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OSTEOSCLEROSIS IN NETHERTON'S DISEASE

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Netherton 病にみられた骨硬化症

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Netherton病は1958年、NethertonがCongenital ichthyosiform erythroderma、“Bamboo baby”，Atopic diathesisを主徴とする1症例を“A unique case of trichorrhexis nodosa”として報告して以来、文献上諸外国において9例、本国において1例をみるのみの極めて稀な疾患である。

最近、本邦での唯一例と思われる本疾患例につき、X線検査を行う機会を得、骨にかなり著明な変化を認めめたので報告する。

症例は8歳の女児で、従来より全身皮膚の乾性脂漏性皸癬、毛髪断端、痙縮素因など定型的なNetherton病の特徴を有し、皮膚科にて経過観察していたものであるが、アフタ性口内炎のため、栄食不能となり、著明な栄養障害をきたして来院した。

臨床検査所見では著明な異常をみないが、尿中アルギニン、アスパラギン酸、セリン、グリシンの増量を認める。入院時の胸部X線像で鎖骨、肋骨等に異常を認めたので、全身の骨撮影を行った。

全身の骨には大、多骨腫縮に似た著明な石灰沈着増強を認め、鎖骨、大腿骨等皮質の著明な肥厚と、顕著の変状がみられた。この所見は手指骨等の著明で、一部では顕著で消失し、指骨末節は短く、先端の狭小化がみられる。頭蓋骨等扁平骨でも、全般的に骨頭影が薄く、板間隔に相当する部分がほとんどみられない。形態的には指骨末節、骨頭にわずかに変形がみられる程度で、著しい変形はない。

大腿骨より得た生検標本では、骨頭が極度に狭い変型的な骨硬化症の像を示した。

本疾患の報告例が少なく、またいずれも皮膚疾患として報告されているため、X線所見における詳細な記載がなく、本症例における所見が疾患固有のものと断するには踏襲するが、現在まで報じられている種々の型の骨硬化性疾患と臨床的にまたX線学的に明らかに異っており、本疾患の1例にみられた特異的な型の骨硬化症としてここに報告した。アミノ酸尿と骨変化の関連も考えられるが、明確には云いがたい。
Netherton's disease is an extremely rare congenital disease characterized by ichthyosiform erythroderma, "bamboo hair", and atopic diathesis. Ten cases have been reported since the first case reported by Netherton in 1958. However, no precise description has been made on roentgenographic abnormalities.

This paper describes the roentgenological skeletal abnormalities observed in a patient with typical manifestations of Netherton's disease.

Case Report

An eight-year-old girl was admitted to the Kobe Children's Hospital because of malnutrition, generalized dry seborrheic scaling, and abnormally short hairs (Figs. 1 and 2). The patient was emaciated because of difficulty in eating secondary to severe oral aphthosis. Family history was non-contributory.

The laboratory test results are summarized in Table 1. Routine examinations of blood and urine gave values mostly within normal limits, though the red blood cells were slightly microcytic-hypochromic.

Urinary amino acid determination using an autoanalyzer revealed an increase of arginine, aspartic acid, serine, glutamic acid, and glycine. In normal subject, arginine, aspartic acid, serine, and glutaminic acid are not excreted in the urine. Renal excretory function was normal, and IVP showed a normal pattern of calyces and pelvis.

A routine chest X-ray film revealed increased density of the ribs, clavicles, and vertebrae (Fig. 3). The total skeletal series disclosed generalized increase of bone density involving both the flat and tubular bones. The increase of bone density was apparently due to endosteal cortical hypertrophy, which caused
Table 1. Laboratory Data

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<th>Blood</th>
<th>Urine</th>
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<tr>
<td>RBC 506 × 10^9/mm³</td>
<td>Amino acids</td>
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<tr>
<td>Hemoglobin 11.5 g/dl</td>
<td>Arginine 16.5 mg/day</td>
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<tr>
<td>Hematocrit 32%</td>
<td>Aspartic acid 11.5 mg/day</td>
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<tr>
<td>WBC 6400/mm³</td>
<td>Serine 16 mg/day</td>
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<tr>
<td>Serum protein 7.6 g/dl</td>
<td>Glutamic acid 18.2 mg/day</td>
</tr>
<tr>
<td>SGOT 29 KU</td>
<td>Glycine 240 mg/day</td>
</tr>
<tr>
<td>SGPT 13 KU</td>
<td>Albumin negative</td>
</tr>
<tr>
<td>Serum alkaline phosphatase 8.3 KAU</td>
<td>Sugar negative</td>
</tr>
<tr>
<td>Na 139 mEq/l</td>
<td>Urobilinogen normal</td>
</tr>
<tr>
<td>K 4.4 mEq/l</td>
<td>Occult blood test negative</td>
</tr>
<tr>
<td>Cl 99 mEq/l</td>
<td>Sediment unremarkable</td>
</tr>
<tr>
<td>Ca 9.8 mg/dl</td>
<td>P 4.0 mg/dl</td>
</tr>
<tr>
<td>P 22.9%</td>
<td>Triosorb test</td>
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Fig. 3. PA view of the chest. There is a marked osteosclerosis in the ribs, clavicles, and vertebrae.

consequent narrowing of the medullary spaces. There was no noticeable increase in thickness or diameter of the bones. Bony architecture was considerably well preserved. In the tubular bones, cortical hypertrophy was prominent exclusively in the diaphyses.

The skull shape was normal, but was densely calcified and the diploic space was hardly recognizable (Fig. 4). The vertebrae also presented dense shadows (Fig. 5).

In the pelvic girdle, there were slight hypoplasia of acetabula and increase of the iliac angles. The pubic bones appeared somewhat osteoporotic. The femurs showed a marked thickening of the cortex and narrowing of the medullary cavity (Fig. 6).

The phalanges of the hands showed similar changes and the medullary spaces were almost obliterated. The distal phalanges appeared particularly dense, short, and slightly tapered distally. The carpal bones were less dense and showed minimal retardation of skeletal maturation (Fig. 7). Other tubular bones of the extremities also showed a similar cortical thickening but appeared to be less
Fig. 4. Increased density of the skull with disappearance of the diploic space. The calvarium is not thickened.

Fig. 5. Lateral view of the spine, showing increased density with coarsened trabeculae.

Fig. 6. Changes in the pelvic girdle, consisting of hypoplasia of the acetabula with increased iliac angles and marked endosteal cortical hyper trophy in the diaphyses of the femurs.
Fig. 7. Marked cortical hypertrophy in the phalanges with encroachment of the medullary spaces. The distal phalanges appear tapered distally.

Fig. 8. Biopsy of the femur showing marked reduction of the medullary cavity.

prominent.

Microscopic examination of the biopsy specimen obtained from just below the greater trochanter of the right femur showed a marked reduction of the medullary spaces. This is typical of osteosclerosis (Fig. 8).
Discussion

There are several types of systemic osteosclerosis, either congenital or acquired. However, none of them has similar roentgerological and clinical features to those of the present case of Netherton’s disease.

Osteopetrosis, pycnodysostosis, and Engelmann’s disease have characteristic X-ray features, and their differential diagnosis is usually no so difficult. Fluorine poisoning, hypoparathyroidism, and hypervitaminosis A and D may also present increased bone density, but these can be fairly easily diagnosed from roentgenological findings and clinical symptoms.

Idiopathic familial osteosclerosis reported by Russell is different in roentgenological characteristics.

Various osseous changes including generalized osteosclerosis very similar to the present case have been described but in our case, physical examinations, laboratory tests, and past history showed nothing suggestive of renal disorders.

Though it is very rare, myelosclerosis may present roentgenological features similar to those of the present case of Netherton’s disease but, in our case, there was no microscopical evidence of myelofibrosis which usually accompanies myelosclerosis, and moreover, the clinical pictures are quite different.

Other possible extrinsic causative factors are drugs used for dermatological treatment and diet. The former was initially suspected as the patient had had vitamin A therapy of 4 months sometime in the past but this was ruled out by the essentially the same X-ray findings of the hands taken before and after the vitamin A therapy. The latter was also ruled out because the hand X-ray films of her parents and sister were normal.

Because of extreme rarity of this disease, detailed pathophysiology of Netherton’s disease has not been clarified.

In 4 out of 8 reported cases, laboratory tests revealed increased urinary excretion of certain amino acids. Particularly, increase of glycine and serine was commonly found in three of these cases. Some investigators have suggested the significance of abnormal aminoaciduria in Netherton’s disease, but this is not yet fully understood. Skeletal change and aminoaciduria may possibly be related but this still remains obscure.

Summary

Osteosclerosis observed in a case of Netherton’s disease was reported. This type of osteosclerosis is with unusual roentgenological and clinical characteristics and may possibly be pathognomonic in Netherton’s disease.

(Dermatological findings in this case are detailed in a paper by M. Ebara and T. Okubo)

References