

DEPOSITION OF HOMOGENSIC ACID IN LONG BONES WITH DIAPHYSEAL LYTIC CHANGES IN A PATIENT WITH OCHRONOSIS

Zrinka Jajić, Ivo Jajić and Tomislav Nemčić

Department of Rheumatology, Sestre milosrdnice University Hospital, Zagreb, Croatia

SUMMARY - Presentation is made of a 58-year-old female patient with alkaptonuria and ochronosis. Calcification and ossification of intervertebral disks in the lumbar, thoracic and cervical spine were developed. In addition, diaphyseal lytic changes of the femur, tibia and fibula were observed. The lesions were diffuse and unequal. Diaphysis of the long bones had a 'moth-eaten' bone appearance. No data on such changes were found in the available literature.

Key words: *Ochronosis; Ochronosis - pathology; Ochronosis - complications; Homogentisic acid*

Introduction

Ochronosis is caused by inherent flaw due to the absence of the enzyme homogentisic acid oxidase¹. This enzyme normally aids in the oxidation of tyrosine/phenylalanine in the complete breakdown of amino acids to water and carbon dioxide. Excessive homogentisic acid in the blood and urine results in the deposition of black pigment in soft tissues and cartilage (meniscus, disk, joints, ear, nose). To our knowledge, there are no literature reports on the pigment deposition in bone marrow and bone tissue leading to lytic lesions. That is why the case presented appears to be quite interesting and intriguing.

Case Report

Our patient was a 58-year-old woman, a housewife, suffering from alkaptonuria from birth. She had two adult children. She had no had any serious illness. In 1998, she fell and sustained fracture of the left femur neck. After the

operation and implantation of total hip prosthesis, she underwent rehabilitation and walked on a crutch for a long time. Radiologic examination was performed several hours after the fracture.

On presentation, blue auricles, tip of the nose, both sclerae and fingertips were observed. Thoracic kyphosis and reduced cervical and lumbar lordosis were present. Spine movements (inclination and reclination) were reduced. The patient had been becoming shorter, and she could reach ever lower spot on her leg with her fingers. The costal arch 'sat' on the iliac crest.

Laboratory findings: ESR 30, erythrocytes 4.02, hemoglobin 111, leukocytes 9.1. Other hematology and biochemistry findings were normal. The homogentisic acid test was positive in the blood and urine². Biochemical markers of bone turnover, and bone or synovium tissue PHD were not determined.

Radiologic finding: Beside ochronotic changes including calcification and ossification of the intervertebral disks in the lumbar, thoracic and cervical spine (Fig. 1) and ochronotic peripheral arthropathy, diaphyseal lytic changes of the femur, tibia and fibula were also recorded (Figs. 2 and 3). Osteolytic changes diffusely affected bone tissue, especially in the sponge area, wherefrom the lesions extended into the cortex causing erosions. Radiologic images showed the bone tissue appearing like a 'moth-eaten' bone. Os-

Correspondence to: *Zrinka Jajić, M.D., Ph.D.*, Department of Rheumatology, Sestre milosrdnice University Hospital, Vinogradska c. 29, HR-10000 Zagreb, Croatia

Received February 1, 2000, accepted in revised April 14, 2000



Fig. 1. Calcificatio and ossification of the intervertebral disk in the lumbar and thoracic spine.



Fig. 2. Lytic changes in the diaphyseal area of the femur.



Fig. 3. Lytic changes in the diaphyseal area of the tibia and fibula.

teoporosis that intensifies lytic lesions was also present. No such changes were found in the skeleton of the upper limbs. DEXA was not performed.

Discussion

There are no radiologic changes early in the course of the disease. Changes occur in the second and third decade, and most distinctive findings are calcification and ossification of multiple intervertebral disks, which result in reduced inclination and reclination of the spine. Changes of peripheral joints usually develop secondary to the changes of the spine⁵. Subchondral cysts are not pronounced in ochronosis, and lytic changes have not been mentioned in the available literature¹⁻⁶.

Homogentisic acid is being deposited in the joint cartilage causing its destruction. Similarly, it is deposited in the bone tissue causing lytic lesions, their severity depending on the homogentisic acid amount. Lytic changes are likely to more easily develop in an osteoporotic area.

In conclusion, we consider that the lytic changes of the diaphyseal bone were due to the effect of homogentisic acid, which is secreted in excess in patients with ochronosis.

References

1. LaDU BN, ZANNONI UG, LASTER L, SEEGMILLER JE. The nature of the defect in tyrosine metabolism in alkaptonuria. *J Biol Chem* 1958;330:251.
2. SEEGMILLER JE, ZANNONI UG, LASTER L et al. An enzymatic spectrophotometric method for the determination of homogentisic acid in plasma and urine. *J Biol Chem* 1961;236:774-7.
3. RESNICK D, NIWAYAMA G. *Diagnosis of bone and joint disorders*. Philadelphia: WB Saunders Company, 1981.
4. SCHUMACHER HR. Ochronosis. In: KOOPMAN WJ, ed. *Arthritis and allied conditions. Textbook of rheumatology*. Baltimore, Philadelphia, London, Paris, Bangkok, Buenos Aires, Hong Kong, Munich, Sydney, Tokyo, Wroclaw: Williams and Wilkins & Waverly Company, 1997:2189.
5. KUNTZ D, BURDNI T. Ochronosis. In: KLIPPEL JH, DIEPPE PA, eds. *Rheumatology*. St. Louis, Baltimore, Boston, Chicago, London, Philadelphia, Sydney, Toronto: Mosby Co., 1994:244.
6. RESNICK D, YU JS, SARTORIS D. Imaging. In: KELLEY WN, HARRIS FD, RUDDY S, SLEDGE CB. *Textbook of rheumatology*. Philadelphia, London, Toronto, Montreal, Sydney, Tokyo: WB Saunders Company, 1997:626.

Sažetak

ODLAGANJE HOMOGENITIZINSKE KISELINE U DUGE KOSTI S LITIČKIM PROMJENAMA
DIJAFIZA U BOLESNICE S OHRONOZOM*Z. Jajić, I. Jajić i T. Nemčić*

Prikazana je 58-godišnja bolesnica s alkaptonurijom i ohronozom. Nađena je kalcifikacija i osifikacija intervertebralnog diska lumbalne, torakalne i vratne kralješnice. Usto, bile su razvijene litičke promjene femura, tibije i fibule. Lezije su bile difuzne. Dijafize dugih cjevastih kostiju izgledale su kao da su ih 'izjeli moljci'. U dostupnoj literaturi nije nađen opis takvih promjena.

Ključne riječi: *Ohronoza; Ohronoza, patologija; Ohronozoa, komplikacije; Homogentizinska kiselina*