Bone microarchitecture deteriorations and a fragility fracture in a patient with beta and alpha heterozygous thalassemia: a case report

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Summary To date there are few studies that have investigated bone mineral density (BMD) and markers of bone metabolism in patients with thalassemia minor form. None of the previous trials presented bone structure analysis in the patient populations. We present the case of a 24-year-old Turkish woman with heterozygous beta and alpha thalassemia who sustained a low-trauma fracture of the inferior pubic ramus. Despite normal markers of bone metabolism, the dual X-ray absorptiometry (DXA) showed decreased areal bone mineral density. Furthermore, severely reduced bone structure parameters and reduced volumetric bone mineral density was assessed by high-resolution peripheral quantitative computed tomography (HR-pQCT). Due to these diagnostic findings at time of peak bone mass, an osteoanabolic therapy with teriparatide for 24 months was initiated. The findings concerning BMD and bone structure in this patient can be seen as caused by the beta and alpha thalassemia.

Keywords Bone microarchitecture · HR-pQCT · Thalassemia

Introduction

Thalassemias name a group of hereditary diseases of hemoglobin synthesis due to a defect in production of one or more of the globin chains of hemoglobin [1]. In more severe forms of thalassemia, ineffective erythropoiesis necessitates transfusion therapy [2]. Reduction in bone mineral density (BMD), increased fractures, deformity and chronic bone pain are well known problems in patients with beta thalassemia major [3–6]. To date there are few studies that have investigated BMD and markers of bone metabolism in patients with thalassemia minor [7, 8]. None of the previous trials demonstrated bone structure analysis in these patients. We present the case of a patient with bone structure deterioration and a low-trauma fracture with heterozygous beta and alpha thalassemia as underlying diseases.

Case report

A 24-year-old Turkish woman with known non-transfusion dependent thalassemia was admitted to a specialized trauma center due to an undisplaced low-traumatic fracture of the inferior pubic ramus on the right side. The trauma was sustained when the patient was walking downstairs. First treatment involved an analgesic therapy, anticoagulation therapy and early mobilization with progress in weight-bearing strength.

To better understand the cause of the fracture the patient was admitted to a specialized bone center. The patient's medical history revealed no signs of secondary osteoporosis or endocrinological disorders. The family anamneses further revealed beta thalassemia of both the patient's mother and her grandmother with no fractures in their respective medical histories. Sex hormones as well as gonadotropin levels were clarified before admission to the bone center and were within normal range. She neither had received any chelation therapy nor any hormone supplementation. The patient had no births and her menstrual cycle was normal and regular. The hemoglobin electrophoreses test as well as genetic testing for thalassemia was conducted. The results
showed that the patient is heterozygous for both beta thalassemia and alpha thalassemia (-α²/aa deletion mutation).

On clinical examination, a reduced BMI of 15.2 kg/m² (weight 42 kg; height 166 cm) was observed. Due to a transient depressive period the patient lost 6 kg (from BMI 17.4 to 15.2 kg/m²) and regained weight again after several months. Psychiatric and dietetic examinations investigating a possible eating disorder did not show any indications of diseases such as anorexia and bulimia. Furthermore, the investigations demonstrated a well-balanced and calcium-rich dietary behavior.

**Laboratory values**

Laboratory investigations (fasting, before 10 am) demonstrated high levels of erythrocytes and iron with reduced values of hemoglobin, MCV, MCH, MCHC and 25-hydroxyvitamin D. Serum values reflecting bone metabolism including procollagen aminoterminal propeptide type I (PINP, osteoblast activity), calcium, phosphate, intact parathyroid hormone (iPTH), type-1 collagen crosslinked C-telopeptide (CTX, osteoclast activity) levels were all in normal range (Table 1).

**Areal BMD, volumetric BMD and bone microarchitecture**

A dual-energy x-ray absorptiometry (DXA) bone densitometry revealed a Z-score of less than –2 reflecting a diminished age-adjusted BMD (see Table 1). High-resolution peripheral quantitative computed tomography (HR-pQCT, Scanco, Bruttisellen, Switzerland) was performed according to the manufacturer’s recommendations on calibration and scanning procedures. With an in vivo resolution of 82 μm, HR-pQCT
was used to noninvasively assess volumetric bone mineral density and bone microarchitecture at the distal tibia and ultradistal radius. At the tibia (Fig. 1) normal cortical vBMD but very low total vBMD and trabecular vBMD were observed. The trabecular bone volume (BV/TV), number of trabeculae (Tb.N) and the trabecular thickness (Tb.Th) were also decreased. In addition, a high level of inhomogeneity of trabeculae was shown by this measurement. Additionally, the cortical thickness was decreased (Table 1).

At the radius (Fig. 2) as a non-weight-bearing bone site, similar alterations in trabecular bone were observed. In contrast the cortical vBMD was slightly increased and cortical thickness as well as total vBMD were within normal range (Table 1).

Due to 25-hydroxyvitamin D insufficiency and the deterioration of bone microarchitecture in conjunction with a fragility fracture, a supplementation with cholecalciferol and calcium as well as a primary osteoanabolic treatment with teriparatide was initiated. After 9 months of osteoanabolic therapy a combination with denosumab as an antiresorptive treatment is planned. Close follow-up and aftercare programs were arranged on the patient’s behalf. The patient was informed that data concerning the case would be submitted for publication and she provided written consent.

### Discussion

We report on a young woman with a genetically proven heterozygous form of beta and alpha thalassemia who had sustained a low-trauma fracture of the inferior pubic ramus. Among normal markers of bone metabolism, significantly decreased values of trabecular volumetric BMD and clearly reduced bone microarchitecture at the time point of peak bone mass were found.

A number of genetic and acquired factors that affect bone density in patients with thalassemia have already been detailed [6]. Toumba et al. describe the mechanism of pathogenesis in thalassemia major as multifactorial. Lack of sex steroids and impaired growth hormone in thalassemic patients due to pituitary damage, as well as other endocrine complica-
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11. Muschitz C, Kocijan R, Fahrleitner-Pammer A, Pavo I, X. Feichtinger, R. Kocijan, H. Resch and C. Muschitz declare that they have no competing interests.

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