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DEFECTIVE NEUTROPHIL MOBILITY IN TEN PATIENTS WITH VITAMIN D-DEFICIENT RICKETS

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ABSTRACT

We studied the immune system, especially the chemotactic activity of neutrophils, in ten patients with vitamin D-deficient rickets and compared the results with ten healthy controls of matched age.

Among all immune system factors, the chemotactic studies persistantly showed remarkable deficiency in leukocyte mobility, both random motion and migration. When compared with controls, the findings were significant. It was postulated that the increased susceptibility of the patients with vitamin D-deficient rickets to infection is mainly due to defective neutrophil mobility.

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INTRODUCTION

Children suffering from vitamin D-deficient rickets are known to be susceptible to infection, mainly in the gastrointestinal and respiratory tracts. A few reports are described about vitamin D-deficient rickets and the defect in chemotaxis in the literature.[1] This defect has been postulated to be the predisposing factor in such patients. This study was carried out to investigate the immunity state, especially neutrophil mobility, in children with vitamin D-dificient rickets.

MATERIALS AND METHODS

Studies were performed on ten children (five boys, five girls) with clinical, biological and radiological manifestations of vitamin D-deficient rickets. The age ofthe patients ranged from three to 36 months. All the children had a history of recurrent gastrointestinal or respiratory tract infection. None of the patients had associated malnutrition. Serum IgM, IgG, IgA, C3 and C4 were measured in seven patients by radial immunodiffusion of Mancini (Behringer manufacture). Total hemolytic complement (CH50) was detected by Mayer's method[2] in six patients. The chemotactic tests were done by the modified technique of Boyden & Agget.[3,4] To measure neutrophil mobility, neutrophils were isolated from heparinized blood by dextran sedimentation, washed in Hank's medium, and resuspended at 2 ml. Chemotactic factor was generated from the serum of a healthy donor by *Escherichia coli* endotoxin (Difco) in Hank's medium. The mobility of the neutrophils in 0.25 ml of this suspension through a millipore membrane of three microns pore diameter was measured by the method of Boyden, Agget, Farhoudi, et al.[3,4,5]

After three hours of incubation, the membrane was separated, washed free of red cells, stained with hematoxylin and mounted on slides. The values of 75 microns and 40 microns were chosen for determining defective mobility in migration and random mobility, respectively. In addition to the patients, neutrophil mobility was also measured in ten healthy age-matched children as controls.

RESULTS

The age, sex, clinical manifestations and non-immunological laboratory findings of the ten studied patients are summarized in Tables I and II. The immunological findings of the patients are shown in Table III as follows: serum levels of IgG, IgA, and IgM within normal range for age, complement function and serum C4 values normal in seven patients, but C3 levels below normal in two patients. The chemotactic studies showed absolute deficiency in leukocyte mobility, both

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Table I. Clinical findings of ten patients with vitamin D-dificient rickets. Tehran University of Medical Sciences (1984-1985).

PATIENT	SEX	AGE	MANIFESTATION	DIAGNOSIS
1	F	10 mo	FTT	resistant rickets
2	F	13 mo	respiratory infection	rickets
3	M	6 mo	constipation, convulsion	rickets
4	F	3 mo	convulsion, UTI	DiGeorge syndrome
5	M	5 mo	convulsion	rickets
6	M	14 mo	resp. inf., convulsion	rickets, pneumonia
7	F	3 yr	leg deformities	rickets
8	M	5 mo	resp. inf., convulsion	rickets, pneumonia
9	M	13 mo	cong. heart disease	rickets, VSD
10	F	20 mo	FTT	rickets

Table II. Laboratory findings of ten patients with rickets.

PATIENT	CBC	Ca	P	Alk phos	U/A	RADIOGRAPHY
1	N	↓	↓	↑	N	fracture, rickets
2	N	N	↓	↑	N	rickets
3	N	↓	↓	↑	N	rickets
4	N	↓	↑	↑	UTI	rickets, absent thymus
5	N	↓	↓	↑	N	rickets
6	N	N	↓	↑	N	rickets
7	N	N	↓	↑	N	rickets
8	N	N	↓	↑	N	rickets
9	N	↓	↓	↑	N	rickets
10	N	↓	↓	↑	N	rickets

in random motion and migration. The statistical analysis of the chemotactic studies from the patients and the controls revealed a statistically significant impairment of neutrophil mobility (Figures 1 and 2, Tables I, II, III).

DISCUSSION

Neutrophil chemotaxis is an important constituent of phagocytosis and the immune mechanisms against bacterial invasion, and defective leukocyte mobility has been associated with recurrent infections in affected individuals.

Impaired leukocyte mobility has been described as a secondary disorder in various disease states such as diabetes mellitus, rheumatoid arthritis, and malnutrition.[9]

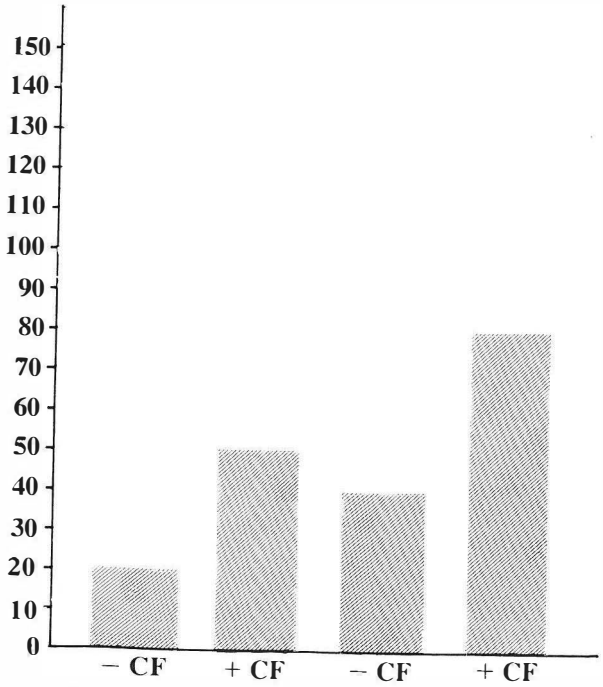

Figure 1. Chemotaxis in ten patients with rickets.

Our study, in concordance with other investigations, indicates that there is a secondary defective neutrophil mobility in patients with vitamin D-deficient rickets. It is likely that this impairment is the main, if not the only factor that accounts for recurrent infections in these patients.

The precise mechanisms of neutrophil mobility have not yet been determined. There are a number of proteins such as actin and myosin that form filamentous structures in leukocytes,[7,9] which are structurally and enzymatically similar to the actin-myosin system in muscles. Neutrophil movement is therefore probably achieved by the contraction of these microfilaments.

The polymerization and depolymerization of the actin network effected by the tubulin skeletal system, appears to be essential for many of the functions of the neutrophils, including attachment to surfaces, phagocytosis, movement, and degranulation.[10-12]

It is postulated
phatemia in vitamin D-deficient rickets may produce intracellular changes sufficient to interfere with normal contractility of the microfilaments, and thus leukocyte mobility. Since the contractility of intracellular microfilaments, as the main means of leukocyte mobility, is dependent upon normal calcium an

Chemotactic Factor	Patients	Controls
− CF	20.6 ± 7.58	33.3 ± 9.40
+ CF	51.5 ± 16.5	79.5 ± 15.72

p 0.001 + CF
p 0.001 − CF
T test = 3.886 D.F. = 18
T test = 3.852

Figure 2. Data findings in ten patients with rickets.

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Table III. Immunological findings in ten patients with rickets.

Patient	Age	Immunoglobulins (mg/dl)			Complement			Chemotaxis Patients		Controls		Opsonins
		IgG	IgA	IgM	CH50	C3	C4	− CF	+ CF	− CF	+ CF	
1	10 mo	1750	178	215				20	50	36	80	ND
2	13 mo	575	39	59	80%	94	27	20	62	30	100	ND
3	6 mo	570	48	177	90%	103	27	20	44	30	75	ND
4	3 mo		ND			ND		38	68	40	80	ND
5	5 mo	75	trace	145	80%	63	23	20	50	20	50	ND
6	14 mo	450	41	69	90%	120	59	10	18	50	100	ND
7	3 yr	1250	190	176	80%	56	22	25	75	50	85	low
8	5 mo	651	85	359	60%		28	10	30	25	55	low
9	13 mo		ND			ND		25	55	40	80	ND
10	20 mo		ND			ND		18	63	32	90	ND

ND = not detectable

metabolism, it is suggested that hypocalcemia and hypophosphatemia in vitamin D-deficient rickets are the responsible factors which interfere with the normal contractility of the microfilaments, resulting in impaired leukocyte mobility.

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