The Turkish Journal of Pediatrics 1997; 39: 247-251

HYPOPHOSPHATEMIC VITAMIN-D RESISTANT RICKETS ASSOCIATED WITH EPIDERMAL NEVUS SYNDROME*

A Case Report

*Ayşegül Tokatlı MD***, *Turgay Coşkun MD****, *İmran Özalp MD****

SUMMARY: Tokatlı A, Coşkun T, Özalp İ. (Metabolism and Nutrition Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Hypophosphatemic vitamin-D-resistant rickets associated with epidermal nevus syndrome: a case report. Turk J Pediatr 1997; 39: 247-251.

Epidermal nevus syndrome is characterized by congenital anomalies affecting multiple body systems, especially the skin, skeleton and central nervous system. A form of rickets/osteomalacia that is markedly resistant to treatment with vitamin D has been reported in children with this syndrome. We report the clinical and laboratory observations in a child with epidermal nevi and severe hypophosphatemic rickets/ osteomalacia. *Key words: epidermal nevus syndrome, hypophosphatemic vitamin-D-resistant rickets/osteomalacia.*

Epidermal nevi are organoid nevi arising from the pluripotential germinative cells in the basal layer of the embryonic epidermis[1]. The nevi are classified by their predominant component as sebaceous, verrucous or comedoneous.

The term epidermal nevus syndrome (ENS) refers to the association of epidermal nevi with congenital anomalies affecting multiple body systems[1-3]. Synonyms for this syndrome are Solomon syndrome, linear nevus syndrome or Schimmelpenning-Feuerstein-Mims syndrome. The most frequent association has been central nervous system involvement; abnormalities in other organ systems are seen less frequently. Hypophosphatemic rickets/osteomalacia in ENS has been reported in recent years, and it has been suggested that vitamin-D-resistant rickets/osteomalacia is a variant of tumor-induced rickets/osteomalacia[4,5].

Here we present the clinical and laboratory observations in a child with epidermal nevi and severe hypophosphatemic rickets/osteomalacia.

Case Report

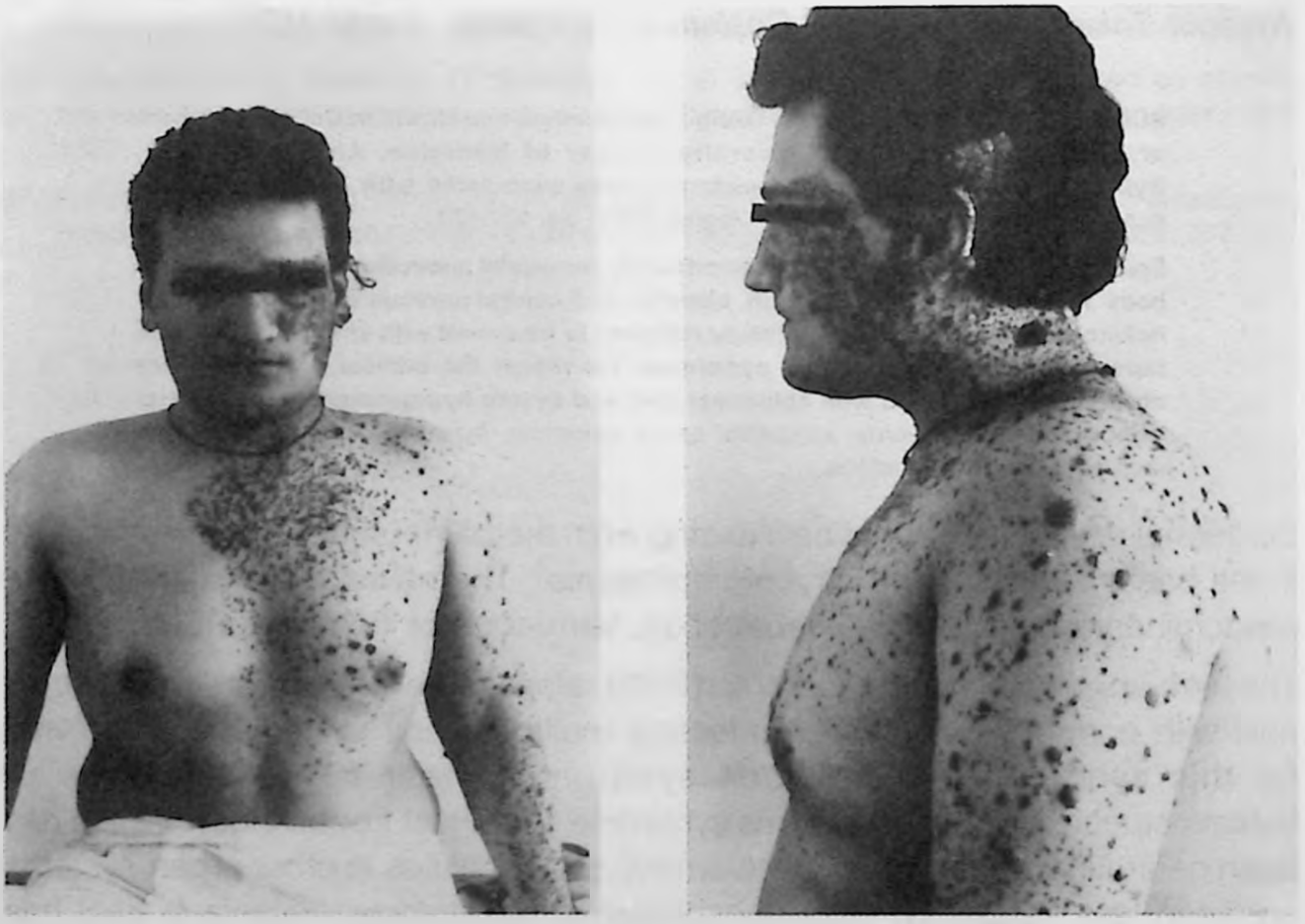
A five-year-old boy was referred to Hacettepe Children's Hospital in 1981 because of vitamin D-resistant rickets. The patient was the first child born to healthy, unrelated parents with no family history of skin or bone disease. At

* From the Metabolism and Nutrition Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara.

** Associate Professor of Pediatrics, Hacettepe University Faculty of Medicine.

*** Professor of Pediatrics, Hacettepe University Faculty of Medicine.

birth, extensive nevi involving the left side of the body were noted, as well as a large verrucous-sebaceus plaque over the left postauricular area, and multiple raised melanotic nevi covering the left side of the face, chest, back, left arm and left leg (Figs. 1-3).



Figs. 1 and 2: Patient at 16 years of age showing nevi on the left side of the body.

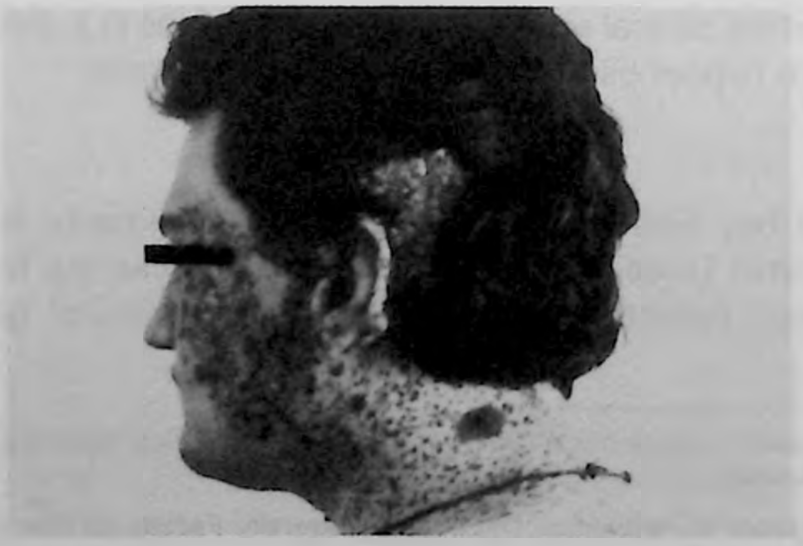


Fig. 3: Close-up view of the large verrucous nevus on the left side of the scalp.

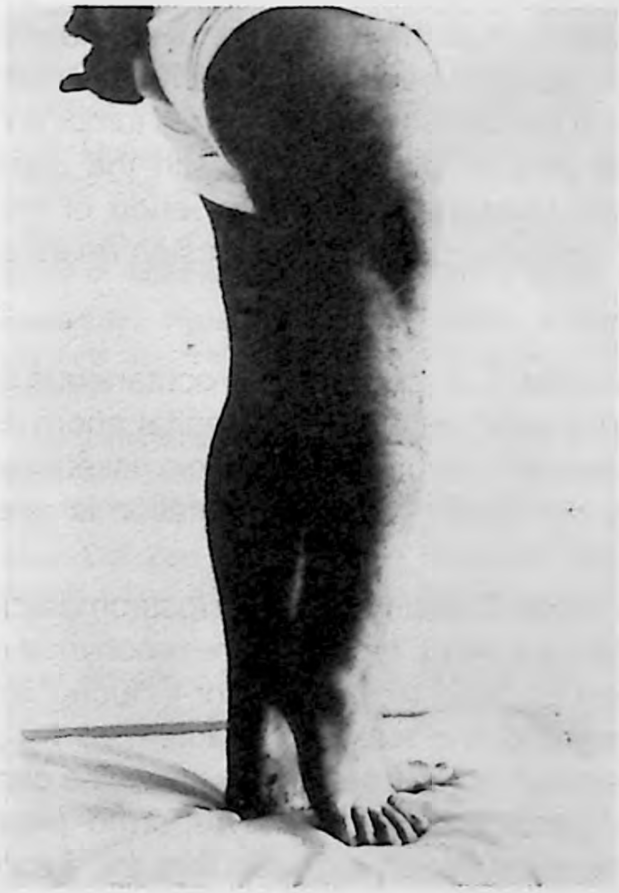


Fig. 4: Note the difference in leg length and the skin lesions on the left leg.

At the age of two years, a difference in the length of the patient's two legs was noticed; his right leg was shorter than the left (Fig. 4). At that time, the patient was investigated elsewhere, the rickets was recognised, and he was prescribed vitamin D several times. At the age of five years, he was referred to our hospital because of vitamin D-resistant rickets. On admission, besides the leg-length difference and the skin lesions which had already been fully noticed at birth, enlargement of the costochondral junctions, wrist and ankles as well as knock-knees were noted. His linear growth had been below the 3 third percentile, but his developmental milestones were normal. The serum calcium concentration was 10.6 mg/dl, serum phosphorus 1.7 mg/dl, and alkaline phosphatase 25 U/L. Active rickets was observed on roentgenograms. At that time, therapy was started with vitamin D 50.000 IU/day and phosphorus 2 g/day p.o. From ages five to 11, the child received vitamin D at doses up to 50.000 IU/day as well as oral phosphorus supplementation with no evidence of radiographic or biochemical healing. He continued to complain of bone pain. After substitution of vitamin D with 1-α hydroxyvitamin D_3, the patient's general condition gradually improved; however, despite phosphorus therapy he was still hypophosphatemic.

Because of the known relation between hypophosphatemic rickets/osteomalacia and epidermal nevi, excision of the skin lesion was planned, but the extensive distribution of the skin lesion in our patient precluded total surgical extirpation. After surgical removal of the verrucous-sebaceous tumor on the scalp, his serum phosphorus level was able to be regulated with the combination of calcitriol [1,25 $(OH)_2D$] and oral phosphorus. Over a period of months, his bone pain disappeared. Biopsy specimens of the scalp lesion revealed nevus sebaceous.

Discussion

Epidermal nevus syndrome is a sporadic neurocutaneous disorder that consists of epidermal nevi and a wide variety of congenital anomalies of the brain, eye, skeleton and other systems[1-3]. Hypophosphatemic rickets/osteomalacia has been described in patients with ENS[4-7]. This combination is rare and has been only sporadically described.

Hypophosphatemic vitamin D-resistant rickets/osteomalacia has been reported in association with various tumors, including mesenchymal and ossifying tumors, and this phenomenon has been termed "tumor-induced rickets/osteomalacia"[8]. Tumor-induced rickets/osteomalacia is characterized by remission of rickets/osteomalacia after resection of the coexisting tumor. The clinical and biochemical reversal of the rickets/osteomalacia in the reported patients with ENS upon surgical removal of the skin lesions suggests that the disorder may be a variant of tumor-induced rickets/osteomalacia. It has been shown that material extracted from the skin lesion of the patient with ENS and rickets/osteomalacia caused phosphaturia in an experimental animal[9]. However, if there is a relation between the skin lesion and rickets-osteomalacia, there is no explanation as to why the complication of rickets/osteomalacia is rare in ENS. Some authors suggest that tumors with different histologic patterns will be found associated with hypophosphatemic vitamin D-resistant rickets/osteomalacia; some types of tumors are responsible for the patient's phosphaturia, but the others do not cause renal phosphate loss which in turn is responsible for the rickets/osteomalacia[9].

The clinical and biochemical findings in our patient were fully compatible with ENS and hypophosphatemic vitamin-D-resistant rickets/osteomalacia. Treatment with vitamin D and phosphorus did not result in complete healing of rickets/osteomalacia. However, removal of parts of skin lesions influenced the rickets/osteomalacia. This result emphasizes that successful therapy for rickets/osteomalacia in ENS cannot be achieved with the mere combination of calcitriol and phosphorus.

REFERENCES

1. Rogers M, McCrossin I, Commens C. Epidermal nevi and epidermal nevus syndrome. A review of 131 cases. J Am Acad Dermatol 1989; 20: 476-488.
2. Pavone I, Curatolo P, Rizzo R, et al. Epidermal nevus syndrome: a neurologic variant with hemimegalencephaly, gyral malformation, mental retardation, seizures, and facial hemihypertrophy. Neurology 1991; 41: 266-271.

3. Feuerstein RC, Mims LC. Linear nevus sebaceous with convulsions and mental retardation. Am J Dis Child 1962; 104: 675-679.
4. Besser FS. Linear sebaceous nevi with convulsions and mental retardation (Feuerstein-Mims' syndrome), vitamin-D-resistant rickets. Proc Roy Soc Med 1976; 69: 518-520.
5. Skovby F, Svejgaard E, Moller J. Hypophosphatemic rickets in linear sebaceous nevus sequence. J Pediatr 1987; 111: 855-857.
6. Carey DE, Drezner MK, Hamdan JA, et al. Hypophosphatemic rickets/osteomalacia in linear sebaceous nevus syndrome: a variant of tumor-induced osteomalacia. J Pediatr 1986; 109: 994-1000.
7. Goldblum JR, Headington TH. Hypophosphatemic vitamin D-resistant rickets and multiple spindle and epithelioid nevi associated with linear nevus sebaceus syndrome. J Am Acad Dermatol 1993; 29: 109-111.
8. Fukumoto Y, Tarui S, Tsukiyama K, et al. Tumor-induced vitamin D-resistant hypophosphatemic osteomalacia associated with proximal renal tubular dysfunction and 1.25-dihydroxyvitamin D deficiency. J Clin Endocrinol Metab 1979; 49: 873-878.
9. Aschinberg LC, Solomon LM, Zeis PM, Justine P, Rosenthal IM. Vitamin D-resistant rickets associated with epidermal nevus syndrome: demonstration of a phosphaturic substance in the dermal lesion. J Pediatr 1977; 91: 56-60.
10. Oranje AP, Przyrembel H, Meradji M, Loonen MCB, de Klerk JBC. Solomon's epidermal nevus syndrome (Schimmelpenning-Feurstein-Mims) and hypophosphatemic vitamin-D-resistant rickets. Arch Dermatol 1994; 130: 1167-1171.