A Young Male with Quadriparesis and Skin Lesions

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A 21-year-old male presented with spastic quadriparesis, 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 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.

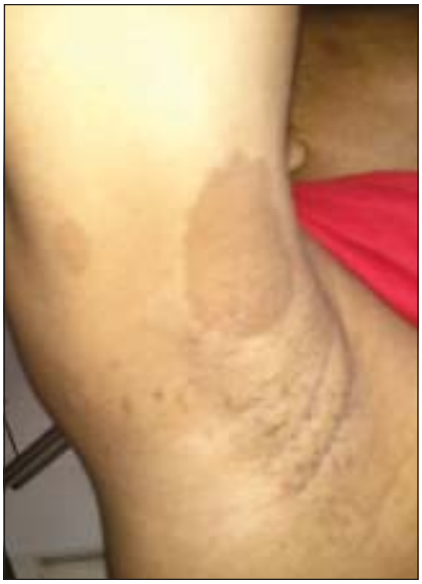

Fig.-1: Café-au-lait macule

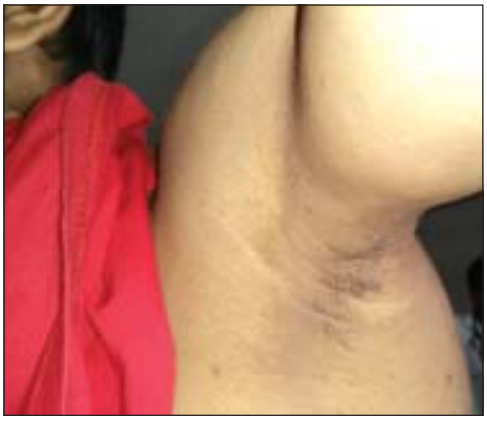

Fig.-2: *Crowe's sign / Axillary freckles*

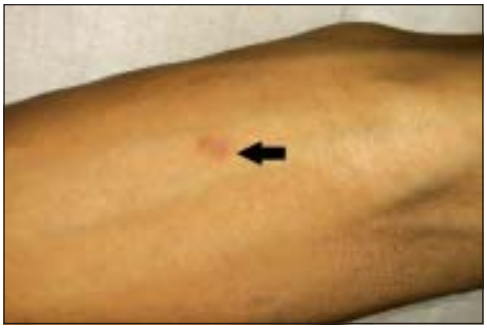

Fig.-3: *Subcutaneous neurofibroma*

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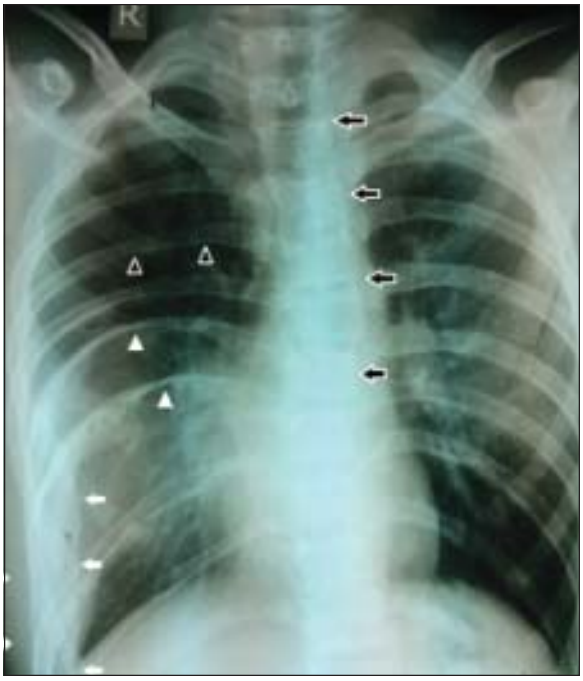

Fig.-4:*Chest x-ray postero-anterior view showing scoliosis (black arrows), extrathoracic soft tissue shadow with invasion of the pleural space (white arrows), consistent with plexiform neurofibroma, rib notching (black arrow-heads) and "twisted-ribbon" ribs (white arrow-heads)*

Discussion:

von Recklinghausen's disease or Neurofibromatosis type 1, is an autosomal dominant disorder, first described in 1882 by Frederichvon 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 frecklesor Crowe's sign(small, usually found in axillary and inguinal region, but may also be present in areaswhere skinfolds are in apposition, including the neck, above the eyelids and under the breasts in women), Lisch nodules (benignmelanocytic hamartomas ofthe iris that is pathognomonic for NF1,do not impair vision or causeany 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, cancontinue to grow during adolescence and early adulthood, can extend into surrounding structures,causing substantial pain and bone destruction, have a lifetime risk of malignanttransformation), skeletal dysplasia (short stature, osteopenia, scoliosis, sphenoidwing dysplasia, congenital tibial dysplasia, pseudarthrosis), cardiovascular abnormalities, ranging from congenitalheart disease(cardio vascularanomaly, pulmonary artery stenosis) to vasculopathy(renal and cerebral artery stenosis, aortic coarctation,arteriovenous malformations)and hypertension, and neurocognitive deficits.[1,2]Associated malignant tumors with varying lifetime risk include glioma of the optic pathway, malignant peripheral nerve-sheath tumour, gastrointestinal stromal tumour, breast cancer, leukaemia, phaeochromocytoma, duodenal carcinoid tumour, rhabdomyosarcoma etc.[1]

Diagnosis of neurofibromatosistype 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 toestablish a diagnosis of neurofibromatosis type 1: (1) six or more café-au-lait macules (>0·5 cm at largestdiameter in a prepubertal child or >1·5 cm in post-pubertalindividuals), (2)axillary freckling or freckling in inguinal regions, (3)two or more neurofibromas of any type or one or moreplexiform 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 1diagnosed by the above criteria.[3]*NF1* genetic testing is reserved for unusualpresentations 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.[4]In chest radiographs, ribs appear notched, due to erosion by neurofibromas in intercostals nerves in the neurovascular grooves,[4] whereas "twisted-ribbon" ribs reflect mesodermal bone dysplasia.[5]Plexiform neurofibromas are poorly delineated diffusely infiltratingmultiple 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 becomingpossible.[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 beaware of the diverse features of this disorder, both clinical and radiological, and be vigilant to detect the disorder early.

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LETTER TO THE EDITOR

(J Banagladesh Coll Phys Surg 2015; 33:184-185)

To

Editor-in-Chief

Journal of Bangladesh College of Physicians and Surgeons.

Sir,

I would like to thank you for publishing the article' Influence of Number of Parity on Bone Mineral Density among Postmenopausal Women'.I have gone through it and found the content nice. I would like to share some of my observations and comments.

Osteoporosis and osteopania among postmenopausal Bangladeshi women are common problem. Low bone mass is the important. Genetic factors play a significant role in determining bone mass. Others are controllable lifestyle factors such as diet and physical activity, environmental factors such as pregnancy and period of lactation. Amenorrhea (cessation of menstrual periods) after the onset of puberty, before menopause, and after menopause is a very serious threat to bone health[1].

Teen pregnant mother that have not yet reached peak bone mass, the 30 g of calcium required for the fetal skeleton competes with the calcium demands for the teen's mineral accretion.It remains controversial whether peak bone mass is compromised in women who experience teen pregnancies[2].

Several changes occur during pregnancy and lactation that can affect bone mass, including changes in reproductive hormones and in hormones that affect calcium metabolism. Since fetal and infant bone growth during pregnancy and lactation depends on calcium transfer from the mother, there is possibility that pregnancy and lactation affect risk for bone mineral loss later in life. Intestinal calcium absorption increases during pregnancy to meet many of the fetal calcium needs, but maternal bone losses may occur in the last months of pregnancy [3].Bone mass may increase due to greater estrogen level in the third trimester of pregnancy. The mother's skeleton also loses bone during breastfeeding, but this loss is largely restored during weaning, as ovulation and menses are re-established. This bone loss and its subsequent restoration appear to be independent of lifestyle behaviors, including dietary calcium intake and physical activity patterns [4]. Some studies indicate that neither extended lactation nor multiple pregnancies are associated with subsequent osteoporosis, whether measured by BMD levels or by assessment of fracture risk[5]. In contrast some studies report, the risk of hip fracture in women has been found to decrease by 5-10 percent with each additional child, and there is no apparent association between the duration of lactation and fracture risk[6]. Some researchers' belief that, pregnancy and lactation in healthy adult women do not appear to cause lasting harm to the skeleton. Sadat Ali et al,in their study found that, increased parity protects women from osteoporosis and the severity of the disease . In a study, women with more than 10 pregnancies and extended lactation had BMD levels similar to those in women who have not been pregnant[7]. Cumming RG et al observed that, parity does not have positive correlation to increased risk of fracture[8]. A number of confounding variables influence the effect of parity on BMD, which may contribute to the divergent results in the studies.

Because of the lack of evidence of the potential effects of parity on bone mineral density, the significance of the observed changes in BMD in every bone site and parity remains unclear. Therefore, further well designed observational studies with large sample size should be carried out to confirm these results.Overall I think the article is updated, informative. I would like to thank the authers for their hard work on time demanding common problem .

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Author's Relpy

Thank you madam for careful reading and criticism about my article.There are lot of studies done in different countries to see the relation between parity and bone mineral density. Ozdemir et al, Gurey et al, Hreshchyshyn et al, Ghannam NN shows negative correlation between parity and numbers of pregnancy. Karlsson C et al, Sadat Ali, Cumming R G et al found no relation. Hoffman et al shows BMD increase in subsequent pregnancy. The results of this study were automaticaly generated in machine and subsequent analysis shows negative correlation. Other confounding variables also influence the effect of patity on BMD. I also strongly agree that further well design ed study with larger sample size should be carried out.

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