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Case Report

A case report of neonatal osteopetrosis

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ABSTRACT

Osteopetrosis is a rare bone disease that occurs due to failure in bone resorption. Osteoclast dysfunction and persistent calcification of primary chondroids and bones are the cause of the disease. Osteopetrosis is a rare hereditary condition known as abnormal bone resorption. Considering the importance of prompt and timely diagnosis and follow-up and treatment with significant complications, we decided to report a case of neonatal osteopetrosis diagnosed 12 h following admission to the neonatal intensive care unit of Imam Reza Hospital. The 7-day-old male neonate was hospitalised due to abdominal mass and thrombocytopenia. Hepatosplenomegaly and thrombocytopenia were diagnosed on examination and tests. Finally, the infant was referred to the neonatal intensive care unit of Imam Reza Hospital in Mashhad at 7 days of age for further evaluation. Chest X-ray taken as part of sepsis workup showed increased rib and arm bone density. A facial X-ray was taken, and eye sign detected for the diagnosis of osteopetrosis. In every neonate with hepatosplenomegaly, thrombocytopenia, and increased bone density, in addition to a neonatal sepsis workup, a facial X-ray should be taken initially to observe signs and confirm osteopetrosis.

Reporte de un caso de osteopetrosis neonatal

Palabras clave:
Neonatal
Trombocitopenia
Signo de ojo
Osteopetrosis

RESUMEN

La osteopetrosis es una rara enfermedad ósea originada por una falla en la resorción ósea, debido a la disfunción de los osteoclastos y la calcificación persistente de condroides y huesos primarios. Se trata de una condición hereditaria rara, conocida como reabsorción ósea anormal. Considerando la importancia del diagnóstico rápido y oportuno y el seguimiento y tratamiento con complicaciones significativas, decidimos reportar un caso de osteopetrosis neonatal diagnosticado después de 12 horas de ingreso a la unidad de cuidados intensivos neonatales del Hospital Imam Reza. El neonato, de sexo masculino, de 7 días, fue hospitalizado por la presencia de una masa abdominal y trombocitopenia. En los exámenes se

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diagnosticó hepatoesplenomegalia y trombocitopenia. Finalmente, a los 7 días fue remitido a la Unidad de Cuidados Intensivos Neonatales del Hospital Imam Reza en Mashhad para una evaluación adicional. En la radiografía de tórax tomada dentro de un estudio de sepsis, se observó un aumento de la densidad de los huesos de las costillas y los brazos. Para el diagnóstico de la enfermedad de osteopetrosis, se tomó una radiografía de la cara y se detectaron signos oculares. En cada neonato con hepatoesplenomegalia, trombocitopenia y aumento de la densidad ósea, además del papel de la sepsis neonatal, en un primer momento se debe tomar una radiografía de la cara para observar signos y confirmar la osteopetrosis.

Introduction

Osteopetrosis is a diseases. It consists of two words bone and stone meaning osteo and petros, respectively. This rare disorder occurs due to loss bone resorption.[1] The cause of ones can be Osteoclast dysfunction and tenacious calcification of primary chondroids and bones. Osteopetrosis is a rare hereditary condition known as abnormal bone resorption.[2]

The most common method to diagnose this disease is based on clinical evaluation and radiography.[2] Symptoms of congenital osteopetrosis include anemia, severe thrombocytopenia, leukoerythroblastosis, progressive hepatomegaly, cerebral nerve palsy, optic nerve and blindness atrophy, hydrocephalus, multiple bone fractures, hypochondriacal seizures, hypokalemic seizures.[3]

The major types of osteopetrosis include severe autosomal recessive form (OMIM 259700) with frequency of 125,000 births and mild autosomal dominant form (OMIM 1666000) with frequency of 12,000 births. Both types of mutations lead to acidification defection for normal osteoclast function. Severe form is usually diagnosed in childhood or early childhood due to macroscale, hepatosplenomegaly, deafness, blindness and severe anemia.[4]

Considering the importance of prompt and timely diagnosis and follow-up and treatment to prevent more serious complications, we decided to report a case of neonatal osteopetrosis who was diagnosed after 12 h of hospital admission in the neonatal intensive care unit of Imam Reza Hospital in Mashhad.

Case presentation

The male newborn was at term or 38 completed week's gestational age due to in touch of abdominal mass was hospitalized in Bojnourd hospital (North Khorasan). Birth weight, height and head circumference were 3390 kg, 51 cm, 35 cm and 35 cm, respectively. Maternal blood group was O^+ and neonatal blood group was O^-.

The patient's history indicates that the infant was the second seek child that born in Bojnourd (North Khorasan province) and his parents had a familial marriage. The mother had a history of gestational diabetes mellitus which was controlled by diet. There is no family history of osteoporosis in parents. In examinations and tests, hepatosplenomegaly and thrombocytopenia were detected. The patient was treated with intravenous immunoglobulin (IVIG). (Primary platelet count: 30,000 and maternal platelet count was normal). Finally, the infant was referred to the Neonatal Intensive Care Unit of Imam Reza Hospital in Mashhad at 7 days of age for further evaluation. The liver and spleen were touched on examination. Other examinations and vital signs were normal.

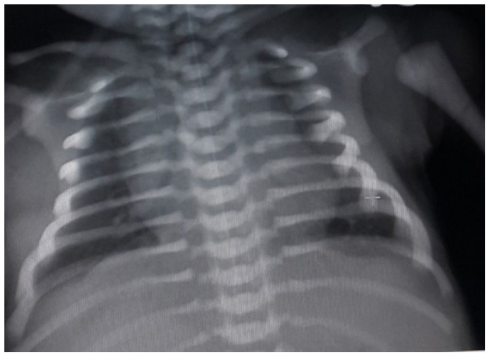

Fig. 1 – X-ray of the chest with increased rib and arm bone density.

Table 1 – Results of biochemical tests.

Na: 134	CRP: 0.3
K: 4.7	ESR: 6
Ca: 9.5	Blood culture: negative
Mg: 2.4	Urea: 22
U/A, U/C: Normal	Ceratinin: 0.6

On ultrasound imaging, liver diameter was 67 mm and spleen with span 77 mm were larger than normal. Due to hepatosplenomegaly and thrombocytogenesis in order to reject of neonatal sepsis, some tests including ESR (erythrocyte sedimentation rate test), CRP(C Reactive Protein), blood culture and chest X-ray were done. In Chest X-ray increasing of rib and arm bones density was observed (Fig. 1), therefore the face X-ray was taken and the diagnosis of osteoporosis with the Eye glass sign, was confirmed (Fig. 2). Other testings were normal for sepsis and congenital infections .The following results were reported in laboratory studies (Table 1).

The results of white blood cell, hemoglobin, MCV (MEAN CORPOSCULAR VOLUME) and platelet counts are as follows (Table 2).

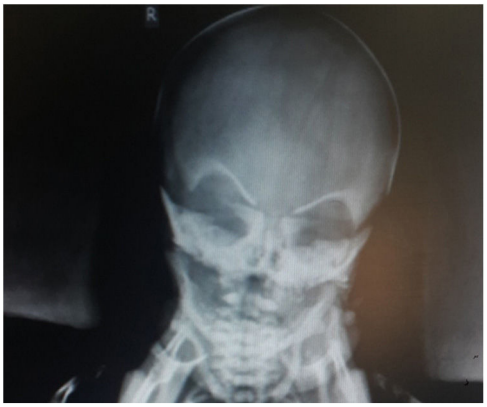

Fig. 2 – Facial imaging and diagnosis of osteoporosis with eye symptoms.

Table 2 – The white blood cell, hemoglobin, MCV and platelet counts process.

WBC	23.9 L:46.8	16.5 L:40 N:46	24.5	18.5 L:50
HB	14	12.6	14.4	11.7
MCV	95.7	96.36	95.43	94.4
Plt	72	46	43	23

Discussion

Osteopetrosis is more commonly known as marble bone disease (Albers-Schönberg or Marble bone). Multiple genetical or biochemical defect can product it, and reduce bone resorption.[5] Clinical Osteopetrosis is a heterogeneous group with increased bone density in radiographs.[5] In the present study, due to the excessive increasing of bone density in chest X-ray, suspected osteopetrosis and "Eye Glass" sign was seen in facial X-ray.

Lee Sh et al. survived neonates with hepatosplenomegaly, anemia, thrombocytopenia, congenital infections including CMV. Congenital CMV infection was diagnosed by virus isolation in urine, blood or saliva in the first 3 weeks of life. Diagnostic methods included routine culture of the virus with immunofluorescence and PCR. Although this patient had not been tested for CMV in the first 3 weeks of life, she had clinical manifestations similar to congenital infection. There was no evidence of intracranial calcification on brain CT scan, but sclerotic changes of the skull were noted, which could be osteopetrosis. Subsequent radiologic studies confirmed osteoporosis,[5] in the present study, initially suspected of congenital infections such as CMV and Rubella Torch, but tests was negatively reported. Reports have shown that hematologic abnormalities can occur both in CMV infection and osteopetrosis. Also in the early phase of antiviral treatment, the cause of anemia, thrombocytopenia and measurement of liver functional test are unclear, because severe anemia and thrombocytopenia persisted over 5 weeks of antiviral drugs.[6]

Skeletal fragility is a clinical feature that is known to be a complication of osteopetrosis.[7] No effective treatment for osteopetrosis has been identified so far, but timely diagnosis and management can greatly protect the patient from dangerous complications.[8] The only definitive and available treatment is hematopoietic stem cell transplant disease,[9] but another study by Johanson showed that timely gene therapy can be more successful than bone marrow transplant.[10] In Johansson study survived the role of familiar marriage in the occurrence of osteopetrosis, they reported that the prevalence of osteopetrosis was higher in populations that had familiar marriage.[10] Our case was result familiar marriage, so in patient with this history must to be attention for osteopetrosis disease.

Molecular investigation of the patient with heterozygous compound mutation in TCIRG1 and heterozygous splice site mutation in CLCN7. CLCN7 recognizes the specific chloride ion channel, CLCN7, which is associated with the TCIRG1 gene product, the a3 subunit of the V-ATPase. CLCN7 has a good function in the neutralization current, is effective for proton pumping, and is important for acid secretion in absorption lacunae, acid coating for bone matrix degradation. Most forms of osteopetrosis are due to dysfunction of osteoclasts, while to a lesser extent those due to disorders of osteoclastogenesis. The most common event after transplantation is graft failure due to delayed hematopoietic regeneration due to small or almost absent bone marrow space and graft-versus-host disease (GvHD).

Combined mutation in TCIRG1 and CLCN7 causes problems in the transplant process and it is better to have this knowledge before treatment. Considering the importance of early diagnosis and timely initiation of treatment, any infant with thrombocytopenia and organomegalia should be one of the most important differential diagnoses of osteopetrosis. In the study of Gul et al., symptoms of the disease were described as decreasing volume and activity of bone marrow, liver enlargement, spleen, and various infections,[11] In our study, due to hepatosplenomegaly and thrombocytopenia, other causes such as sepsis were evaluated in the patient, that all of the evaluations was negative.

Due to lack of proper response to treatment, with suspected alloimmune Thrombocytopenia, a course of IVIG therapy has been used. The patient was treated with intravenous immunoglobulin (IVIG). (Primary platelet count: 30,000 and maternal platelet count was normal). The mother had a history of gestational diabetes mellitus which was controlled by diet and his parents had a familial marriage. The values of the full description of the patient's file are as follows phosphorus:

5.2 mg/dl
TSH:5 mc Iu/l
T4:10 ng/dl
T3:95 ng/dl
PTH:5.4 ml

Significant increasing in serum acid phosphatase due to loss of osteoclast cells is reported in these patients,[12] but in the present study, this case study was not investigated, so needs to more studies.

Conclusion

According to recent studies and reports of this rare disease, in each patient with familiar marriage, hepatosplenomegaly,

thrombocytopenia and also due to increase of bone density in chest X-ray, diagnosis of osteopetrosis is strongly recommended. To confirm of this disease and seen of "Eye Glass" sign should be done facial X-ray in order to fast diagnosis and referral to neonatal hematologist for bone marrow transplamention or other treatment.

Ethical considerations

The consent of the patient is not necessary for the publication of the article because her anonymity is fully preserved, the authors declare that this article does not contain personal information that allows to identify the patients. The authors declare that informed consent has been obtained for experiments with human subjects. Human privacy rights must always be respected. We confirm that there is no conflict of interest related to this article. Ethical approval and informed consent, all procedures performed in studies involving human participants were in accordance with 1964Helsinki declaration and its later amendments or comparable ethical standards.

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Consent to participate

We agree to participate in the research project and the following is explained to us: Research may be of direct benefit to Our participation is completely voluntary. Our right to cancel the study at any time without any consequences for us.

Consent to publish

We give my consent for the publication of identifiable details, which can include photograph(s) and/or videos and/or case history and/or details within the text ("Material") to be published in the above Article. Therefore, anyone can read material published in the article.

Availability of data and materials

The authors declare that this article does not contain personal information that would allow the identification of patients. A 7-day-old male infant was admitted to the hospital due to abdominal mass and thrombocytopenia. Informed consent was not required because the diagnostic process and tests did not cause a disturbance in the vital function of the baby.

Conflict of interest

None.

1) This material is the authors' own original work, which has not been previously published elsewhere.
2) The paper is not currently being considered for publication elsewhere.
3) The paper reflects the authors' own research and analysis in a truthful and complete manner.
4) The paper properly credits the meaningful contributions of co-authors and co-researchers.
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