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Hepatic Osteodystrophy in Congenital Biliary Atresia

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先天性胆道閉鎖症における肝性骨異栄養症

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先天性胆道閉鎖症73例（1971～1980年）のX線写真を再評価し，13例（17.8%）に諸種の骨変化を認めた．

骨幹端にクル病所見を認めたもの9例，骨折を認めたもの6例，及びクル病所見と骨折の共存した例は2例であった．また，全体にみられた所見は全身の骨の著明な脱灰所見であった．

骨幹端におけるクル病所見は当然のことながら成長が盛んな部，例えば橈骨尺骨の遠位端，大腿骨遠位端，脛骨近位端に強くみられた．骨折は長管骨の近位あるいは遠位1/3に好発していた．一部にはLooser's zoneと区別つかぬものもあった．

retrospectiveにみて骨変化の発症をみると，骨幹端のクル病変化は2カ月～1歳7カ月，平均7カ月，骨所は10カ月～10歳，平均2歳2カ月であった．この年齢分布の差はかなり明らかである．

先天性胆道閉鎖症における骨変化は，まず肝障害（胆汁性肝硬変）による蛋白合成の抑制やビタミンD活性化の第1段階における水酸化が障害されることにより生ずるものと考えられるが，臨床的には他の因子も関与していることは当然推察される．今回は骨変化に注目してX線写真の再評価を行ったが，本症では，特に全身病としての取扱いが重要であると考えられる．骨変化に対する治療として活性ビタミンDの大量投与やカルシトニン投与が考えられるが，今の所奏効した例は経験してない．

Introduction

Vitamin D is hydroxylated at the carbon 25 position to form 25-hydroxyvitamin D [25-OH-D]. This occurs primarily in the liver. Additional hydroxylation of 25-OH-D occurs at the 1 position producing 1, 25-dihydroxyvitamin D [1, 25-$(OH)_2$-D], physiologically active form of vitamin D. This occurs primarily in the kidneys. Therefore, impaired functions of the liver and kidneys cause disturbance of vitamin D metabolism with resultant osteodystrophic conditions.

Congenital biliary atresia is one of major hepatobiliary abnormalities in infants, and one of the causes of

so-called hepatic osteodystrophy.

Retrospective analyses of the skeletal changes of congenital biliary atresia were performed. This paper concerns interesting clinico-radiological aspects of these changes.

Materials and Results

One hundred and ninety-two cases with congenital biliary atresia were experienced at Department of Pediatric Surgery, Juntendo University Hospital during 1971-1980 (nine year period). Roentgenograms of seventy-three cases with congenital biliary atresia could be reviewed. Out of these, thirteen cases were found to have skeletal changes. The skeletal changes included rachitic changes of the metaphysis and fractures, associated with generalized osteopenia. Metaphyseal rachitic changes were seen in nine cases and occurred at rapid growing ends of the bones. Fractues were seen in six cases, out of which two cases accompanied rachitic changes. Thirteen fractures were radiographically identified in six cases, and fracture sites were as follows; 4 femora, 3 humeri, 2 tibiae, 1 scapula, 1 rib, 1 ulna, and 1 radius. The fractures occurred predominantly in proximal and distal thirds of the long bones. Some of the fractures were indistinguishable from Looser's zone radiographically. Table 1 showed clinico-radiological manifestations of the cases with skeletal changes. Rachitic changes of the metaphysis were more common in younger infants. Age of the infants with rachitic changes ranged from 2 months to 1 year 7 months with average of 7 months. Fractures were much more common in older infants. Age of the cases with fractures ranged 10 months to 7 years with average of 2 years and 2 months.

Case Presentation

Representative cases were shown next.

Case 1; S.I. (No.2) 3 months old girl.

Jaundice was pointed out at the age of 3 months. Hepatoportojejunostomy was performed. After surgery, she suffered from repeated pulmonary infections. Chest film showed bronchopneumonic changes in both

Table 1 Radiological manifestations of 13 cases with skeletal changes in congenital biliary atresia

case NO	sex	age of onset, skeletal changes	rachitic change	fracture	fracture sites	surgical procedure
1	F	2mo.	+	−		hepatoportojejunostomy at 1 mo.
2	F	3mo.	+	−		hepatoportojejunostomy at 2 mo.
3	F	5mo.	+	−		hepatoportojejunostomy at 5 mo.
4	F	5mo.	+	−		sublingual thoracic duct drainage at 5 mo.
5	F	8mo.	+	−		choledochojejunostomy at 6 mo.
6	F	7mo.	+	−		hepatoportojejunostomy at 5 mo.
7	M	3mo.	+	−		(autopsy)
8	F	10mo.	−	+	rt. humerus	hepatoportojejunostomy at 2 mo.
9	F	1yr. 1mo.	+	+	rib. rt humerus	hepatoportojejunostomy at 2.5mo.
10	M	1yr. 1mo.	−	+	lt. humerus	hepatoportojejunostomy at 2.5mo.
11	M	1yr. 4mo.	−	+	lt. scapula	hepatoportojejunostomy at 7 mo.
12	F	1yr. 7mo.	+	+	lt. & rt. femora lt. & rt. tibiae rt. radius lt. ulna	hepatoportojejunostomy at 2 mo.
13	F	7yr.	−	+	lt. & rt. femora	cholecystoduodenostomy at 6 mo. sublingual thoracic duct drainage at 7 mo.

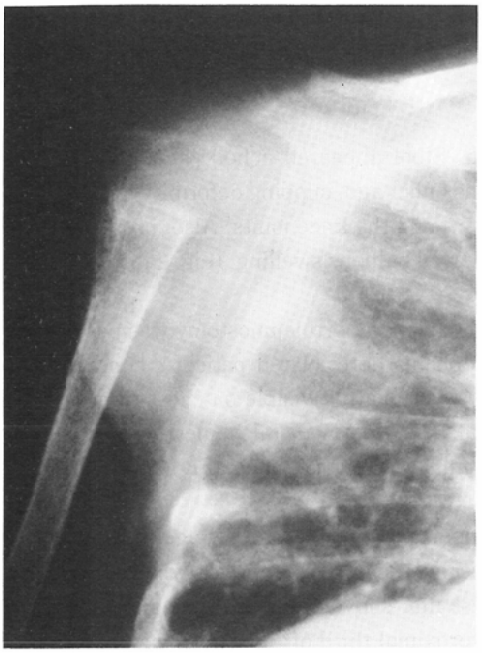
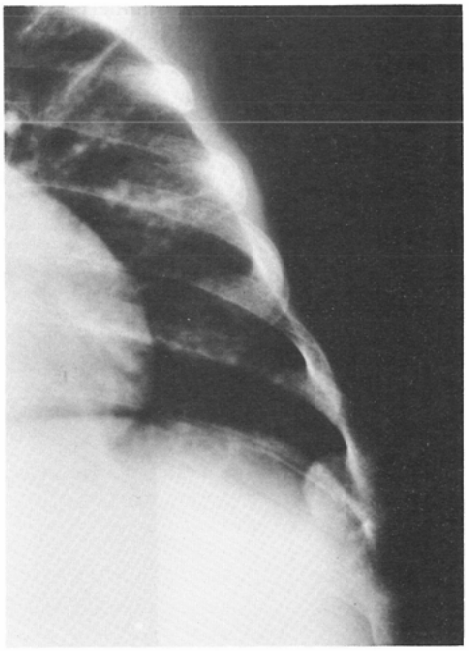


Fig. 1 S.I. (No.2) 3 months old girl;
There was squaring deformity in the proximal metaphysis of the right humerus. There was a generalized demineralization of the bones.

a

b



c

Fig. 2a, b, c K.g. (No.5) 8 months old girl:
There were cupping deformity and irregularity in the distal metaphyses of the ulna, radius and distal femur (a, b). Distal ends of the ribs showed bulbous swelling (c).

lungs. Bone density was decreased with thin cortices and indistinct bony trabeculae. There was frayed appearance in the proximal humeral metaphyses. There was no evidence of cupping deformity but squaring deformity in the metaphyses. (Fig. 1)

Case 2; K.G. (No. 5) 8 months old girl;

She had progressive jaundice at the age of one month. Stool appeared acholic at 2 months of age. Choledochojejunostomy (Roux-Y) was performed. At 8 months of her age, cupping deformity and irregularity were identified in the distal metaphyses of the forearms and around the knee joints. Also, proximal humeral metaphyses showed frayed appearance. Distal ends of ribs showed bulbous swelling. (Fig. 2abc)

Case 3; A.I. (No. 9) 1 year and 1 month old girl;

Acholic stool was pointed out at 3 weeks of neonatal period. Hepatoportojejunostomy was performed but repeated pulmonary infections and development of hydrocephalus deteriolated patient's condition. Chest film showed bilateral pneumonic consolidation. Bony cortices were hardly visible on chest film, because of marked demineralization. There were bilateral metaphyseal fractures of distal humeri with minimal impaction. Indistinctness of the metaphyses were seen in distal humeri, radii and ulnae. (Fig. 3)

Case 4; M.I. (No. 12) 1 year and 7 months old girl;

This was a case with multiple fractures. She had hepatoportojejunostomy at her age of 3 months with resultant improvement of her jaundice. Bone changes were discovered on 4th admission when she had severe respiratory distress and deteriolated general condition. Chest film showed bilateral pneumonia. Fractures were noted in distal third of femoral shafts, proximal tibiae, proximal third of right ulna, and proximal third of left radius. Callus formation was seen in minimal degree. Laboratory data showed severe anemia, hepatic dysfunction, elevated serum alkaline phosphatase and borderline low serum calcium. Metaphyseal rachitic changes were seen in proximal humeri, distal radii, distal ulnae, proximal femora, proximal tibiae, distal tibiae, and distal fibulae. Periosteal reaction was identified along the shafts of both humeri, radii, and ulnae.

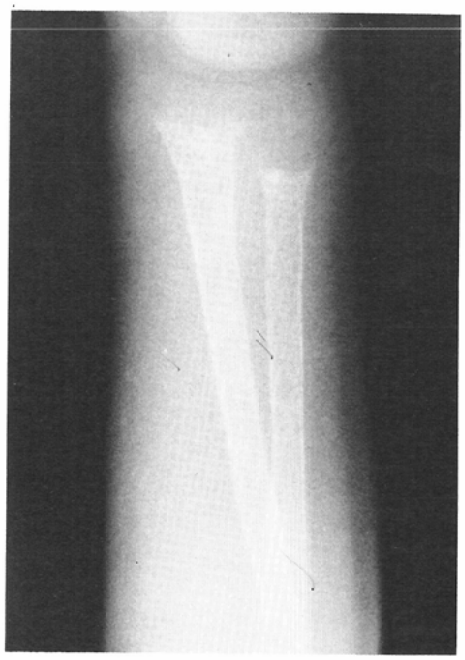
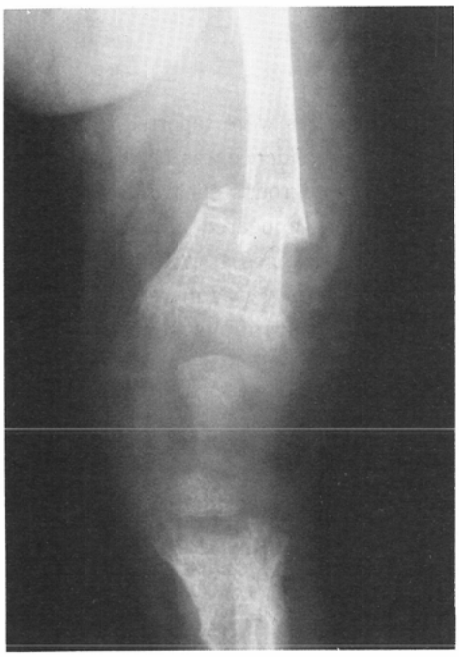
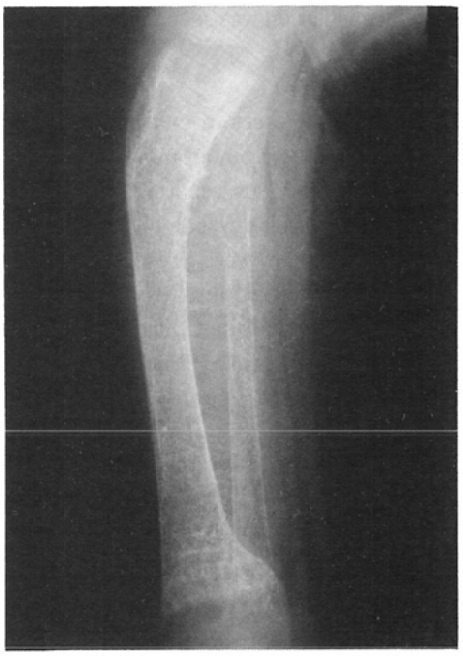


Fig. 3 A.I. (No. 9) 1 year and 1 month old girl; Poor definition and cupping deformity were seen in the distal metaphyses of the radius and ulna.



a



c

b

Fig. 4a, b, c M.I. (No. 12) 1 year and 7 month old girl;
Fractures were seen in the distal femur and proximal tibia. Ricketic changes were present in the metaphyses (a). Periosteal reaction was identified along the diaphyses of the radius and ulna with diaphyseal freacture (b). Spiculations were seen in the tibial diaphysis (c).

Periosteal spiculation was seen in the tibial and femoral shafts.

Discussion

In 1975, eight cases of congenital biliary atresia with skeletal changes were reported by us[1]. In this series, review of roentgenogram revealed 13 cases with skeletal change. Incidence was 17.8% (13/73) during 1971-1980. In previous report, bones changes were divided into three groups such as epi-metaphyseal change (rachitic), diaphyseal change (dystrophic) and fracture. There appeared a tendency that epi-metaphyseal changes were present in younger infants and diaphyseal changes as well as fractures were predominantly observed in older infants. In the present series, this tendency was more distinct. Rachitic changes of the metaphyses were observed in infants younger than one year of age. Fractures were seen predominantly in age group older than one year. Fractures occured in osteopenic bones, allowing for the fact that some of the fractures were indistinguishable from pseudofracture (Looser's zone) radiographically.

Rachitic changes were observed in younger infants. Rapid growing ends of bones were favorite sites of rachitic changes. However, bone changes with congenital biliary atresia could present as a manifestation of total damage of skeleton[2)3)4)7)]. It was quite interesting that rachitic changes were observed in cases of 2 months old and 3 months old respectively. Usually vitamine D deficiency rickets was thought to be uncommon before 3 months of age. The broad spectrum of congenital rickets should be considered in differential diagnosis. Hypophosphatasia should be included in differential diagnosis because jaundice was likely to be a prominent clinical feature.

In biliary atresia, metabolic disturbance is resulted from impairment of the passage of bile salts into alimentary canal. In consequence, inadequate emulsification of fat results in incomplete absorption of vitamin D. In addition, in the course of the disease, liver cirrhosis develops and hydroxylation of vitamin D is impaired. Vitamin D and hence calcium absorption were thus in turn diminished.

Toomy et al.[5] reported 14 cases of rickets associated with cholestasis and parenteral nutrition in premature infants. In their series, the first radiographic sign of rickets was decreased bone density which appeared usually by one month of age. By two months, swelling of the anterior rib ends was noted. Rachitic changes were identified in 2—3 months. Fractures were present usually after 2 months of age. Allowing for difference in age distribution, the sequence of bone changes were identical with our series. Assessment of the bone density on radiographs is insensitive, and radiographs of the infants are usually unsatisfactory, giving much more difficulty in radiographic assessment of bony mineralization.

In addition to hepatobiliary abnormalities, many other factors may be responsible for skeletal changes. Several authors have described rickets in low-birth-weight infants[6)7)8)]. Prolonged jaundice is known to result in metabolic bone diseases[9)]. Prognosis of congenital biliary atresia is usually much discouraging, especially in cases with associated skeletal changes. Most of the cases died of severe pneumonia and some died of hepatic insufficiency. Rupture of esophageal varices is also cause of death. Clinician should be alert not to enhance the skeletal changes in congenital biliary atresia and identify the skeletal changes earlier in order to give better clinical care to the patients.

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