

A Young Male with Quadripareisis and Skin Lesions

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A 21-year-old male presented with spastic quadripareisis, developed gradually over months. He had no pain or restricted movement of neck. Other than features of upper-motor-neuron-lesion of all four limbs, physical examination revealed, multiple Café-au-lait macules (>2cm in diameter) [Fig. 1], bilateral



Fig.-1: Café-au-lait macule

axillary freckles [Fig. 2], multiple subcutaneous neurofibroma [Fig. 3] scoliosis, and a tender soft tissue mass at right lower chest. Chest x-ray postero-anterior view showed scoliosis, extrathoracic soft tissue shadow with invasion of the pleural space, consistent with plexiform neurofibroma, rib notching and “twisted-ribbon” ribs [Fig. 4]. Based on clinical and radiological findings, he was diagnosed as neurofibromatosis type 1. MRI of spine revealed multiple neurofibromas, at cervical and dorsal levels. He was offered neurosurgical management. But he decided for treatment at local health-facility, and was lost to follow-up.



Fig.-2: Crowe's sign / Axillary freckles

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Fig.-3: Subcutaneous neurofibroma



Fig.-4: Chest x-ray postero-anterior view showing scoliosis (black arrows), extrathoracic soft tissue shadow with invasion of the pleural space (white arrows), consistent with plexiform neurofibroma, rib notching (black arrow-heads) and "twisted-ribbon" ribs (white arrow-heads)

Discussion:

von Recklinghausen's disease or Neurofibromatosis type 1, is an autosomal dominant disorder, first described in 1882 by Frederich von Recklinghausen. It is a relatively common inherited condition (worldwide incidence of ~1 per 2500 to 3000 individuals, irrespective of age, gender or ethnicity), caused by a germ-line-inactivating mutation in the *NF1* gene on chromosome 17q11.2, having high predisposition to develop benign and malignant tumours, and associated with increased mortality and morbidity. The disease manifestation is usually apparent from birth, with varying features of multi-organ involvement, especially the nervous system.^{1,2}

Common non-malignant features are café-au-lait macules (earliest clinical manifestation, develops within first 2 years), intertriginous freckles or Crowe's sign (small, usually found in axillary and inguinal region, but may also be present in areas where skinfolds are in apposition, including the neck, above the eyelids and

under the breasts in women), Lisch nodules (benign melanocytic hamartomas of the iris that is pathognomonic for NF1, do not impair vision or cause any medical problems, best detected on slit-lamp examination), neurofibromas (benign Schwann-cell tumours, with four subtypes: cutaneous, subcutaneous, nodular or diffuse plexiform, and spinal, result in discomfort or disfigurement, sometimes both sensory and motor deficits), plexiform neurofibromas (arise from multiple nerve fascicles, typically manifest at birth, can continue to grow during adolescence and early adulthood, can extend into surrounding structures, causing substantial pain and bone destruction, have a lifetime risk of malignant transformation), skeletal dysplasia (short stature, osteopenia, scoliosis, sphenoid wing dysplasia, congenital tibial dysplasia, pseudarthrosis), cardiovascular abnormalities, ranging from congenital heart disease (cardiovascular anomaly, pulmonary artery stenosis) to vasculopathy (renal and cerebral artery stenosis, aortic coarctation, arteriovenous malformations) and hypertension, and neurocognitive deficits.^{1,2} Associated malignant tumours with varying lifetime risk include glioma of the optic pathway, malignant peripheral nerve-sheath tumour, gastrointestinal stromal tumour, breast cancer, leukaemia, pheochromocytoma, duodenal carcinoid tumour, rhabdomyosarcoma etc.¹

Diagnosis of neurofibromatosis type 1 is most commonly made using established clinical criteria (National Institute of Health consensus criteria).^{1,2} Two or more of the following clinical features are sufficient to establish a diagnosis of neurofibromatosis type 1: (1) six or more café-au-lait macules (>0.5 cm at largest diameter in a prepubertal child or >1.5 cm in post-pubertal individuals), (2) axillary freckling or freckling in inguinal regions, (3) two or more neurofibromas of any type or one or more plexiform neurofibromas, (4) two or more Lisch nodules, (5) a distinctive osseous lesion, (6) an optic pathway glioma, and (7) A first-degree relative with neurofibromatosis type 1 diagnosed by the above criteria.³ *NF1* genetic testing is reserved for unusual presentations or reproductive decision-making.¹

Routine and cheap investigations like chest radiograph can be very important in diagnosis. Kyphoscoliosis, a hallmark of neurofibromatosis, can easily be visualized,

if not evident physically.⁴In chest radiographs, ribs appear notched, due to erosion by neurofibromas in intercostal nerves in the neurovascular grooves,⁴ whereas “twisted-ribbon” ribs reflect mesodermal bone dysplasia.⁵Plexiform neurofibromas are poorly delineated diffusely infiltrating multiple masses that arise along the axis of the major nerves, better viewed with CT or MRI.⁵

A multidisciplinary approach to care throughout the lifetime of the patient has been suggested for the appropriate management of neurofibromatosis type 1. With the enhancing knowledge on the disorder, swift implementation of newer effective treatments is also becoming possible.¹ Prompt diagnosis is important to provide optimum care. But because of the varying clinical presentation, patients can present to different medical and surgical specialists and, symptoms might not be recognized. So clinicians must be aware of the diverse

features of this disorder, both clinical and radiological, and be vigilant to detect the disorder early.

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