



Original Contribution

LATE BONE CHANGES IN PATIENTS WITH HOMOZYGOUS THALASSAEMIA

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ABSTRACT

Thalassaemic syndromes are relatively often met disease states. The survival of patients increased significantly with the improvement of conventional therapy and some of them reach mature age. Nevertheless, some organ abnormalities with different severity are observed, including also the bone-muscle system. Erythroid hyperplasia results in bone-marrow expansion in the skull and other bones which may lead to fractures. A relation between the type of genetic mutations and the severity of bone changes is observed. This gives rise to diagnostic, therapeutic and psychosocial problems. Spontaneous fractures of vertebrae in the backbone result in severe pain syndrome and demand continuous treatment. The authors present a series of radiologic changes of bones of patients with different types of β - thalassemia. It is reported that regular blood transfusions and iron – chelating therapy improve the quality of life and reduce the risk of complications. Bone changes are present among the endocrine abnormalities and outline a significant problem for these patients.

Key words: β - thalassemia, Chelating therapy, Bone-marrow expansion

INTRODUCTION

The introduction of effective methods of treatment from the mid-70s increased the survival of patients with talassaemia. The patients between 20 and 40 years of age are exposed to higher risk of new complications, some of which are life-threatening, owing to iron intoxication of vital organs.

A great number of patients complain of bone pains with different intensity and headache. This is considered to be a result of osteoporosis.

In the past, especially in irregularly transfused and treated with chelators patients the cases of bone deformities, pains and pathologic fractures were not rare.

There are a few reference data concerning bone changes and fracture rates in thalassaemic patients (1, 2). For that reason we decided to study the frequency and the type of bone fractures in a group of patients with β -thalassaemia.

MATERIALS AND METHODS

Forty-four patients were selected in this study (Range 1-35). Twenty of them were boys and 23 were girls.

Apart from hematological and molecular analyses, radiographs, CT and MRI were also done.

Information was collected about each patient, including his state by the time of fracture: age, mean Hb level before transfusion, mean serum ferritin level, mean aminotransferase level, rate of pubertal development, secondary amenorrhea, hypothyroidism, hypoparathyroidism. The traumas were distributed in 3 groups according to their severity – mild, middle and severe. The severe trauma usually was a consequence of a serious incident; the middle one was a result of falling (during usual daily activities or playing); the mild one was occurred unobvious.

RESULTS

The frequency of bone fractures in the studied group of patients was 14 %. Four men and 2 women have had fractures. The distribution by age and sex is shown in Table 1.

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Most frequently fractures were found in patients older than 20 years and between 15 and 20 years of age.

Fractures can be seen in almost all bones, especially the bones of extremities, long bones of the arm (radius and ulna), the leg (tibia and fibula) and of the hand (falangeal and metacarpal). Fractures of vertebrae of the backbone were found in a patient aged 35 with homozygous β^0/β^0 -thalassaemia, caused by a frameshift mutation in codon 5. Multiple and repeated fractures have been observed seen in the same patient, with 2 and sometimes more bones involved. Repeated fractures are of different type (Figure 1a,b, Figure 2, Figure 3 a,b and Figure 4).

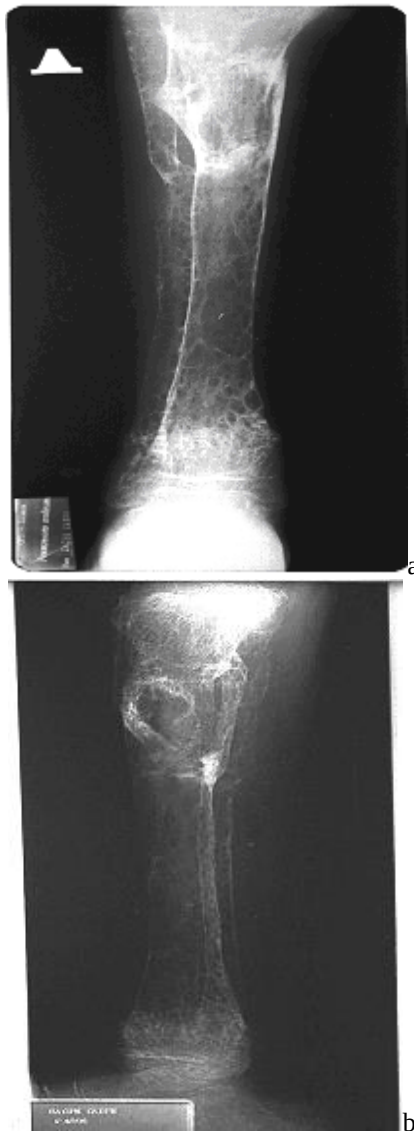


Figure 1a, b. Radiographic imaging of right tibia and fibula face and profile. Mild deformity of tibia, transverse thickening. Osteoporotic bones with coarse netting structure like honeycomb in distal part, unevenly enlarged bone-marrow channel, thinned corticallis with uneven contours. In proximal part transverse lines of thickening are seen, looking line lines of growth. In the same zone symmetrical periosal linear reaction of an old type is seen, with non-malignant characteristics as a result of old fracture undergone.



Figure 2. Radiographic imaging of pelvis of the patient D.B. Mild deformity of pelvis. Pelvic bones are with preserved shape, thinned corticallis, net-line osteoporotic structure.

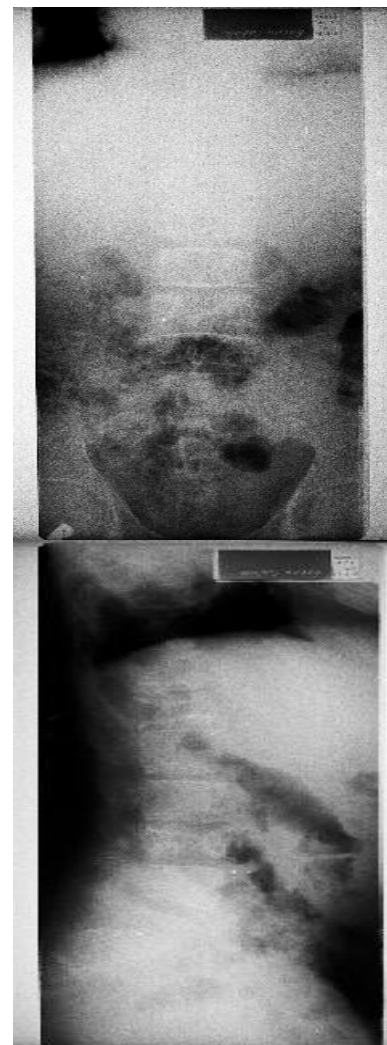


Figure 3 a, b. Radiographic imaging of lumbar vertebrae - face and profile. Compressional fractures of L1 and L4 as a result of minor traumatic injury because of severe changes, that could be found in corpus vertebrae of all vertebrae.

Proximal parts of thighs show similar changes in structure, with predominance of longitudinal dessication, corticallis is thinned with uneven inner contours. Femoral necks

are with thinned corticalis and net-like structure. On the same graphy a compressional fracture of L4 and obvious osteoporotic changes of vertebrae – L5 is with net-like structure and thinned corticalis – could also be seen.

We have found severe traumas in 16 % of the patients, middle in 2 % and mild in 22 %.

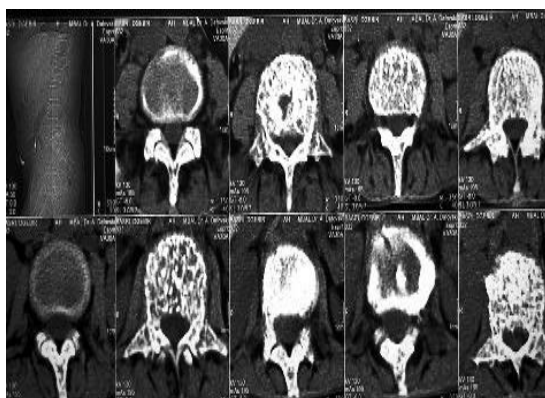


Figure 4. CT imaging of L1 and L4. Tomograms show structural changes and deformity of bone-marrow channel of fractured L1 and L5 vertebrae. Vertebral structure looks like moth-eaten.

Table 1. Distribution by Age and Sex in Thalassaemic Patients with Bone Fractures.

Age Years	Men Number	Women Number	Total Number
1 – 6			
7 – 14	1		1
15 – 20	1	1	2
> 20	2	1	3

Mean Hb levels before transfusion by the time of appearance of fractures are shown in Table 2. As seen in the table, fractures were found in patients with Hb levels lower than 10 g/dl. Mean serum ferritin levels in patients before occurrence of fractures are shown in Table 3. One patient had serum ferritin level lower than 1000 ng/ml, 3 – between 2000 and 4000 ng/ml and 2 – higher than 5000 ng/ml. The levels of ASAT and ALAT were higher than 40 u/l in 56 % of patients and normal (lower than 40u/l) in the remaining 44%. This is shown in Table 4.

Table 2. Pretransfusion Hb Level in 6 Patients with β -thalassaemia by the Time of Occurrence of the Fracture.

Hb level g/dl	Men		Women		Total	
	N	%	N	%	N	%
< 8,0	2	33,3	2	33,3	4	66,7
8,0 – 9,0	1	16,7	1	16,7	2	33,3
9,0 – 10,0	-		-		-	
> 10,0	-		-		-	

Table 3. Serum Ferritin Level (ng/ml) before Fractures.

Ferritin ng/ml	Men		Women		Total	
	N	%	N	%	N	%
< 1000	1	16,7			1	16,7
1000–4000	2	33,3	1	16,7	2	50,0
> 5000	1	16,7	1	16,7	3	33,3

Table 4. ALAT and ASAT Level in 34 Patients.

ALAT ASAT	Men		Women		Total	
	N	%	N	%	N	%
Normal		24	-	20	-	44
Increased		35	-	21	-	56

DISCUSSION

Our results show significantly higher frequency of fractures in thalassaemia patients than those of the remaining population of the same age. The fractures are nearly 70 % more frequent than those of the remaining population. Michelson J. and Cohen A. (1) have reported the same observations.

The investigations of L. Ruggiero and V. De Sanctis (3) have shown, that young patients receive fractures more often than the older, while in the rest of the population 50 % of the fractures are seen in older patients, 23 % in teenagers and 27 % in children.

Most of our studied patients have had pathologic fractures in mild or middle trauma.

Our study shows that many factors participate in the fracture genesis in thalassaemic patients. Bone-marrow infiltration, chronic anemia, chronic liver diseases resulting from hemosiderosis from repeated transfusions, increased intestinal iron resorption are involved in the ethiopathogenesis of bone mass reduction.

Endocrine dysfunction of gonads, thyroid gland and parathyroid glands resulting from hemosiderosis are also involved in the pathogenesis of bone mass reduction. This might play a significant role in the pathogenesis of osteopenia in thalassaemic patients (4,5). It is important to underline the higher incidence of puberty disorders and the appearance of secondary amenorrhea in studied patients with bone fractures.

Many investigations show interrelation between bone changes and fractures and the way of treatment with transfusions and chelators. Bone thinning is stronger in patients with less transfusions and shorter desferioxamine courses (6, 7). Correlation between Hb levels and fractures shown in the present study is in conformity with the results reported by Katz et al. The same authors have

found out that hemoglobin level higher than 9 g/dl obviously decreases osteoporosis and risk of fractures (8).

In conclusion, we consider that early prophylaxis of demineralization is important for more effective fight with osteopenia, osteoporosis and fracture in thalassemic patients. Probably biphosphonates would prove and would be an effective remedy in this direction.

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