A NEW VARIANT OF 1,25-DIHYDROXYVITAMIN D-RECEPTOR -DEFECT RICKETS AND ALOPECIA. ASSOCIATED WITH MENTAL RETARDATION AND HEARING LOSS.

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ABSTRACT :

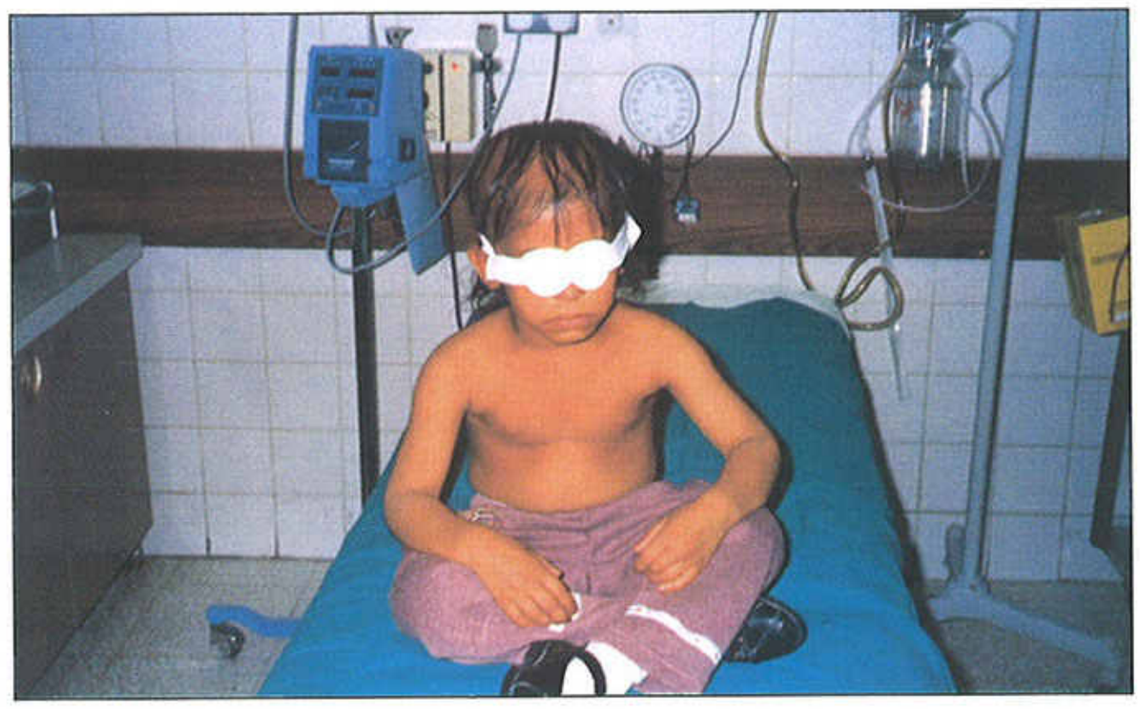
Three patients (two brothers and a sister) with clinically different severity of Vitamin D dependent rickets type II with alopecia, were found to have different degrees of mental retardation and sensorineural deafness. Up to our knowledge, mental retardation and hearing loss have not been described before in this disease. Previous reports of vitamin D dependent rickets type II with alopecia are reviewed and the unusual features of our patients are discussed.

INTRODUCTION :

1,25-Dihydroxyvitamin D-receptor-defects rickets(also called vitamin D-dependent rickets type II) is a hereditary disease of target organ resistance to 1,25-dihydroxyvitamin D (1,25-(OH)2 D), which is a biologically active vitamin D metabolite.1 The characteristic clinical features of this disease are rickets, hypocalcaemia, hypophosphatasia, secondary hyperparathyroidism, and elevated serum levels of both alkaline phosphatase activity and 1,25-(OH)2D2. Alopecia was observed in 15 of 23 patients reported to have vitamin D-dependent rickets type II 3,4. A relationship between alopecia and marked resistance to treatment has been recognised 5. Recently, we discovered new associations with this syndrome, namely mental retardation and sensorineural hearing loss.

PATIENTS

A 17-years-old boy (patient 1), a 15-years-old boy (patient 2, Fig 3 & 4) and a 3-years-old girl (patient 3, Fig 1 & 2) are the only sibs for a consangious parents



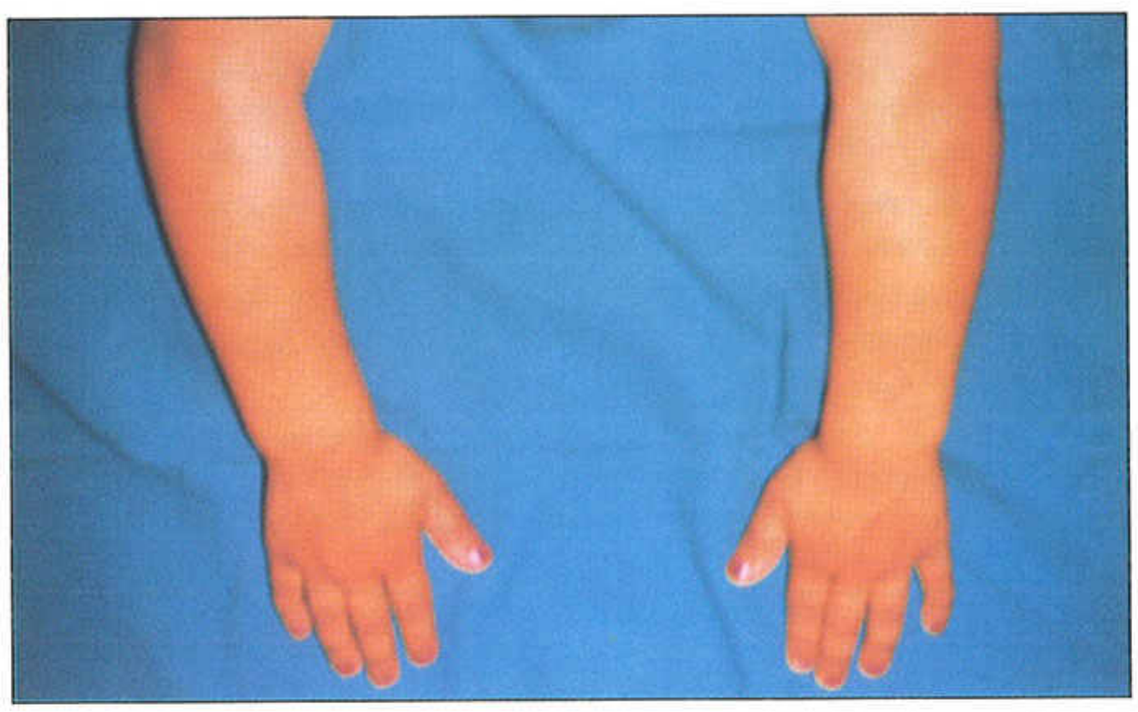


Fig 1 and 2 Younger sister showing rachitic changes and alopecia

(first degree cousins). They were reported to Farwania Hospital for evaluation of alopecia and bone deformities. These patients were the outcome of a normal vaginal delivery at full term and were presented to our Hospital at the ages of one and half-years, 6-months and 7-months, respectively. All of them had clinical evidence of rickets, muscle weakness and hepatosplenomegally. Loss of scalp hair was noticed between the age of 3 to 6 months,the alopecia was in the form of diffuse thinning of hair with patches of complete hair loss, the hair in general was fragile and lusterless. They were all short and failing to thrive. They were noticed to be mentally retarded, and formal development assessment (gross motor, adaptive, language, personal and social) revealed a maturity of 73%,69%, and 60% of normal. On testing their hearing with audiogram and brain stem evoked potential, all of them were found to have sensorineural hearing loss. Chromosomal study was normal for all of them. Before treatment, their calcium levels were

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1.7,1.99,2.4 mmol/L (normal range 2.2-2.6 mmol/L), the phosphorus level was 2.6,1.15,2.48 mg/dL (normal range 4.5- 6.2 mg/dL), the alkaline phosphatase activities were 966, 1015, 961 IU/L (normal range up to 465 IU/L), and the parathyroid hormone levels were 0.8,1.1,1.3, ng/mL in patients 1,2 and 3 respectively. The urine examination revealed generalized aminoacidria.

The level of 1,25-(OH)2D level was high in all three patients. Reentgenographic examination revealed cupping and fraying at knee and wrist with deformities of lower limbs. These patients were treated with high doses of 1-alpha-(OH) D3, for prolonged periods with good response in patients 1 and 2 with complete reversal of biochemical data and radiological findings to normal, however, alopecia, mental retardation, and hearing loss remained unchanged. In patient 3, there were very poor response to treatment, still with clinically evident rickets and other features of the syndrome.

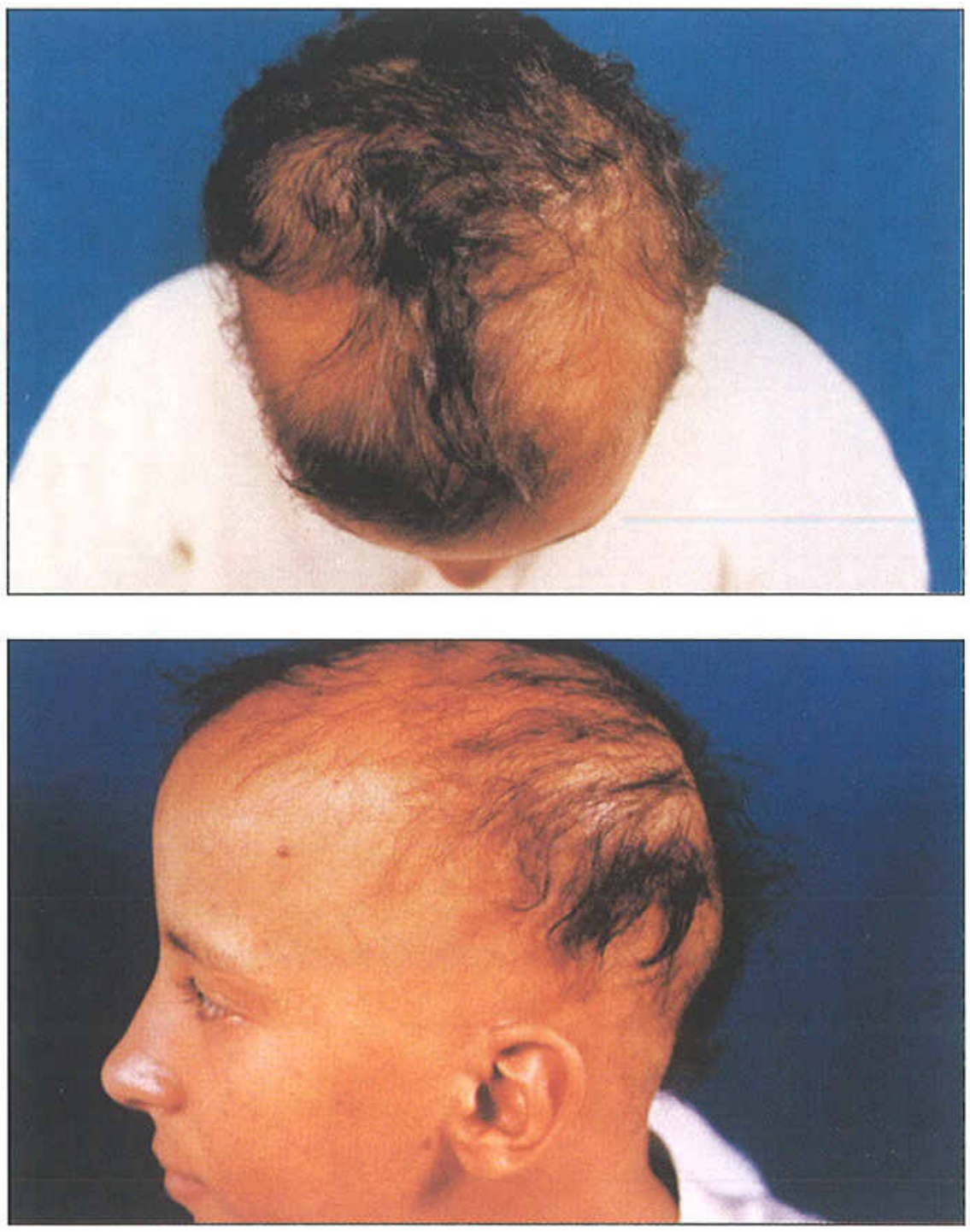

Fig 3 and 4 Two brothers showing hair changes

DISCUSSION

Vitamin D-dependent rickets type II (VDDR type II) is a syndrome first described by Brooks et. al in 1978 6. It is a hereditary disease of target organ resistance to dihydroxyvitamin D, which is a biologically active vitamin D metabolite 1. Alopecia has been reported in some individuals with VDDR type II and is considered as a marker of more refractiveness to therapy 7. In the present study we found three children belonging to one family (two brothers and one sister) with classical features of VDDR type II. In addition to these features, they were found to have mental retardation and sensorineural hearing loss. The elder two brothers responded to treatment with high doses of vitamin D, but this was not the case with their younger sister, who was known to have the severest degree of mental retardation. Whether mental retardation is another marker for refractiveness to treatment, remains questionable. None of our patients showed any improvement regarding alopecia, mental retardation, or hearing loss. We recommend to assess hearing and mental status in all cases of VDDR type II with alopecia, as this may be a separate entity, or another proof of clinical heterogeneity of this syndrome.

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