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Temporary brittle bone disease: fractures in medical care

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Abstract

Temporary brittle bone disease is the name given to a syndrome first reported in 1990, in which fractures occur in infants in the first year of life. The fractures include rib fractures and metaphyseal fractures which are mostly asymptomatic.

The radiological features of this disorder mimic those often ascribed to typical non-accidental injury. The subject has been controversial, some authors suggesting that the disorder does not exist.

This study reports five infants with typical features of temporary brittle bone disease in whom all or most of the fractures took place while in hospital. A non-accidental cause can be eliminated with some confidence, and these cases provide evidence in support of the existence of temporary brittle bone disease.

INTRODUCTION

Over the last 20 years, we and others have described a condition characterized by multiple fractures in young children, which we have called temporary brittle bone disease (1–4). The disorder appears to be distinct from osteogenesis imperfecta in that the period of fracturing is brief and there is no increased tendency to fracture thereafter. To date, no evidence of a mutation in the genes coding for type 1 and type 2 collagen has been identified.

Temporary brittle bone disease causes fractures in the first year of life and, to a large extent in the first six months. Long bone fractures do occur and are sometimes the reason for the presentation, but rib fractures and metaphyseal fractures are common and generally asymptomatic. As with other bone disorders causing fractures at this age, there is often a significant lack of the clinical evidence of trauma that might be expected had the fractures been caused by inflicted injury. The disorder appears to be particularly common in twins and in infants born pre-term.

The clinical and radiological features of this disorder mimic those often ascribed to 'typical' non-accidental injury. For this reason, the identification of temporary brittle bone disease has been the source of much controversy (5–9). It has sometimes been suggested that the disorder does not exist but simply represents a mistaken diagnosis in cases of non-accidental injury.

One part of the argument in support of the existence of temporary brittle bone disease is the finding of typical features in cases where a non-accidental cause can be eliminated with some confidence. This study describes five such patients.

PATIENTS

Some details of the five patients are summarized in Table 1. All the patients were born in the United Kingdom and all except case 5 were of Caucasian parentage.

Case 1

A female infant was born at 28 weeks' gestation by emergency caesarean section because of worsening maternal hypertension. She developed severe respiratory distress syndrome and a right upper lobe collapse. She also had a patent ductus arteriosus, which responded to fluid restriction and frusemide. At 8 weeks of age, she was noted to have five healing fractures of the ribs. One week later, two further fractures were seen. Two weeks later, six additional fractures in various stages of healing were noted. Figure 1 shows the chest film at this stage. She was in a neonatal unit throughout this period; she was discharged to a local hospital at the age of 12 weeks, where a further healing rib fracture was identified on admission. All the fractures appeared to be asymptomatic. Radiologically, there was no sign of rickets or osteopenia. The serum alkaline phosphatase was normal. In all, four fractures were in posterior positions, seven were lateral and three were anterior. No further fracture occurred in 6 years' follow-up.

Case 2

A male infant was born at full term by ventouse extraction. On the day of delivery, he was admitted to a neonatal unit for 4 h before being returned to his mother. She noticed a 'crackle or pop noise every now and then and [he] would flinch'. When he was held, she could feel a 'popping sensation' in his back. She reported this to one midwife who reassured her. The signs were again noticeable on the second day and, after she had again drawn it to the attention of the staff, an X-ray was taken which demonstrated a recent posterior fracture of the sixth right rib with slight displacement. There was also a probable undisplaced fracture of the right seventh rib posteriorly. It was asserted that such posterior rib fractures did not occur at birth and were characteristic of non-accidental injury. The police and social services were summoned but, because it was clear that the fracture had

Table 1 Details of the patients

Case	Gender	Gestation	Birth weight	Fractures	Follow-up
1	F	28 weeks	780 g	14 rib fractures in hospital from 7 weeks to 11 weeks of age	6 years
2	M	40 weeks	4309 g	One definite and one probable posterior rib fracture found on day after birth while in hospital	10 years
3	M	36 weeks	2082 g	13 rib fractures from 4 weeks to 10 weeks of age (six in hospital between 6 and 10 weeks)	18 years
4	F	36 weeks	2196 g	17 rib fractures from 6 weeks to 10 weeks of age, at least 14 in hospital	18 years
5	F	35 weeks	1516 g	22 rib fractures in hospital from 3 weeks to 6 weeks. One possible metaphyseal fracture in hospital	1 year

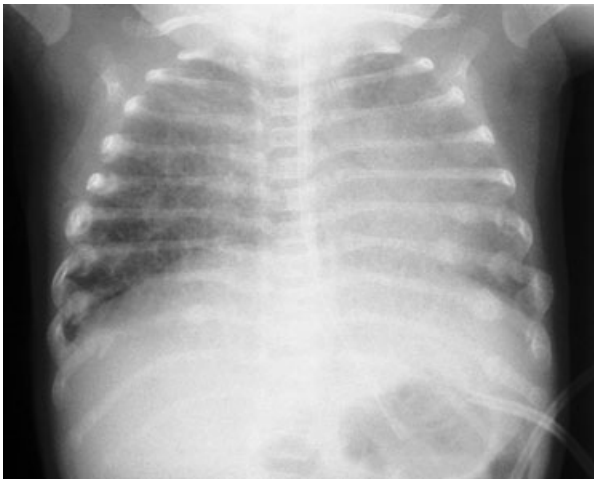

Figure 1 Case 1: Chest X-ray at the age of 11 weeks to show multiple fractures in different stages of healing. All the rib fractures had occurred in hospital.

occurred in hospital, it was accepted that a non-accidental cause was very improbable. A skull X-ray showed some widening of the suture lines. No further fracture occurred in 10 years' follow-up.

Case 3

A male infant, one of twins, was delivered at 36 weeks' gestation by elective caesarean section because of maternal hypertension and breech position. Weight gain was poor but he was discharged at the age of 1 week. He was readmitted at 3 weeks of age because of persistent vomiting after every feed. The vomiting was described as projectile. He was discharged after 4 days. He was readmitted at 5 weeks of age for the same reason but discharged after 5 days. At 6 weeks of age, he was again admitted because rib fractures had been found on his twin sister. His chest film showed virtually symmetrical healing fractures of ribs ten, eleven and twelve on both sides. There was also a recent fracture on the posterior part of the right ninth rib. The fractures appeared to be asymptomatic. Over the next 6 weeks, a further six rib fractures occurred; there was no doubt radiologically that these were sustained in hospital. In all, nine fractures were posterior, two were postero-lateral and two were anterior. While in hospital, he developed a right inguinal hernia. He was discharged at the age of 12 weeks and no further fracture occurred. The hernia resolved spontaneously. Follow-up over the subsequent 18 years was uneventful.

Case 4

A female infant, the twin of case 3, was born by elective caesarean section at 36 weeks' gestation. She made good progress at home but, at 6 weeks of age, developed bruising around both ears, petechial haemorrhages on the face and a large abdominal swelling, thought to be an abdominal wall hernia. A chest X-ray on admission showed no rib fractures. Later the same day, she was noted to have in-drawing of the left costal margin on breathing and some crepitus. An X-ray on the morning of admission showed no rib fracture. Later the same day after transfer to another hospital, an X-ray showed recent fractures in lateral parts of ribs seven, eight and nine on the left. In addition, recent fractures of posterior parts of ribs eight, nine, ten and eleven on the right were seen. The possibility that the lateral fractures had occurred prior to admission could not be excluded from the earlier film, but the area of the posterior fractures was well visualized and these fractures were not present on the earlier film.

Two weeks later, a further chest film showed the previously noted fractures, all with evidence of early healing consistent with their having been fresh when first seen. In addition, seven new rib fractures with early healing were

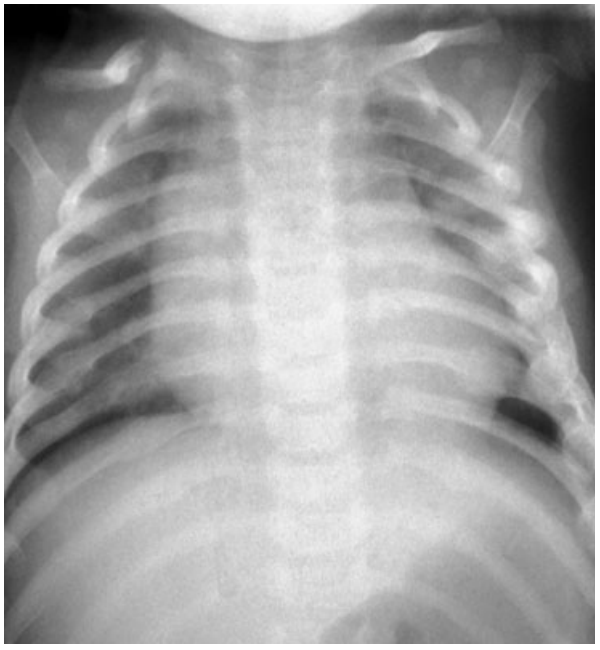

Figure 2 Case 4: Chest X-ray at the age of 12 weeks to show multiple rib fractures. All the fractures had occurred in hospital with the possible exception of the lateral fractures of the left 7th, 8th and 9th ribs.

seen. Three further rib fractures were visible 2 weeks later. Figure 2 shows the chest at this stage. The fractures appeared to be asymptomatic. In all, four fractures were in posterior positions, two were in postero-lateral positions and eleven were lateral. While in hospital, she developed an inguinal hernia. She was discharged at the age of 12 weeks and no further fracture occurred. The herniae resolved spontaneously. Follow-up over the subsequent 18 years was uneventful.

Case 5

A female infant of African parentage was delivered by elective caesarean section at 35 weeks' gestation because of severe maternal hypertension. She remained in the neonatal unit because of her mother's continuing illness. At 3 weeks of age, she became unwell and was thought to have a chest infection. Two recent rib fractures were visible on X-ray. Two days later, the film showed five further rib fractures. Four further rib fractures were noted 2 days later. The next chest X-ray was taken at 5 weeks of age; the films showed all the previously noted fractures with obvious callus formation together with six additional healing fractures and two recent fractures. A possible metaphyseal fracture at the distal left femur was also seen. Three further new fractures were seen at 6 weeks of age. In all, thirteen of the rib fractures were posterior, two were in the posterior axillary line and seven were in antero-lateral positions.

This child was in hospital for the whole period from birth to the age of 15 weeks.

The diagnosis of osteogenesis imperfecta was initially considered, but there was no clinical feature to support this and a traumatic cause was also considered. The nurses reported seeing the mother holding the child tightly on visits. However, it is clear from the timing of the fractures that only seven of the rib fractures could have occurred at times when the mother was present. No further fracture occurred over the next year, but further follow-up was not practicable because the child and her mother returned to her home country.

DISCUSSION

The five patients in this report form part of a much larger group of children investigated for multiple unexplained fractures in early childhood. In the majority of cases, these fractures occurred or appeared to occur after the child had returned home and it was entirely reasonable to include non-accidental injury as part of the differential diagnosis. The importance of these five patients is that, for various reasons, the children were in hospital at times when all or most of the fractures occurred. In each case, the diagnosis of non-accidental injury was either not considered or could readily be discounted in the light of the fracture history. It seems likely therefore that these cases represent significant evidence for the existence of a temporary brittle bone disease.

What is the nature of this condition? One possibility is osteogenesis imperfecta. This seems unlikely in that osteogenesis imperfecta severe enough to cause the number of fractures seen in this group in early infancy could be expected to show other good evidence for its existence at the time and subsequently; none was seen.

Another possibility is vitamin D deficiency rickets, which is now recognized as much more common than previously thought. It does cause fractures and pseudofractures in infancy (10). While none of these cases had radiological appearances typical of rickets, vitamin D deficiency cannot be excluded as a contributory factor.

Another possibility, at least in case 1, is bone disease of prematurity. This has been recognized for many years as a cause of rib fractures and metaphyseal fractures, and may cause fractures of different radiological ages (11–16). Earlier reports of temporary brittle bone disease have emphasized the frequency with which patients with this condition had been born pre-term. However, there were in those series many patients with an apparently identical syndrome who were not born pre-term. It could be that the condition described in this study is a single disorder both in pre-term and full-term infants, but simply more common in pre-term infants. The condition would be considered to be bone disease of prematurity in a child under full supervision in hospital but might be regarded as non-accidental injury in a child under parental care at home (4,15).

Earlier work (1–4) has explored the possibility of various metabolic and mechanical causes for this syndrome and, indeed, many factors could contribute to its development. Miller and Hangartner (17) have drawn attention to the frequency of intrauterine confinement as a possible factor; decreased intrauterine movement and twin pregnancies are over-represented in these patients. Metabolic causes, particularly copper deficiency and vitamin C deficiency, have been explored. Both copper and vitamin C are essential for normal maturation of collagen and the similarity of this temporary condition to classical osteogenesis imperfecta could be explained by a temporary disorder of collagen maturation. In the series in this study, copper deficiency was postulated in case 1 but not investigated at the time. It was investigated in cases 3 and 4. In these cases, both serum copper and superoxide dismutase levels were within reference ranges at the time the fractures were occurring. Such findings do not exclude the possibility that an abnormality was present in copper metabolism (or indeed in vitamin C status) during intrauterine life when the collagen of the bones was being established. One additional pointer to a transient collagen disorder is provided by the spontaneous resolution of the herniae in cases 3 and 4.

One feature of this group of patients is the very large number of rib fractures which occurred under close medical supervision and without any other evidence of trauma. An infant's ribs are widely regarded as flexible and resistant to fracture. For example, fractures are uncommon when chests are compressed in cardiovascular resuscitation. Similarly, when rib fractures occur as a result of known trauma, more than about four rib fractures represent injury so severe that survival is unlikely (18). In contrast, a much larger number of fractures were seen in these patients with little evidence of injury or distress.

One concern about the concept of temporary brittle bone disease is the supposed improbability of a bone disease that causes fractures for a limited period (9). However, these cases demonstrate that the natural history of the condition, as of bone disease of prematurity (11,15), is that of a self-limiting disorder. When fractures take place at home but not after a child is taken into care, it is often inferred that the diagnosis of non-accidental injury is self-evident. However, in cases 3 and 4, many fractures occurred in hospital but the fracturing ceased when the children went home at the age of 12 weeks.

The findings in these five patients are important in contributing to the evidence for the reality of a syndrome characterized by temporary bone fragility and should stimulate increased effort to identify the causes.

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