometimes coined for café-au-lait macules and neurofibromas occurring at a single body segment.[5,6] This condition is presumably caused by mosaicism or hyper-expression of the phenotype along a particular body segment. When these lesions are bilateral, and usually symmetrical, the term "bilateral segmental neurofibromatosis" might be applicable.[7,8] This variant is usually adult-onset, and might be associated with malignancies of the internal organs. Despite neurofibromas limited to bilateral upper limbs, our patient does exhibit truncal café-au-lait macules. We thus believe that segmental neurofibromatosis or bilateral segmental neurofibromatosis are not the proper diagnostic labels for our patient.

The diagnosis of NF-1 is important as long-term multidisciplinary follow-up is necessary for the detection and management of complications.[9] Despite recent advances in understanding the gene and the protein amino acid neurofibromin responsible for NF-1,[10,11] the diagnosis of NF-1 remaines clinical. Sophisticated molecular diagnostic investigations and mutation analyses are not available in most parts of the world including India. We therefore believe that dermatologists and other clinicians diagnosing and managing patients with NF-1 should be alerted to this uncommon clinical presentation of a common phakomatosis.

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