Schimmelpenning syndrome presenting with hypophosphataemic rickets

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Introduction

Schimmelpenning syndrome was first described in 1957 by Schimmelpenning[1]. It is characterized by sebaceous linear naevi with associated neurological, cardiovascular, ocular, urogenital and skeletal abnormalities[2,3,4]. These naevi can secrete phosphoric proteins like Fibroblast Growth Factor 23 (FGF23) and Matrix Extracellular Phosphoglycoprotein (MEPE), leading to hypophosphataemic rickets, which results in deformity and growth failure in children[5,6]. We report a child with diffuse linear sebaceous naevi since birth who presented with bow legs and growth failure due to hypophosphataemic rickets at three years of age.

Case report

A 3-year-old girl presented with pigmented naevi involving her scalp, neck and upper limbs. She was born with one naevus on the scalp and a few scattered naevi on the neck, which increased in size and number and spread along the left arm with growth. Additionally, she had bilateral progressive bowing of the legs with worsening limb pains, mainly with activities. However, she was developmentally normal except for her avoidance of running and jumping owing to the pain. She displayed difficulties in scholastic performance. She neither had seizures nor a family history of bone disease or dermatological issues.

On examination, her weight was 11.9kg (just above 3rd centile), and her height was 85cm (just below 3rd centile).

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There was a large sebaceous naevus in her scalp (Figure 1), verrucose lesions on her forehead and scattered pigmented sebaceous naevi of varying sizes involving her neck and upper arms (Figure 2 a & b). There was bilateral bowing of legs without other clinical signs of rickets. Cardiovascular and neurological systems and vision were clinically normal.

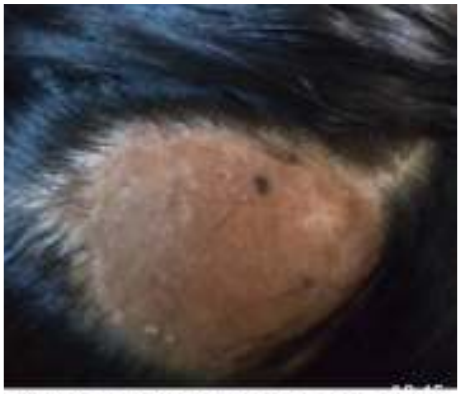

Figure 1: ***Sebaceous naevus on the scalp***

Biochemical evaluation demonstrated hypophosphataemia with a bone profile of serum calcium 2.33 mmol/L (normal range 2.2-2.7mmol/L), serum phosphate 0.92mmol/L (normal range 1.45-1.78 mmol/L) and alkaline phosphatase 874U/L (normal range 60-425U/L). The 25-OH vitamin D level was 71.2 nmol/L (<50 nmol/L - insufficient). At presentation, the parathyroid hormone (PTH) level was 7.8pmol/L (1.59-7.21pmol/L). Urinary investigations showed significant phosphaturia with a markedly reduced tubular reabsorption. Urine phosphate: creatinine was 7.38mmol/mmol (normal range 1.45-2.1). The tubular reabsorption of phosphate was 55.4% (>95% normal). Maximum tubular reabsorption of phosphate [Tubular maximum phosphate reabsorption per glomerular filtration rate (TmP /GFR)] was 0.51mmol/l (normal range 1.05-1.78). There was no associated hypercalciuria (calcium: creatinine 0.03 mmol/mmol (normal range 0.04-0.09mmol/L)). X-ray of lower limbs showed rickets with cupping and fraying of femoral epiphysis (Figure 3). Her 2D-echocardiography, ultrasound scan of abdomen and visual assessment were normal.

(a) (b) (c) (d)

Figure 2: ***Verrucose sebaceous naevus and scattered pigmented naevi on (a) forehead (b) neck (c) right side of face, (d) left side of face***

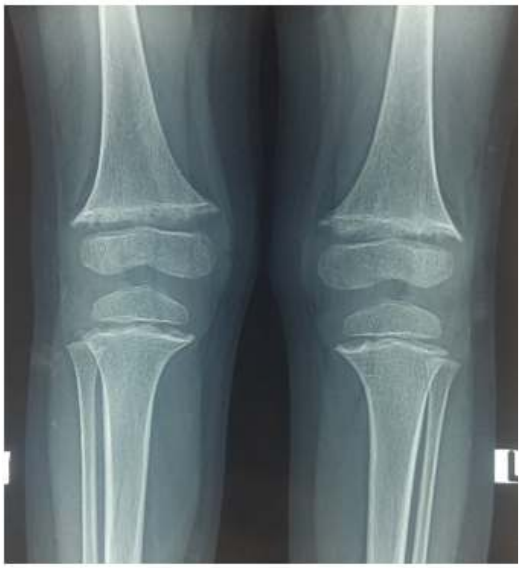

Figure 3: ***X-ray lower limb with cupping and fraying of epiphysis***

She underwent resection of growing naevi on the forehead and right upper limb. The histology showed papillomatosis, keratosis, and acanthosis suggestive of epidermal sebaceous naevi. There was no histological evidence of malignant transformation.

Considering the underlying pathogenesis for hypophosphataemic rickets, she was started on phosphate buffer 4ml 6 hourly (24 mmol/day) with oral 1-α-calcidiol 0.25µg/day. She is on medication for hypophosphataemic rickets with a good biochemical response and improved growth parameters and is under ongoing surveillance for new-onset visual defects.

Discussion

We report a child with Schimmelpenning syndrome who presented with multiple naevi and hypophosphataemic rickets. This is a multisystem disorder that occurs sporadically. It is also thought to originate with mosaicism[5]. This may be the reason for the varied presentation and the system involvement.

The key feature of Schimmelpenning syndrome is the extensively distributed sebaceous naevi, most commonly on the scalp (59.3%) and the face (32.6%)[3,4]. In addition to those sites, her left arm had been involved extensively in our child. As differentiation of the sebaceous cells depends on the androgens, naevi may not show the typical histological pattern before puberty. The commonest malignant transformations are basal cell carcinoma and trichoblastoma, which are rare before puberty[5]. Hence, vigilant dermatological follow-up is mandatory.

Hypophosphataemic rickets has been described with Schimmelpenning syndrome and can lead to severe deformity, growth failure and osteopenia with fractures. The morbidity can be reduced with appropriate treatment. The mechanism for phosphaturia is not well established and is thought to be due to the naevi-induced secretion of proteins, FGF23 and MEPE[5,6]. FGF-23 acts on the FGFR1c receptor and induces renal phosphate excretion. Further, it inhibits 1-α hydroxylase activity[6]. Thus, these children should be treated with active vitamin D metabolites (1-α calcidiol or calcitriol) to prevent secondary hyperparathyroidism. This is the possible reason for our child's slightly elevated PTH level at the initial presentation. Excision or dermabrasion of giant nevus may help control poorly responding hypophosphataemic rickets[5]. In our child, hypophosphataemic rickets is currently well

managed medically. However, she has undergone resection of a few lesions due to cosmetic reasons and the risk of malignant transformation.

Neurological abnormalities are commonly associated with Schimmelpenning syndrome. However, neuroimaging in an asymptomatic child is not indicated[3]. Our child is neurologically normal; hence she has not undergone cranial imaging yet. Nearly 59% shows ophthalmic involvement, colobomas and corneal abnormalities being the major ones found. Horseshoe kidneys and the duplex collecting systems are the commonly reported urinary abnormalities[3]. However, our child did n0t show these system involvements up to date.

In conclusion, Schimmelpenning syndrome is rare with multisystemic involvement, including hypophosphataemic rickets. Early diagnosis and appropriate specific treatment will reduce skeletal deformity, growth retardation and osteopenia.

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