DIFFERENTIAL DIAGNOSIS OF DECREASED BONE DENSITY IN AN INFANT WITHOUT FRACTURES AND GENETIC TESTS. AN AUTOPSY REPORT

Emran Lyutfi[1], George Stoyanov[2], Deyan Dzhenkov[2]

[1]Student, Medical University of Varna
[2]Department of General and Clinical Pathology, Forensic Medicine and Deontology, Faculty of Medicine, Medical University of Varna

ABSTRACT

Decreased bone density is classically associated with the osteogenesis imperfecta (OI) group of disorders, rickets, and malabsorption. The morphological evaluation, especially without genetic testing and detailed previous medical documentation, is difficult. Hematoxylin and eosin, and special stains give details on the changes in the bone matrix and the severity of dysmorphological bone formation. Herein we present a case report of a diseased infant with surgically corrected ileal atresia and impaired bone formation, without any other morphological changes in the internal organs. Interpretation of the changes, on the background of the lacking medical documentation and genetic tests, was based on the pathophysiological mechanisms of malabsorption and non-specific changes observed and reported in the OI spectrum of disorders.

Keywords: *bone development, ileal diseases, malabsorption syndromes, osteogenesis imperfecta, rickets*

INTRODUCTION

Case report:

Decreased bone density in the pediatric population is a rare condition classically associated with the osteogenesis imperfecta (OI) group (1- 3).

However, a myriad of other diseases can mimic the condition. In the autopsy practice, the differential diagnosis is important, especially in cases where medical documentation is scarce or non-existent, or genetic tests for OI have not been performed.

Herein we report the autopsy and histological findings in a three-month-old female infant with surgically corrected ileal atresia and flexion contractures of the lower limbs.

Address for correspondence:
Emran Lyutfi
Medical University of Varna
55 Marin Drinov St
9002 Varna
Bulgaria
e-mail: heliacaquila@gmail.com

Received: November 03, 2018
Accepted: December 17, 2018

MATERIALS AND METHODS

Autopsy report:

Upon general observation only a flexion-adduction contracture of the lower limbs was noted as well as the site of surgical correction of ileal atresia with an ileostomy. The measurements were as follows: height – 51 cm, weight – 2.500 g, head circumference - 35 cm, large fontanelle sized 6x4cm, and opened small fontanelle sized 2x2cm with an abundance of Wormian bones.

Organ measurements were as follows: left lung – 37 g, right lung – 33 g, with edematous section with foamy serous fluid draining from the cut surface on compression; heart – 18 g, with a membranous obstruction of the foramen ovale; liver – 157 g, with preserved consistency; the gastrointestinal tract was undisturbed, filled with digested food particles, the suture sites of the anastomosis were well-healed, with no signs of inflammation; left kidney – 11 g, right kidney – 12 g, without notable abnormalities; spleen – 10 g, without notable abnormalities; cerebrum, cerebellum, brain stem, and spinal cord – 435 g, notably edematous.

Dissection of the musculoskeletal system revealed irregular margins of the costochondral borders (Fig. 1) and grossly visible decreased trabecular bone matrix of both the ribs and the calcaneus (Fig. 2). No fractures were noted.

Fig. 1. Gross view of the costochondral border

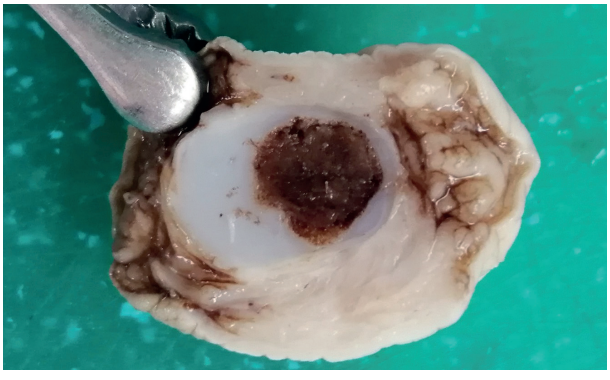

Fig. 2. Section through the calcaneus with no grossly visible trabecular bone

Upon request, additional medical documentation, no test for OI had been performed, however, an x-ray performed postoperatively showed no signs of OI or impaired bone formation (Fig. 3). The patient was delivered naturally, after an unfollowed pregnancy, at the 34th week of gestation.

Organ histology revealed neonatal morphology of the organs, without evident changes, apart from the edema in the lungs and central nervous system.

Bone histology, without decalcification, stained both with hematoxylin and eosin (H&E) and Azan's stain, revealed no change in the formation of lamellar bone, however, there was nearly no trabecular bone, with degenerative phenomena at the costochondral border (Fig. 4). The scleral thickness and structure on H&E and Azan revealed no change in the deposition of the extracellular matrix (Fig. 5).

The osseous changes, although severe, were not considered a result of the OI spectrum of diseases,

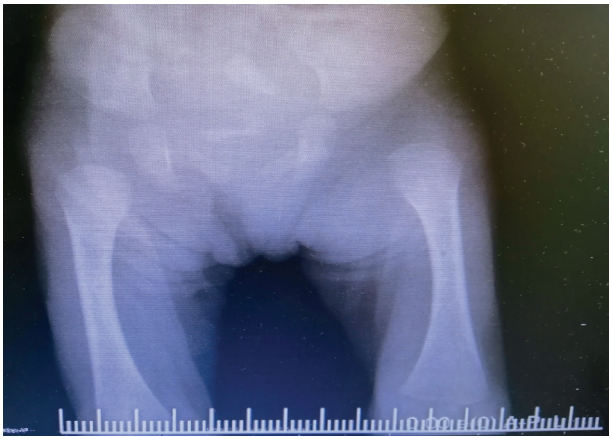

Fig. 3. X-ray carried out during hospital stay, no evidence of bone pathology

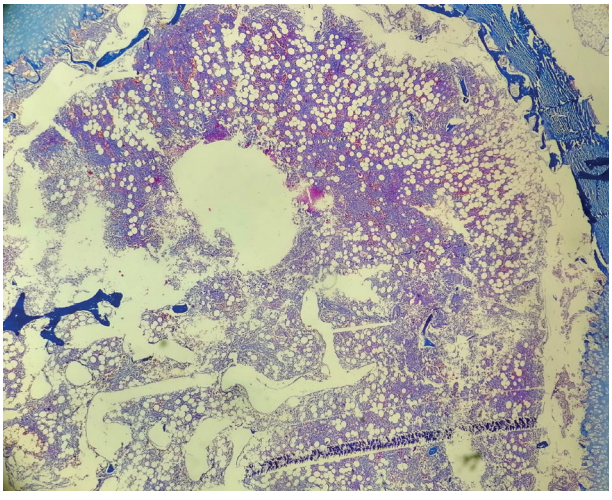

Fig. 4. Calcaneus, Azan stain 40x, only a few trabecular bone fragments seen across the bone marrow

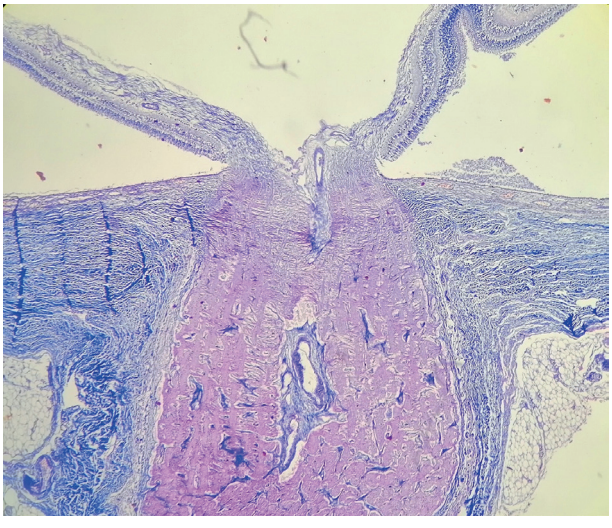

Fig. 5. Sclera, Azan stain 40x, section through the optical nerve, the delaminated retina is seen

despite the flexor-adductor contracture being suggestive of Bruck syndrome (4-6).

The cause of death was determined as a complication of the ileal atresia, with the osseous changes being attributed to prematurity, malabsorption, and increased metabolic needs of the organism.

DISCUSSION

Although decreased bone formation should always sway the pathologist in the direction of the OI group of conditions, the lack of genetic tests, especially on the background of normal bone development and lack of fractures, always poses a diagnostic dilemma (1).

Wormian bones and an unclosed fontanelle in infants delivered at term are widely considered as pathognomonic for the OI spectrum of conditions. However, in infants delivered prematurely, especially ones with severe organ pathology, this should not be taken as a sure sign of OI (2,3,5).

As illustrated in our case, bone density and formation may be hindered by malabsorption or increased metabolic needs, especially in premature infants (7). Scleral histology is especially important in such cases to differentiate between mineralization issues or collagen deposition issues.

Rickets is also a condition that should be considered in such cases, especially in infants with prolonged hospital stay and increased metabolic needs. However, rickets also affects bone in a wider pattern with caput quadratum and deformations of the ribs (8-10).

Malabsorption, although rare in presentation with impeded bone formation only, should always be considered. Increased metabolic need as in our case, together with malabsorption, regardless of the cause, can also have a similar presentation in adults, presenting as premature osteoporosis (7).

CONCLUSION

Genetic tests and detailed clinical information are key in determining the cause for decreased bone density in infants. Morphological study alone can rarely identify the cause unless a detailed approach is undertaken. As illustrated by our case, mimicry of OI can be caused by malabsorption, especially with severe gastrointestinal pathology.

REFERENCES

1. Cassella JP, Stamp TCB, Ali SY. A morphological and ultrastructural study of bone in osteogenesis imperfecta. Calcif Tissue Int. 1996;58(3):155-65. doi:10.1007/BF02526881.
2. Harrington J, Sochett E, Howard A. Update on the evaluation and treatment of osteogenesis imperfecta. Pediatr Clin North Am. 2014;61(6):1243-57. doi:10.1016/j.pcl.2014.08.010.
3. Van Dijk FS, Cobben JM, Kariminejad A, Maugeri A, Nikkels PG, van Rijn RR, et al. Osteogenesis imperfecta: A review with clinical examples. Mol Syndromol. 2011;2(1):1-20. doi:10.1159/000332228.
4. Bank RA, Robins SP, Wijmenga C, Breslau-Siderius LJ, Bardoel AF, van der Sluijs HA, et al. Defective collagen crosslinking in bone, but not in ligament or cartilage, in Bruck syndrome: indications for a bone-specific telopeptide lysyl hydroxylase on chromosome 17. Proc Natl Acad Sci U S A. 1999;96(3):1054-8. doi:10.1073/pnas.96.3.1054.
5. Mokete L, Robertson A, Viljoen D, Beighton P. Bruck syndrome: congenital joint contractures with bone fragility. J Orthop Sci. 2005;10(6):641-6. doi:10.1007/s00776-005-0958-9.
6. Afşarlar ÇE, Peltek-Kendirci HN, Erdoğan D, Özgüner İF, Çavuşoğlu YH, Karaman A, et al. The first case of Bruck syndrome associated with gastroschisis. Turk J Pediatr. 55(6):651-4.
7. Keller J, Layer P. The pathophysiology of malabsorption. Visz Gastrointest Med Surg. 2014;30(3):150-4. doi:10.1159/000364794.
8. Al-Jundi SH, Dabous IM, Al-Jamal GA. Craniofacial morphology in patients with hypophosphataemic vitamin-D-resistant rickets: A cephalometric study. J Oral Rehabil. 2009;36(7):483-90. doi:10.1111/j.1365-2842.2009.01963.x.
9. Nordahl J, Hollberg K, Mengarelli-Widholm S, Andersson G, Reinholt FP. Morphological and functional features of clasts in low phosphate, vitamin D-deficiency rickets. Calcif Tissue Int. 2000;67(5):400-7. doi:10.1007/s002230001151.
10. Gjørup H, Kjær I, Sonnesen L, Haubek D, Beck-Nielsen SS, Hintze H, et al. Craniofacial morphology in patients with hypophosphatemic rickets: A cephalometric study focusing on differences between bone of cartilaginous and intramembranous origin. Am J Med Genet Part A. 2011;155(11):2654-60. doi:10.1002/ajmg.a.34242.