Linear Nevus Sebaceous with Vitamin D3 Resistant Rickets (Schimmelpenning Syndrome)

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ABSTRACT

Introduction: Schimmelpenning syndrome is a neurocutaenous condition characterized by one or more sebaceous nevi, usually on the face or scalp, associated with anomalies of the central nervous system, ocular system, skeletal system, cardiovascular system and genitourinary system. It is also called linear nevus sebaceous syndrome, sebaceous nevus syndrome and Jadassohn's nevus phacomatosis. It is one of the types of epidermal nevus syndromes with sebaceous nevi and vitamin D resistant (hypophosphatemic) rickets. There is growing evidence that in these situations, the epidermal nevi produce a phosphaturic factor which causes hypophosphatemic rickets.

Case report: We highlight a case of an 8 years old boy with congenital epidermal nevi on face, scalp and neck, who developed vitamin D resistant rickets at 7 years of age.

Conclusion: We report this case because of its rarity. Nevus sebaceous is the hallmark of Schimmelpenning syndrome, and if physicians are aware of this distinct lesion, an early diagnosis can prevent the development of rickets causing marked disability.

Keywords: Nevus sebaceous, vitamin D resistant, rickets

INTRODUCTION

Schimmelpenning syndrome is a rare multisystem disorder characterized by sebaceous nevi associated with abnormalities outside the skin, most commonly of the brain, eyes and bones.[1] Sebaceous nevi are comprised of an increased number of malformed sebaceous glands along with an overgrowth of epidermis. Epidermal nevus syndrome is sometimes used as a synonym, but more often as a broader term referring to Schimmelpenning syndrome in addition to Nevus Comedonicus syndrome, Becker's nevus syndrome, CHILD syndrome and phacomatosis pigmento-keratotica.[2] There are 9 epidermal nevus syndromes well defined by clinical, histopathological and genetic causes.[3]

Schimmelpenning syndrome is the most common type of epidermal nevus syndromes. Other terms used to describe Schimmelpenning syndrome include linear nevus sebaceous syndrome, Schimmelpenning – Feurstein-Mims syndrome, Jadassohn's nevus phacomatosis and Jadassohn nevus syndrome.[4] Nevus sebaceous was first described by Jadassohn in 1895. The classic Schimmelpenning syndrome was first reported by Gustav Schimmelpenning in 1957[5], sebaceous nevi occur in 1-3/1000 births with equal incidence by sex.[2] Up to 10% individuals with epidermal nevi may develop additional signs and symptoms, though the exact prevalence and incidence of these in general population are unknown.

Exact etiology of Schimmelpenning syndrome is unknown. It is believed to be caused by a mutation in a gene that occurs after fertilization (postzygotic mutation)[3], most likely early during embryonic development.[4] Affected individuals have some cells with a normal copy of this gene and some cells with the abnormal gene (mosaic pattern). Researchers believe that these postzygotic mutations occur randomly for no apparent reason (sporadically).[1] The earlier in embryonic development such a mutation occurs, the more extensive the nevi and greater the likelihood of other organ system involvement.[5] Recent research has identified individuals who had postzygotic mutation of the KRAS and HRAS genes.[3]

The characteristic skin lesion, the sebaceous nevus, most often involves the scalp (59.3%), neck and face (32.6%), arms, legs and trunk may also be affected.[6] Sebaceous nevi are usually salmon or yellow colored, hairless and smooth patches. When scalp is involved, large lesions may be present with associated alopecia. The nevi may be prominent at birth, but sometimes these do not become apparent until after puberty.

Skeletal abnormalities include dental irregularities, scoliosis and vitamin D resistant (hypophosphatemic) rickets – a condition characterized by progressive softening of bone structure, pain and bowing of the legs. In children, growth may slow down, resulting in short stature. Other skeletal abnormalities may include abnormal curvature of the spine, malformation of hip and abnormalities of arms and legs.

There is growing evidence that epidermal nevi produce fibroblast growth factor 23 (FGF 23) which decreases renal tubular reabsorption of phosphate and decreases the activity of renal 1-α hydroxylase enzyme, resulting in decreased serum phosphate levels and decrease in the production of $1,25D_3$. FGF23 measurement should be included in the workup of this type of rickets.[7]

Treatment includes potential surgical removal of the nevi. Depending on the other system(s) involvement, management may need an interdisciplinary team of specialists – the dermatologist, neurologist, ophthalmologist, orthopedic surgeon, oral surgeon, plastic surgeon and psychologist.[3] For hypophosphatemic rickets, treatment is oral calcitriol (30-70 ng/kg/day) and oral phosphate (1-4 gm/24 hours).

CASE REPORT

An 8 years old boy, product of nonconsanguineous marriage, presented to us with congenital skin lesions on right side of face and scalp with spare hair and areas of alopecia (Figure-1). These were diagnosed as epidermal nevus sebaceous by skin biopsy at PGIMER, Chandigarh. There is pigeon chest, rachitic

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How to cite this article: Gupta Anju Darshan Kumar, Aseem Singh, Karnail Singh. Linear nevus sebaceous with vitamin D3 resistant rickets (schimmelpenning syndrome). International Journal of Contemporary Medical Research 2017;4(5):1027-1028.

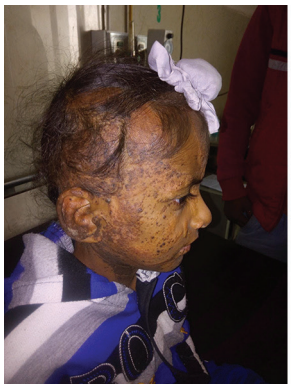
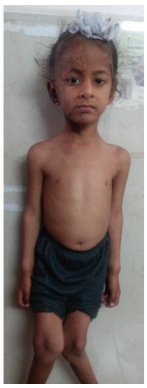
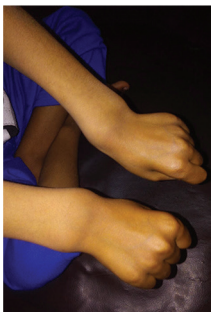

Figure-1: Congenital epidermal nevus with spare hair and areas of alopecia. **Figure-2:** Marked genu valgum, rachitic rosary.; **Figure-3:** Widening of the wrists.

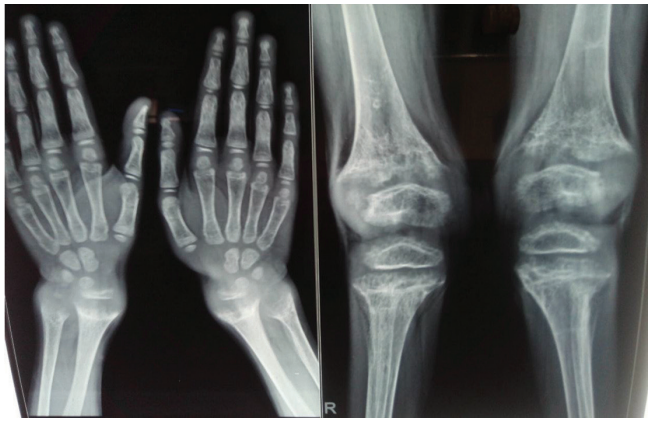

Figure-4: Rachitic changes in the form of fraying, flaying and cupping.

rosary, slight potbelly, marked genu valgum, bowing of legs, double malleoli, widening of wrists (Figures-2,3) and dental irregularities. The child has grade 3 protein-energy malnutrition and grade 2 stunting per Indian Academy of Pediatrics growth charts. X-rays of the knees and wrist show florid rachitic changes in the form of fraying, flaying and cupping (Figure-4). Neurological, ocular and cardiovascular system examination are normal.

Laboratory values reveal normal vitamin D, 25 hydroxy levels (25.9 ng/dl, Ref. range 20-60 ng/ml), raised alkaline phosphatase (1392 u/l, ref. range 86-315 u/l), low serum phosphorous (2.10 mg/dl, ref. range 8.80-10.80 mg/dl) and normal serum calcium levels (total 9.0 mg/dl, ionized 4.2 mg/dl). Blood urea, creatinine and pH are normal as are serum PTH (53.5 pg/ml, ref. range 14-72 pg/ml) and serum 1,25 $(OH)_2$ D3 (73.0 pg/ml, ref. range 16.38-80 pg/ml). Urinary phosphate excretion was 308 mg/24 hours, reference range for adult males and females is 360-1600 mg/24 hours and 170-1200 mg/24 hours respectively. We could not find pediatric values for the same.

DISCUSSION

Epidermal nevus syndrome (ENS) are congenital hamartomas of embryonic origin classified based on their main component. The component may be sebaceous, apocrine, eccrine, follicular or keratinocytic. Ten percent individuals with epidermal nevi have involvement of other organ systems, hence the condition is considered to be an epidermal nevus syndrome. Schimmelpenning syndrome is one of the most common types of ENS. Cases of Schimmelpenning syndrome with complication of severe rickets have been reported.[8] The skeletal abnormalities may include dental irregularities, scoliosis, vitamin D resistant rickets and hypophosphatemia. Additional skeletal malformations may` include bone cysts, underdevelopment of pelvis and incomplete formation of bony structures including ankle, foot and bones of the spinal column. Affected individuals may be prone to fractures, present with bowing deformities of legs, pain in legs and growth retardation.[9] X-ray changes of rickets, decreased serum phosphate, normal serum calcium, normal serum PTH and serum vitamin D_3, decreased or normal serum 1,25 dihydroxy D_3 and increased serum FGF23 favor the diagnosis of this syndrome.[7]

In the case, we are reporting, sebaceous nevi on face, scalp, neck and pinna with development of rickets at 7 years of age despite good diet and adequate sun exposure and good health of other siblings and no response to vitamin D therapy clinch the diagnosis of vitamin D resistant rickets. X-ray findings of rickets, decreased serum phosphate level, normal serum calcium, serum PTH, serum vitamin 1,25 D_3 and 25D_3 levels, increased serum alkaline PO_4 levels and possibly increased urine phosphate levels, all prove our diagnosis of vitamin D resistant (hypophosphatemic) rickets.[10] Serum FGF 23 levels were not possible because of nonavailability of this test in India. Patient was treated with oral calcitriol (0.5 µg orally OD) and oral phosphorus (750 mg/day) and showed subjective improvement in the form of less pain and more muscle power and mobility within a few weeks of this treatment.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 14-04-2017; **Accepted:** 16-05-2017; **Published:** 29-05-2017