Buschke-Ollendorff syndrome: A rare and underdiagnosed entity in preadolescent population

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Introduction

Buschke-Ollendorff syndrome is an uncommon inherited disorder of connective tissue which usually follows a benign course. This makes Buschke-Ollendorff syndrome a relatively underdiagnosed disease. However, accurate clinical diagnosis and follow up is vital to prevent patients being subjected to unnecessary interventions and to curtail parental anxiety. It has an autosomal dominant inheritance with incomplete penetrance. Buschke-Ollendorff syndrome has a preadolescent onset with an equal male to female ratio and no racial predilection has been observed.

Case reports

We like to describe four cases of Buschke-Ollendorff syndrome presented to dermatology clinic over a period of 2 calendar years.

Case 1 – 12 year old girl presented with pain in both legs for months and examination revealed linear plaques over both thighs symmetrically (Figure 1). She was otherwise well and radiography was negative for osteopoikilosis and melorheostosis. Dermatopathology revealed an elastoma (Figure 2).

Figure 1. *Linear skin coloured plaques over anterior thigh.*

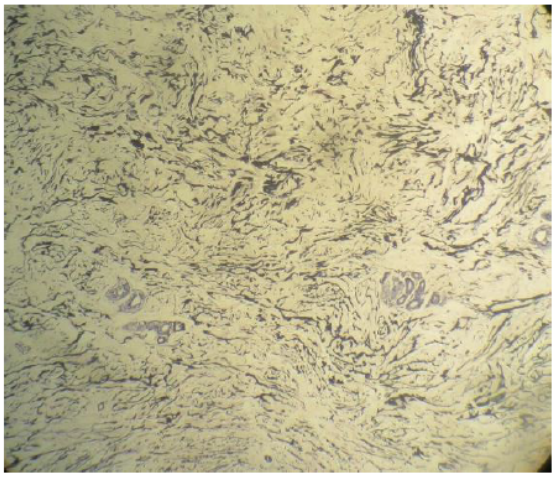

Figure 2. *Orcein staining showing accumulation of interlacing fibers of elastin in dermis.*

Case 2 – 8 years old boy presented with skin lesions over lower abdomen for one year. They were slowly progressing. He complained of right sided hip joint pain for couple of months. Examination revealed subtle, firm, yellowish nodules coalescing to form plaques symmetrically over the lower abdomen (Figure 3). Rest of the clinical examination was unremarkable. Imaging showed osteopoikilosis but no melorheostosis (Figure 6). Histology suggested a collaginoma (Figure 4 and 5).

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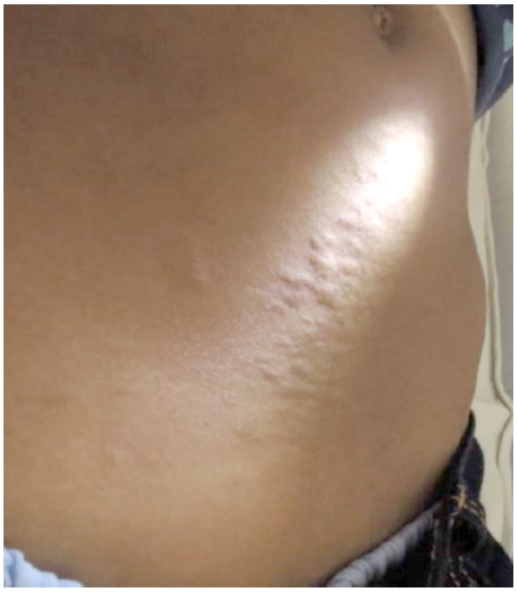

Figure 3. *Typical skin colour thin plaques over trunk.*

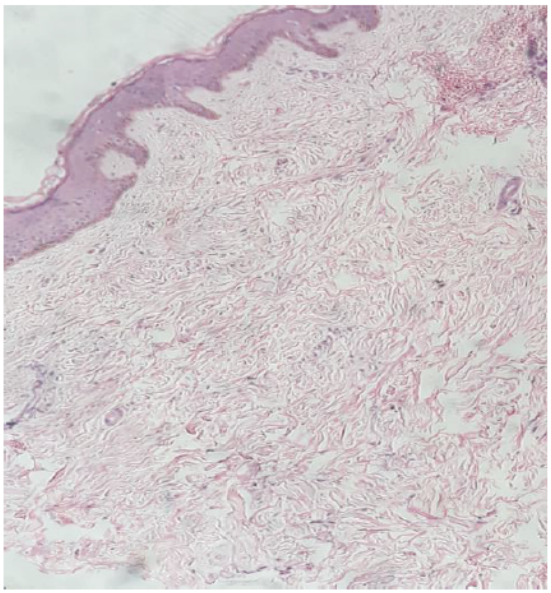

Figure 4. *H & E – thick reticular dermis with broad collagen bands.*

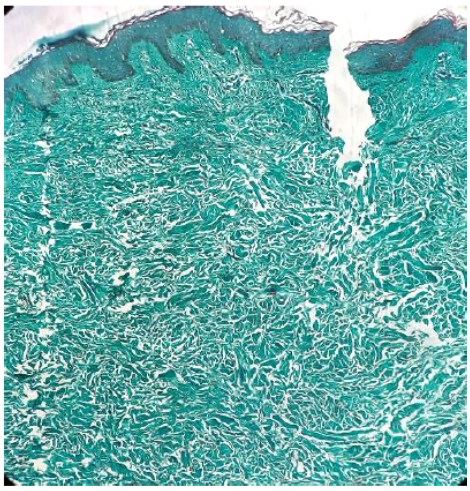

Figure 5. *Masson's trichrome stain confirms presence of collagen.*

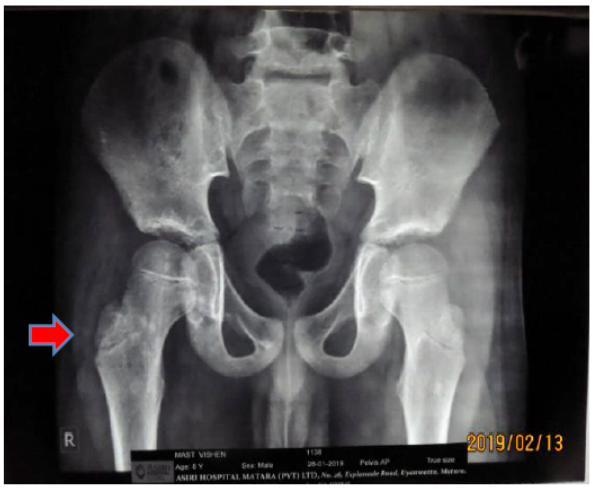

Figure 6. *Early osteopoikilosis.*

Case 3 – 9 years old boy with asymptomatic skin lesions over trunk (Figure 7) for months but no musculoskeletal complains and normal systemic examination. Osteopoikilosis without melorheostosis noticed in radiography (Figure 8). Biopsy of skin lesions revealed a collaginoma.

Case 4 – 7 years old boy presented with typical skin plaques confined to lower abdomen (Figure 9) but slowly progressive asymmetrically over several months. Increased dermal collagen deposition confirmed by Masson's trichrome staining. Typical osteopoikilosis noticed in the long bones (Figure 10).

A family history was absent in all four patients. Ear, cognitive and cardiac evaluations were unremarkable. First patient was lacking skeletal changes and histologically had a pure elastoma. Other three patients had osteopoikilosis and cutaneous histology was positive for a pure collaginomas.

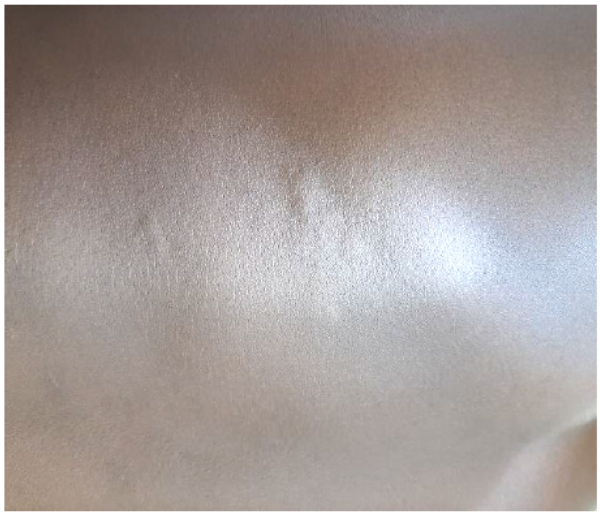

Figure 7. *Thin plaques shown by the light parallel to skin.*

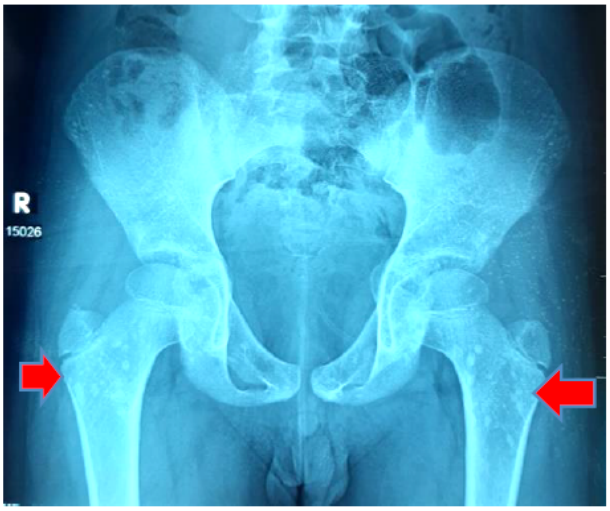

Figure 8. *Osteopoikilosis in femur.*

	Gender	*Age*	*Skin involvement*	*Bone imaging*	*Other system involvement*	*Histology*
Patient 1	Female	12	Linear plaques over thighs, symmetrical	No bone involvement	No	Elastoma
Patient 2	Male	08	Discoid plaques over lower trunk, symmetrical	Osteopoikilosis but no melorheostosis or other changes	No	Collaginoma
Patient 3	Male	09	Discoid plaques over lower trunk, asymmetrical	Osteopoikilosis but no melorheostosis or other changes	No	Collaginoma
Patient 4	Male	07	Discoid plaques over lower trunk,	Osteopoikilosis but no melorheostosis	No	Collaginoma

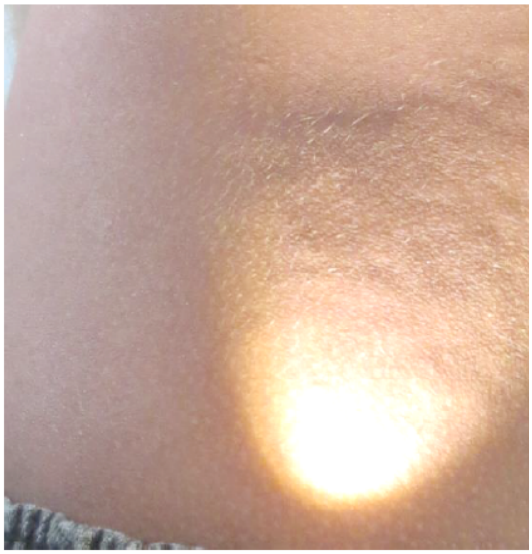

Figure 9. *Thin plaques shown by the light parallel to skin.*

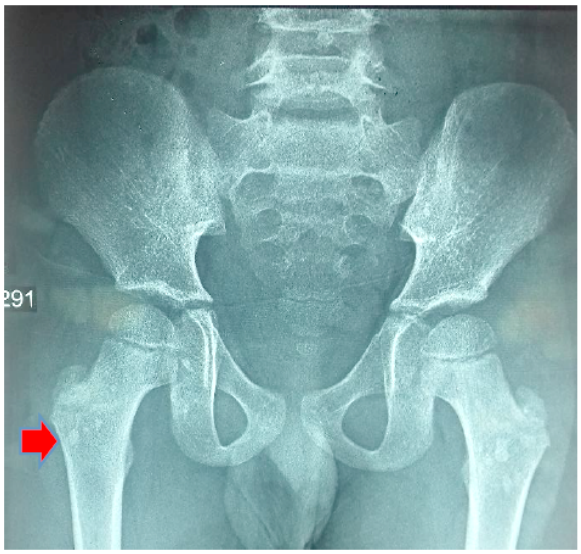

Figure 10. *Osteopoikilosis in femur.*

Discussion

Buschke-Ollendorff syndrome (Dermatofibrosis lenticularis disseminata) is not only rare but also under-diagnosed entity characterized by disseminated connective tissue nevi and focal sclerotic bone involvement. This autosomal dominant disorder is due to a loss of function mutation in the LEM domain-containing protein 3 (LEMD3) gene encoding the LEMD3 protein which antagonize bone morphogenetic proteins (BMP) and tumour growth factor-β (TGFβ) signaling pathways. This leads to abnormal regulation of fibroblasts leading to aberrant expression of dermal collagen and elastic. It is a rare syndrome with an estimated prevalence of 1:20000.

Clinical expression of Buschke-Ollendorff syndrome is variable hence cutaneous and bone manifestations can occur independently with variable phenotype.

Skin lesions present in childhood and favours trunk and proximal extremities. It is characterized by diffuse or localized, asymptomatic slightly elevated, skin coloured papules and plaques which develop slowly over years. Two of our patients had diffuse symmetrical distribution *(dermatofibrosis lenticularis Disseminate)* and in the other two a localized variant characterized of type 2 segmental distribution.

Skeletal manifestations include Osteopoikilosis, melorheostosis, osteoathia striata and mixed sclerotic bone dystrophy. Rarely congenital spinal stenosis, nerve root compression, disc herniation and bone malignancies (osteosarcoma, chondrosarcoma and giant cell tumours) can occur. Melorheostosis is a rare sclerosing bone dysplasia which appears to be allelic with this syndrome, from a second postzygotic somatic mutation but the concurrence of the two diseases was not detected in the four patients.

Other uncommon manifestations include hearing impairment, aortic stenosis and cognitive delay.

Four histological subtypes are noticed. These include pure elastomas, pure collaginomas, mixed connective tissue nevi and cellular connective tissue nevi. Elastomas represent the major histologic subtype. Interestingly 75% (3 out of 4) of our patients were positive for pure collaginomas.

It is interesting to notice that all four patients lack a positive family history which can be due to either incomplete penetrance or de novo mutation. All were positive for connective tissue nevi.

Due to its benign course Buschke-Ollendorff syndrome is easily overlooked. On the other hand, it can lead to an unnecessary anxiety for parents. Less experience on the entity will lead to unnecessary interventions. So it is important for the dermatologists to be aware of Buschke-Ollendorff syndrome.

The complications are rare but well documented hence it is the clinicians' responsibility to arrange longitudinal follow up for patients with Buschke-Ollendorff syndrome.

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