구루병과 수두증을 동반한 Osteopetrosis 증례

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Osteopetrosis Associated with Hydrocephalus and Rickets: A Case Report

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Osteopetrosis or albers-Schonberg disease is extremely rare disease. It is characterized by osteoporosis, stunted growth, deformity, increased likelihood of fractures, also patients suffers anemia, recurrent infections and hepatosplenomegaly. However, we recently came upon a 14-month-old female as the 1st child of osteopetrosis with hydrocephalus and rickets. She has the typical symptoms such as nystagmus, osteosclerosis -especially in skull. Brain Magnetic Resonance Imaging (MRI), MRI shows hydrocephalus and x-ray finding are consistent with rickets. This is the first report of osteopetrosis with hydrocephalus and rickets in Korea by pediatrician.

Key Words: Osteopetrosis; Rickets; Hydrocephalus

Introduction

In 1904 Albers-Schonberg reported three cases of abnormal sclerosis of the bone. The main features were generalized osteosclerosis, lymphadenopathy, hepatosplenomegaly and anemia¹⁾.

In 1926, Karshner suggested the term osteopetrosis (stony bones) "-because in a word it describes the primary pathological condition, bone petrification-". This term has been widely accepted²⁾.

Osteopetrosis, literally "-stone bone-", is also known as marble bone disease and Albers-Schonberg disease. The overall incidence of these conditions is difficult to estimate but autosomal recessive osteopetrosis (ARO) has an incidence of 1 in 250,000 births, and autosomal dominant osteopetrosis (ADO) has an incidence of 1 in 20,000 births³⁾. In health, osseous tissue remodeling results from the balanced processes of bone formation and resorption. Excessive resorption causes osteoporosis, which accounts for most non-traumatic fractures.

Normal bone growth is achieved by a balance between bone formation by osteoblasts and bone resorption (break down of bone matrix) by osteoclasts. In osteopetrosis, the number of osteoclasts may be reduced, normal, or increased. Most importantly, osteoclast dysfunction mediates the pathogenesis of this disease. To date, there has been no case report of osteopetrosis with hydrocephalus and rickets yet. Here, we present a pediatric case of osteopetrosis associated with

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hydrocephalus and rickets.

Case report

A 10 month-old girl was referred to our hospital for nystagmus. The pregnancy and term birth were uneventful. She was delivered by normal spontaneous vaginal delivery in March 2011. Her birth weight was 3.3 kg (50th percentile). She was her parents' second child and had one older sibling.

On examination at 10 months of age she weighed 10.5 kg (50th percentile) and measured 90 cm (97th percentile) in long. Her head circumference was 52 cm (> 97th percentile), the anterior fontanel was widely open with, mild frontal bossing, and a separated suture line. Her development was normal. Spontaneous nystagmus became apparent at 10 months of age and was not positionally related. Her pupils were reactive and eyes followed the light. She presented with right otorrhea(bloody, serous fluid) and tympanic membrane perforation of the right ear and we discovered that her left eardrum was bulging.

Laboratory examination showed increased alkaline phosphatase (ALP) 521 IU/L (normal: 45~129 IU/L), and acid phosphatase 9.5 U/L

(normal: -6.5 U/L) whereas other lab tests were normal including 25-OH vitamin D 29.2 ng/ml (normal: 11-70 ng/mL), osteocalcin (11.8 ng/mL), parathyroid hormone (PTH), 18.2 pg/mL (normal: 15.0-65.0 pg/mL), free T₄ 17.1 pmol/L (normal: 11.5~23 pmol/L), and thyroid-Stimulating hormone (TSH) 0.47 mIU/L (normal: 0.17~4.05 mIU/L). Electrolyte imbalances were not detected on admission and , and there was no evidence of a hematologic disorder. We did not conduct a genetic test.

Brain MRI demonstrated moderate dilation of both lateral ventricles with periventricular interstitial edema (Fig. 1A, 1B). Although she had hydrocephalus, she did not present typical symptoms such as behavior changes, decreased consciousness, lethargy, or neurological symptoms, such as weakness, numbness, or vomiting. Simple skull radiography demonstrated increased thickness of the cranium and calvaria, in addition to increased overall bone density (Fig. 2). Radiography of the forearm and hand revealed rickets, defective metaphyseal modeling, and an irregular border between the growth plate and the metaphysal widening and fraying (Fig. 3).

The femurs also show osteopenic lesions on the metaphysis and epiphysis (Fig. 4). Bone scan revealed abnormal radioisotope accumulation throughout the skull base, especially in the skull base,

Fig. 1. Brain MRI showing moderate dilation of both lateral ventricles with periventricular interstitial edema (1A: T2 weighted image, 1B: Flair image)

Fig. 3. Radiographs of upper extremity showing osteopenic changes suggestive of rickets.

Fig. 2. Skull X-ray showed cranioclerosis and calvarial thickening and skull base sclerosis (2A, 2B) and sphenoidal deformity (2B)

Fig. 4. X-ray of both femurs showed osteopenic lesions on the both metaphysis and osteosclerosis on the both diaphysis area.

Fig. 5. Bone scan reveals increased radiotracer accumulation in all of skull especially in skull base, maxilla, mandible, and diaphyseal area of the long bones.

as well as hyperdense zygomatic maxilla and mandible (Fig. 5). The long bones of the arms and legs appear clubbed and showed diffuse uptake along the diaphysis, while no visible changes in radiotracer accumulation were seen in the metaphyseal area.

Discussion

Our patient presented with ARO, a life-threatening condition that classically manifests in the first few months of life. Increased bone density can paradoxically weaken the bone, resulting in a predisposal to fractures and osteomyelitis. Macrocephaly and frontal bossing develop within the first year, resulting in a typical facial appearance. Such skull changes can result in choanal stenosis and hydrocephalus⁴⁾.

The rickets component of osteopetrorickets is reversible if treated. After treatment, patients experience increased activity, decreased irritability, improved appetite, and protection from recurrent respiratory tract infections. If bone marrow transplantation (BMT) facilities are available, the treatment of rickets is essential for optimal results. Rickets with osteopetrosis is treated with vitamin D3 and high doses of calcium, which improves a child's general well-being⁵⁻⁷⁾. BMT is the only curable therapy for osteopetrosis because it provides monocytic osteoclast precursors. However, in the presence of underlying rickets, the clinical response to BMT is inadequate⁸⁻¹¹⁾.

Our patients showed both typical and atypical features of osteopetrosis. Typical features included a radiological skeletal survey which revealed diffuse bony sclerosis, wide-open anterior fontanels and nystagmus (by nerve entrapment syndrome). However, our patient did not have a hematologic disorder; in fact, her hemoglobin level was normal and she did not show any

other signs of hematologic failure.

Although BMT is the only effective and curable treatment for osteopetrosis, many possible complication including graft-versus-host disease, can impede treatment success^{7,13)}.

Conservative treatments such as vitamin D, erythropoietin, γ -interferon and corticosteroid are usually recommended^{14,15)}. Hence in our case, we used a high-dose steroid 2 mg/kg/day with vitamin D supplementation (400 IU/day).

Infantile osteopetrosis is an extremely rare disease with a poor prognosis unless timely intervention is provided. We believe that the current case is the first of infantile osteopetrosis complicated by rickets and hydrocephalous in Korea. Further studies on the clinical features and prognosis of patients with this disease would help prevent complications.

요약

Osteopetrosis는 골경화증(osteosclerosis), 림프질환(lymphadenopathy), 간비비대(hepatosplenomegaly)와 빈혈을 주소로 하는 드문 질병이다. 이중 상염색체 열성 osteopetrosis는 영아기에 진단되고 골수기능이 심하게 저하되며 구루병을 동반한 경우에는 골수이식을 시행할 수 없어 예후가 불량하다고 알려져 있다. 본 저자는 수두증과 구루병을 보인 10개월 여아에서 steroid와 vitamin D 치료 증례를 보고하는 바이다.

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