

## Rib Enlargement in Premature Infants with Bronchopulmonary Dysplasia<sup>1</sup>

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**Purpose :** The purpose of this study is to describe the rib changes seen in patients with bronchopulmonary dysplasia (BPD).

**Materials and Methods :** Serial chest radiographs of nine premature infants with BPD who showed diffuse rib enlargement were reviewed for hyperinflation, which was compared with the observed degree of rib enlargement. Vibrator chest physiotherapy was performed in all cases, and five infants underwent conventional ventilation plus high frequency oscillatory ventilation therapy. Their calcium level was normal whereas alkaline phosphatase and phosphate levels were high. In all infants except one, liver enzyme levels were normal. For the treatment of patent ductus arteriosus, infection, and BPD, medications including indomethacin, antibiotics, and dexamethasone were administered. Vitamin D was given to all patients with total parenteral nutrition.

**Results :** Rib enlargement was found to be severe (n= 4), moderate (n= 3), or mild (n= 2) with undulating margins or posterior tapering (n= 2). Hyperinflation was noted in eight patients, in seven of whom it was moderate to severe. Among these seven, rib enlargement was severe (n= 2), moderate (n= 3), or mild (n= 2). In one infant with mild hyperinflation, rib enlargement was severe. Bilateral irregular infiltrates and atelectases were noted in all patients.

**Conclusion :** In BPD patients, rib enlargement may be seen. In order to differentiate this process from systemic bone disease or bony dysplasia, an awareness of the rib changes occurring in patients with BPD may be important.

**Index words :** Ribs, abnormalities

Radiography, in infants and children

Infants, newborn, skeletal system

Infants, newborn, respiratory system

Recent advances in neonatal intensive care allow premature babies with very low birth weight to survive with less morbidity and mortality than previously. Since

mechanical ventilation is now more common and is used for longer periods, however, increasing numbers of infants develop chronic lung disease, known as bronchopulmonary dysplasia (BPD). In some such cases, we have found slowly progressing rib enlargement without any other significant bony abnormality. Increased rib width has been found to be associated with BPD (Hedlund GL et al., presented at the Society for Pediatric Radiology meeting, May 1998). Radiological rickets can occur in infants with very low birthweight, and can in-

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Received June 22, 1999; Accepted November 5, 1999

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clude osteopenia, metaphyseal abnormalities and fractures (1, 2). Such cases do not, however, usually show diffuse rib enlargement. Generalized periosteal reaction involving the ribs or long tubular bones has been reported in infants, and is thought to be related to chest physiotherapy or prostaglandin administration (3, 4). High frequency jet ventilation may cause diffuse periosteal new bone formation involving all ribs and long bones with fractures of the extremities (5). We describe the characteristic findings of rib thickening, as seen on plain chest radiographs in infants with BPD, and suggest the involvement of certain etiologic factors.

### Materials and Methods

Over a two-year period, 98 infants were admitted to our neonatal intensive care unit because of low birth weight and prematurity with or without respiratory distress syndrome (RDS). Of these, 32 developed BPD. In nine consecutive infants (five boys and four girls), there was diffuse rib enlargement and evidence of BPD.

Among these nine patients in whom BPD was diagnosed, the condition was secondary to prolonged oxygen and mechanical ventilation therapy for RDS in sev-

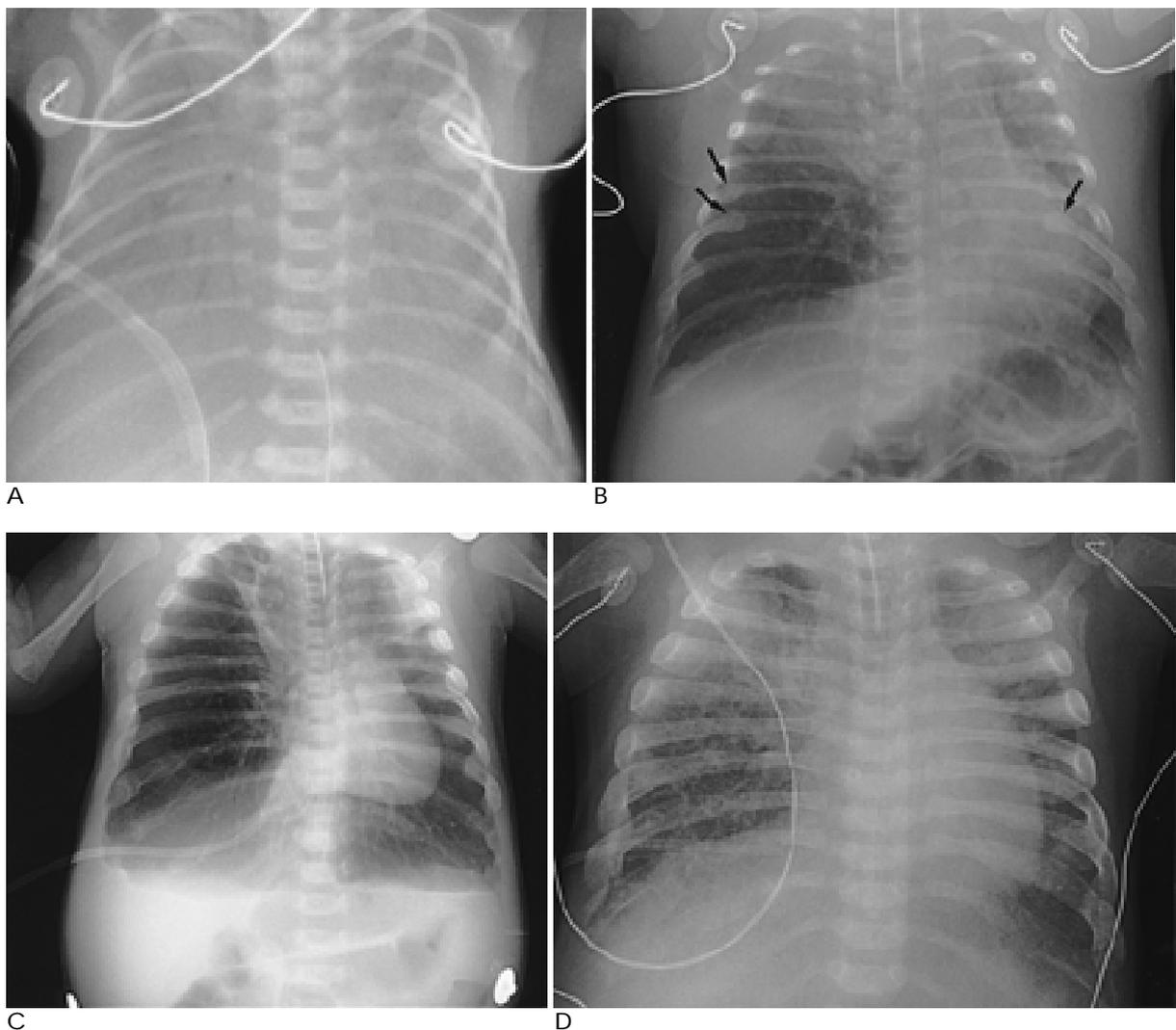


Fig. 1. Case 1 Male infant with BPD and longstanding hyperaeration.

- A. Chest radiograph on the 1st day of life shows severe bilateral air-space disease, indicating severe RDS. Bilateral ribs are normal.
- B. 45 days later, moderate to severe hyperaeration is seen with areas of atelectasis and irregular densities, consistent with BPD. Bilateral ribs show slight undulation without apparent thickening. Multiple healing rib fractures are seen (arrows).
- C. Three months later, severe bilateral hyperaeration is noted with multifocal atelectasis. There is diffuse rib thickening with slight posterior tapering. Both humeri show no evidence of metaphyseal irregularity and the vertebrae are normal.
- D. Five months later, chest radiograph clearly shows bilateral diffuse rib thickening with undulating margins. Posteromedial narrowing is noted producing "canoe-paddle" ribs.

en cases, due to immaturity in one, and to pneumonia in one. The nine infants were born prematurely at a gestational age of 26 to 31 (mean, 28) weeks, and with a birthweight of between 811 and 1700 (mean, 1077) gm. The mean duration of ventilator care and oxygen therapy was 118 (range 53-242) days and 157 (range 70-300) days, respectively. Seven infants had a culture-proven pulmonary infection and were treated with antibiotics. Patent ductus arteriosus was present in all nine, and indomethacin was used. All underwent dexamethasone therapy to relieve the inflammatory reaction associated with BPD, and all received hyperalimentation for between 11 and 79 days. Vitamin D supplements were added. Three patients died due to cor pulmonale secondary to BPD.

Five patients required mechanical ventilation involving both conventional ventilator therapy and high frequency oscillatory ventilation, the duration of the latter ranging from several to 66 days.

In order to reexpand atelectasis and facilitate the expectoration of secretions, all infants underwent vibrator chest physiotherapy, using a facial massager (Mon Charme, 川崎精機, Japan). Infants frequently underwent chest physiotherapy throughout their nursery admission.

When rib enlargement was observed, serum calcium levels were normal, but phosphate and alkaline phos-

phatase levels were high in all patients. Liver enzyme and total bilirubin levels were normal in all patients except one, who had a slightly elevated GOT/GPT level of 54/65.

Serial chest radiographs obtained from the first day of life up to twenty-four months of age were reviewed. Ribs were defined as abnormal when their width increased progressively and undulating margins or relative narrowing of their posterior segment was observed. Hyperinflation of the lungs was defined as mild when there was a slight increase in lung volume, with a preserved diaphragm dome; moderate if a further increase in lung volume with a slight loss of diaphragm dome was noted; or severe if a marked increase in lung volume was accompanied by diaphragmatic flattening or inversion.

Plain abdominal radiographs available for all infants were reviewed for evidence of any other bony abnormality.

### Results

Clinical data are shown in Table 1.

Rib enlargement was severe in four patients, moderate in three, and mild in two (Fig. 1, 2). Eight showed bilateral diffuse rib enlargement (Fig. 1), and in two there was relative narrowing of the posterior medial segment

Table 1. Clinical Data of Presented Cases

Case No./Sex	G-age /Birth wt	Mechanical Ventilation Duration	HFV Duration	Age of Presence of Rib Enlargement	NICU Stay	Last F/U Outcome
1/M	29 wk 1160 gm	242d	-	3mo	8mo	10mo, expired persistent
2/M	27 wk 974 gm	81d	-	3mo	5mo	5mo persistent
3/M	26 wk 1000 gm	154d	66d	2mo	6mo	6mo, expired persistent
4/F	29 wk 1295 gm	94d	9d	4mo	5mo	11mo improved
5/F	29 wk 903 gm	72d	6d	4mo	5mo	24mo improved
6/F	27 wk 813 gm	110d	-	4mo	6mo	7mo, expired persistent
7/M	29 wk 811 gm	53d	5d	3mo	4mo	9mo persistent
8/M	28wk 1040gm	148d	60d	3mo	5mo	5mo persistent
9/F	31 wk 1700 gm	113d	-	3mo	4mo	4mo persistent

G-age: gestational age

HFV: High frequency ventilation

of the ribs, mimicking a “canoe-paddle” appearance (Fig. 1D). In all patients, rib enlargement was found at 2-4 months of age and progressed slowly until 5-21 months (Table 1). In the three patients who died, the ribs were seen on the most recent follow-up chest radiographs as persistently thick.

In all patients, there was evidence of BPD; this included bilateral irregular densities suggesting fibrotic scars, atelectases, and hyperinflation. Bilateral hyperinflation was seen in eight patients, and was severe in four, moderate in three, and mild in one. Among four patients

with severe hyperinflation of the lungs, rib thickening was severe in two, moderate in one, and mild in one. In one infant who showed unilateral severe hyperinflation with contralateral atelectasis, rib thickening was more severe in the hyperinflated thorax (Fig. 2). Among three patients with moderate hyperinflation, rib enlargement was moderate in two and mild in one. In one infant with mild hyperinflation of the lungs, severe rib enlargement was noted.

Bony structures on the abdominal radiographs revealed no evidence of systemic bone disease or dyspla-

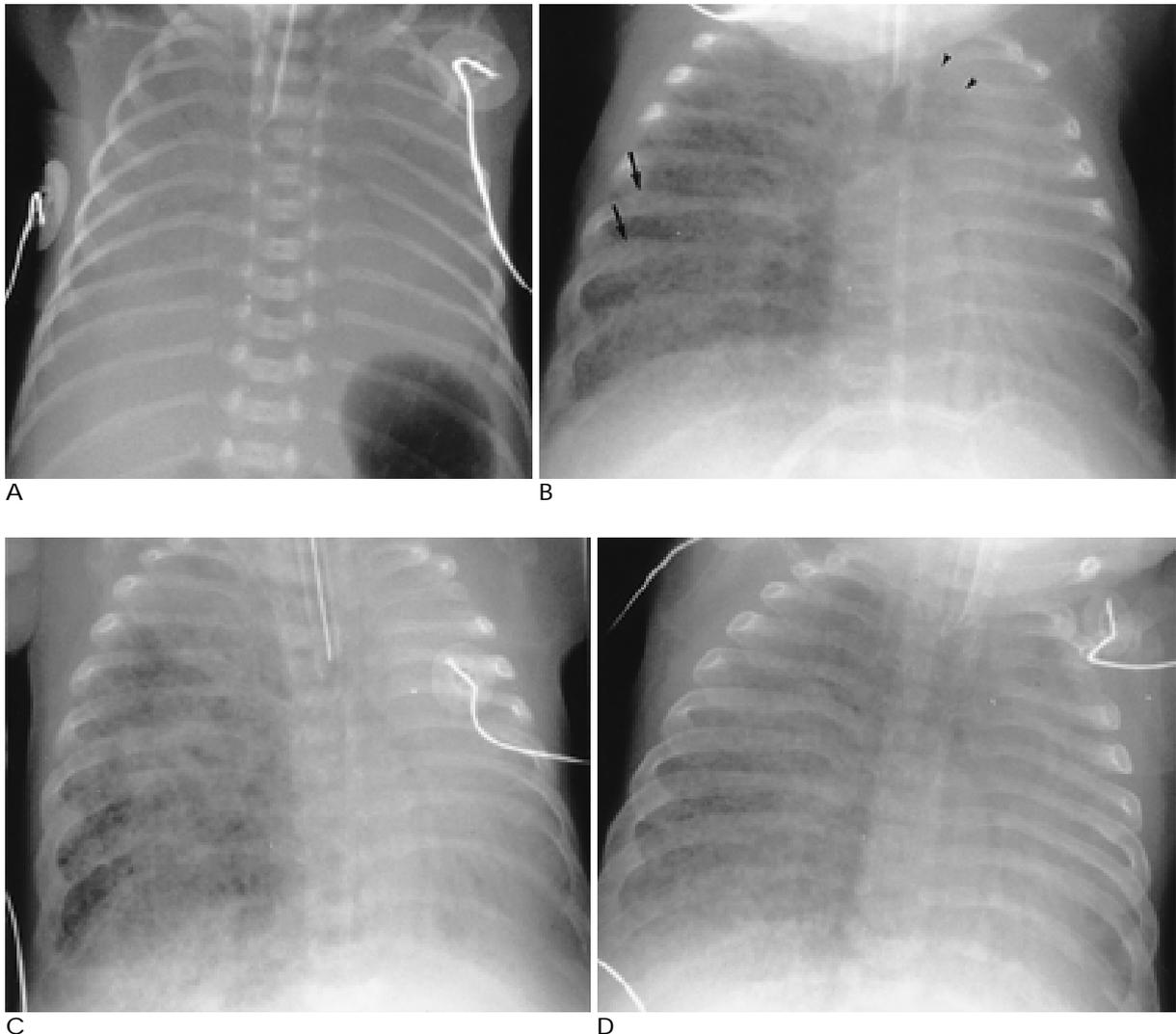


Fig. 2. Case 8 Male infant with RDS and BPD, who showed asymmetric rib enlargement.

A. Chest radiograph on the 1st day of life shows severe RDS with small lung volume. Bilateral ribs are normal.

B. Two months later, complete atelectasis of left lung is seen with hyperexpanded right lung. Irregular infiltrates are seen in right lung. There is right lung edge (arrowheads) herniated to left hemithorax anteriorly. Healed rib fractures (arrows) with suspicious thickening of right lower ribs are noted.

C. One month later, chest radiograph shows severe hyperinflation with atelectases in right lung and persistent left lung collapse. Diffuse rib enlargement is noted in right lower ribs.

D. Two months later, bilateral diffuse rib enlargement is clearly seen, which is more severe in right hemithorax. There has been interval reexpansion of left lung.

sia. In three infants, rib fractures were noted during their stay in hospital (Fig. 1B and 2B); in one of these, there was radiologic evidence of rickets - including rib fractures, osteopenia, and metaphyseal irregularity - several weeks before rib enlargement was apparent.

In two infants, rib enlargement progressed until nine and twenty-one months of age, respectively, and improvement was then noted until the time at which the most recent follow-up chest radiographs were obtained (Table 1). In seven infants, including the three who died, rib enlargement persisted for ten months of follow-up.

### Discussion

Isolated rib enlargement, not associated with other bony abnormality, has rarely been described. Periostitis with rib thickening can be seen in Caffey's disease, but associated abnormality involving the mandible, long tubular bones and scapula is to be expected as well as clinical symptoms (6). Prostaglandin E1 therapy, which is needed to maintain patency of the ductus arteriosus, has been reported to cause periostitis involving the ribs and long bones (4). None of our patient, however, underwent PGE1 therapy. Wood (3) has reported infantile cases that showed generalized periosteal reaction of the ribs resulting from vibrator chest physiotherapy. All our nine patients suffered severe, longstanding BPD, and in order to facilitate the expectoration of secretions and re-expansion of atelectasis, underwent vibrator physiotherapy throughout their period of hospitalization.

High frequency ventilation is used in infants with respiratory failure who are not responsive to conventional ventilation therapy, but has been reported to cause diffuse hypertrophic periosteal new bone formation involving the ribs (5). The suggested explanation is that the high frequency vibration, cause either by high frequency ventilation or a vibrator used in physiotherapy, initiates subperiosteal hemorrhage of the ribs (5). In our series, five patients underwent high frequency oscillatory ventilation therapy as well as vibrator physiotherapy, though we have not seen similar rib changes in other infants whose treatment involved high frequency ventilation.

Although respiratory muscle interaction is complex and its nature is still debatable, hyperinflation seems to affect muscle interaction, leading to the recruitment of expiratory muscles (7). In our series, seven patients showed a moderate to severe degree of hyperinflation.

In cases involving severe and persistent air trapping, the diaphragm is fixed at a lower level, reducing its contribution to respiratory motion. The contribution of the rib cage to chest wall motion and respiration increases, and this may cause intercostal muscle and rib hypertrophy. Nevertheless, in our study, hyperinflation did not correlate with rib enlargement.

Because of combined trace element, mineral, and vitamin deficiency, metabolic bone disease of prematurity is not uncommon in premature infants (6). Radiologic findings, resembling rickets, include osteopenia, flaring of the metaphyses, and multiple fractures, particularly of the ribs. Although rib enlargement is usually not a finding of rickets, repeated fractures and the subsequent healing process may result in rib thickening and/or undulation. Because alkaline phosphatase levels were high, despite normal calcium levels, rickets of prematurity was possible in our patients. An examination of the plain radiographs, however, revealed only one case of full-blown rickets.

Dexamethasone, a potent synthetic steroid with reported side effects of hypertension, hyperglycemia, and an increased frequency of infection, but without known effects on the skeletal system, has been widely used to improve pulmonary function in neonates with BPD (8). The side effects of cyclooxygenase inhibition by indomethacin include oliguria, increased serum creatinine, and transient mild bleeding; there is no known complication involving the skeletal system. In some cases, an excess of vitamin D can cause periosteal new bone deposition, as in vitamin A intoxication but less severe (6). Excessive vitamin D intake cannot, however, be the only cause of rib enlargement: we have not seen similar rib changes in other infants treated with vitamin D and no associated abnormality of the long bones seen on chest and abdomen radiographs was noted.

Chronic pleural disease can cause rib enlargement in adults (9), a condition we have encountered in two non-BPD cases not included in this study: one with pleuro-mediastinal fistula and pleural inflammation after corrective surgery for a tracheoesophageal fistula, and the other involving chronic aspiration pneumonia and recurrent tracheoesophageal fistula. Two patients also underwent vibrator physiotherapy for atelectases. Rib enlargement may be thus seen in patients with chronic lung or pleural diseases other than BPD.

The ribs of children are easily deformed by, for example, weak intrapulmonary retractive forces caused by chronic pneumonia or atelectasis (10). In our cases, mul-

multiple areas of atelectasis were noted. In one patient with unilateral hyperinflated lung and contralateral atelectasis, rib thickening was more severe in the hyperinflated hemithorax than on the opposite side (Fig. 2).

A limitation of our study is that we did not compare the results for BPD patients who showed rib enlargement with those of control BPD in whom this did not occur. In addition, to explain the etiologic factor and pathogenesis, the vibrator-treated group and non-treatment group must be compared. There may be differences in the duration of hospitalization, the duration and frequency of vibrator use, medications, and radiologic findings. In order to compare these groups clinically and radiologically, further study is needed.

Because the pathogenesis of rib enlargement appears to involve subperiosteal hemorrhage or periostitis, and if the provoking factors are eliminated, it is to be expected that on follow-up study, ribs will appear normal. In two of our nine patients, rib enlargement was reversible, and in the remaining seven, partly because of the short follow-up period, the most recent follow-up chest radiographs revealed persistent thickening.

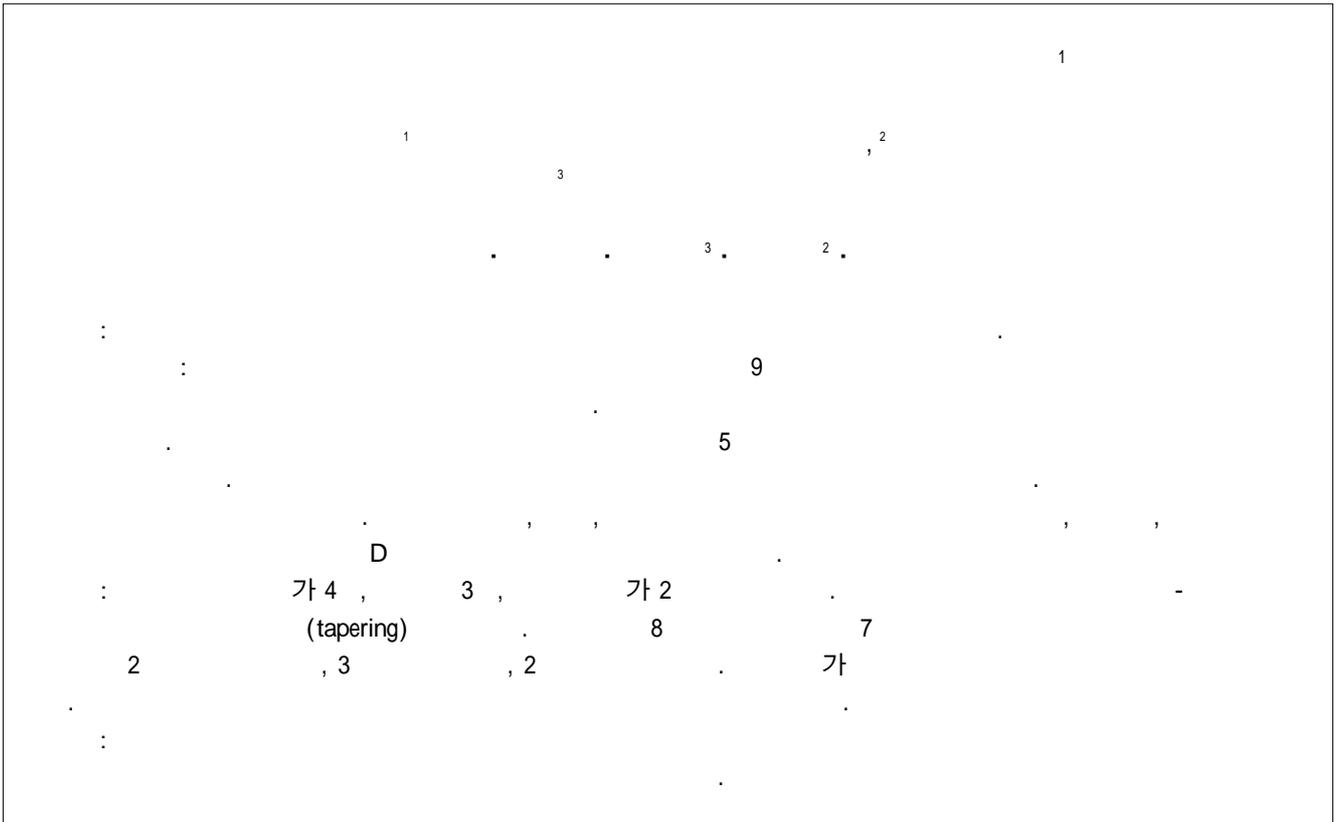
The rib enlargement associated with BPD should not be mistaken for that seen with bony dysplasia. The first case we encountered (Fig. 1) demonstrated "canoe-paddle" ribs, mimicking those seen in cases of mucopolysaccharidosis. Since there was no evidence of associated bone or morphological abnormality, and previous chest radiographs showed normal ribs, the existence of this latter condition could, however, be ruled out.

In conclusion, rib enlargement may be seen in infants with BPD. The mechanism underlying this process is, however, unclear and totally speculative: mechanical

factors (hyperexpanded lungs, atelectasis, high frequency ventilation, and vibrator physiotherapy) and/or metabolic factors may be involved. An awareness of the rib changes occurring in infants with BPD, the absence of other bony abnormalities, and a comparison with previous chest radiographs are thought to be very important when differentiating this process from metabolic bone disease or bony dysplasia.

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