CASE REPORT

Infantile cortical hyperostosis (Caffey disease): a possible misdiagnosis as physical abuse

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Infantile cortical hyperostosis (Caffey disease) is a rare self-limiting inflammatory bony disease of early infancy. We report a 1-month-old Chinese boy with Caffey disease who presented with painful swelling over his shins bilaterally. Physical abuse was initially suspected, but the radiological findings of periosteal thickening over multiple bones (particularly the mandible), symmetrical involvement, diaphyseal involvement with sparing of the epiphysis, made Caffey disease a likely diagnosis. This report highlights that infantile cortical hyperostosis is an important differential diagnosis for children suspected of being abused, and clinicians should have a high index of suspicion to avoid misdiagnosis.

Case report

A 1-month-old Chinese boy was referred to the Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital, Hong Kong, by the Department of Orthopaedics for evaluation of suspected physical abuse. He presented with painful bilateral swelling over his shins. He was born at full term by vacuum extraction, and his birth weight was 2.9 kg. There was no consanguinity. He was looked after by his mother and grandparent, who denied any history of injury, and he was never entrusted to another carer. Apart from the painful swollen legs, the baby had no other systemic symptoms such as poor feeding, fever, or weight loss. There was no family history of child abuse. Physical examination showed a thriving baby with a body weight of 4.8 kg (50th centile) in good health. He had bilateral shin swelling and tenderness, but there were no swelling or tender points over the jaw or upper limbs. There were no external wounds or bruises.

Radiographs showed bilateral asymmetrical solid and mature-looking periosteal reaction involving the diaphysis of the bilateral humeri, radii, femurs, tibiae, and the rami of the mandible. There was associated perifocal soft tissue thickening. Bone density was preserved and the metaphysis of the long bones was normal in appearance. On bone scintigraphy, increased radiotracer uptake was noted along the mandible and diaphysis of the long bones, which corresponded to the periosteal reaction on the radiographs.

Initial blood examination showed thrombocytosis (platelet count, 713 x 10^9 /L [reference range, 150-450 x 10^9 /L]). White cell count, haemoglobin level, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were normal. Serum calcium was normal, although alkaline phosphatase (ALP) level was slightly raised at 394 U/L (reference range, 104-345 U/L).

Social investigation was performed by a social worker, but there was no evidence of child abuse. A clinical diagnosis of infantile cortical hyperostosis was made. Oral indomethacin for symptom control was suggested, but the parents declined. The baby later developed irritability and poor feeding. There was further increase in the leg swelling and new-onset left jaw and arm swelling was noted when the child was aged 3 months. Repeated radiographs showed interval increase in periosteal reaction of the affected bones. The femurs and tibiae showed mild medullary expansion with bowing deformity (Fig 1a). Radiographs of the mandible showed thick periosteal reaction (Fig 1b). Follow-up blood tests revealed leukocytosis of 20.5 x 10^9/L (reference range, 4.5-11.0 x 10^9/L) and an increase in platelet count to 844 x 10^9/L. The initial normal CRP level increased to 30.5 mg/dL and ALP level increased to 691 U/L. At this stage the parents agreed to start oral indomethacin 3 mg/kg/day.

After commencement of indomethacin, the symptoms of tenderness and irritability decreased markedly. The legs, arm, and jaw swellings gradually regressed. The white blood cells, platelets, ALP, and CRP levels were all normalised. Although mild bowing deformity could still be observed (Fig 2a), there was an interval decrease in periosteal reaction (Fig 2b). In view of the clinical improvement, indomethacin was tapered off. However, swelling recurred over the right jaw when the child was 13 months old and the indomethacin dose was increased. The jaw swelling later resolved and indomethacin was stopped.

Key words
Bone diseases; Child abuse; Diagnosis, differential; Hyperostosis, cortical, congenital; Tibia

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可能被誤診為虐兒個案的嬰兒骨皮質增生症

嬰兒骨皮質增生症（Caffey disease）是一種骨骼發炎的自限性疾病，多數在嬰兒早期發病。本文報告一名1個月大患有Caffey disease的男嬰，發病時在脛部兩邊腫痛。起初被懷疑是虐兒個案，但放射學檢查發現在多個骨骼處（尤其是在下頜骨處）有骨膜增生，加上病徵兩邊對稱，牽涉骨幹但未影響骺的症狀都顯示病人很可能患有Caffey disease。這病例顯示對於懷疑虐兒的個案，應考慮嬰兒骨皮質增生症的鑒別式診斷。醫生亦應對此症提高警覺，以免誤診。

There was relapse of the left leg swelling and pain 2 weeks after stopping the treatment, so indomethacin was resumed. The pain soon subsided, but the leg swelling persisted. Indomethacin was finally stopped when the child was 16 months old after resolution of clinical symptoms. The growth and development of the child has since been normal. He could walk steadily at the age of 13 months, and has not had any side-effects of the drug.

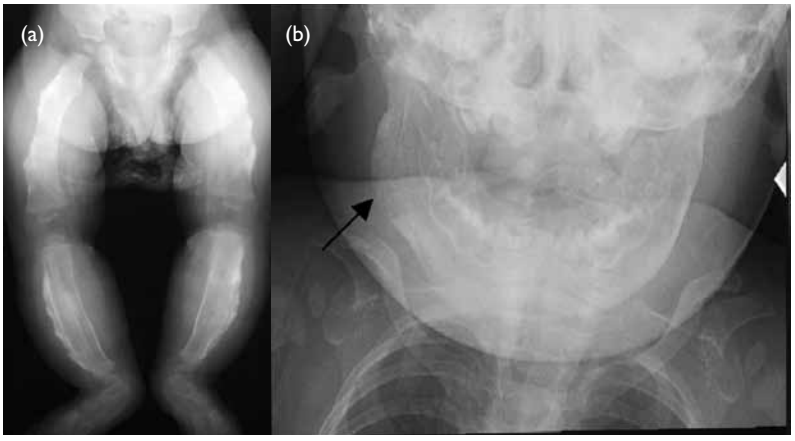

FIG 1. New bone formation at the age of 3 months, over (a) the bilateral lower limbs and (b) the mandible

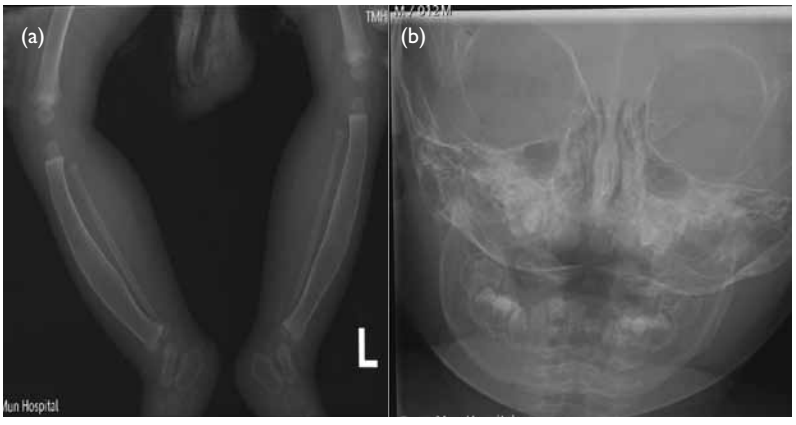

FIG 2. After treatment with indomethacin at the age of 12 months, (a) the cortical thickening over the femurs and tibiae nearly resolved, although the lateral bowing of bilateral tibiae persisted, and (b) the right mandible cortical thickening completely resolved

Discussion

The presence of painful limb swelling and periosteal reaction in a young infant is suggestive of non-accidental injury (NAI), which is an important differential diagnosis. Social investigation, complete skeletal survey, and bone scintigraphy are necessary for evaluation.[1] If there is a confused explanation for the swelling, suspicious signs of unexplained external injury, or a radiological feature of NAI,[1] timely intervention is warranted to prevent further injury. However, a misdiagnosis of child abuse can also pose a significant burden to the child, the parents, and the suspected perpetrator. With enhanced awareness of the presentations of child abuse, an increasing number of patients have been referred to paediatricians for evaluation. Wheeler and Hobbs,[2] in a report of 10 years' experience, found that 50 of 2628 children were misdiagnosed with NAI. These patients were later found to have various other conditions that mimicked NAI, including infantile cortical hyperostosis. The authors suggested that misdiagnosis of NAI is distressing and leads to increased anxiety.[2] It is therefore of crucial importance that clinicians are aware of other conditions that may mimic NAI, for example, infantile cortical hyperostosis.[3]

This patient presented with extensive periosteal reaction over multiple bones. Periosteal reaction is usually seen in fracture repair but can occur in the absence of fracture as a consequence of gripping or twisting force alone. In infants, the periosteum has only a loose attachment to the underlying bone and it readily separates following formation of a subperiosteal haematoma during trauma. Repetitive injuries and severe twisting will lead to florid periosteal reaction that can cloak the bone and extend into the epiphysis, which is characteristic of NAI.[1] In contrast, the periosteal reaction in infantile cortical hyperostosis is usually confined to the diaphysis.

Bone scintigraphy plays an important role in the evaluation of NAI as it is sensitive to subtle fractures, particularly at the ribs, scapula, diaphysis, and spine.[1] In infantile cortical hyperostosis, increased radiotracer uptake is usually seen in the mandible and the diaphysis of the bilateral long bones in contrast to the multiple asymmetric sites in NAI.

Infantile cortical hyperostosis is characterised by an infantile episode of subperiosteal new bone formation. The condition was first described by Caffey and Silverman in 1945.[4] The age of onset is usually younger than 5 months.[5] Clinical features include fever, hyperirritability, painful swelling in the extremities, tenderness, and pseudoparalysis.[6] There is no fracture present. There may be anaemia,

moderate leukocytosis, thrombocytosis, and increased ESR, CRP, and ALP levels, confirming an inflammatory process.[6,7] The bones involved include the mandible, clavicles, long bones, ribs, scapulae, ilia, and skull. The mandible is the bone affected most frequently, and its involvement is virtually pathognomonic.[4] On radiographs there is massive periosteal new bone formation with perifocal soft tissue thickening. The hyperostosis typically affects the mandible and diaphysis of the bilateral tubular bones with the epiphysis being spared. The periosteal reaction is solid and mature in nature without cortical destruction, in contrast to the interrupted and spiculated type of periosteal reaction in aggressive lesions. The hyperostosis may be reamed out from inside, resulting in a thin-walled bone with large medullary cavity[7] as demonstrated in this patient.

Although infantile cortical hyperostosis is sporadic, a few familial cases suggest that its inheritance is autosomal dominant with variable penetrance.[8] A novel missense mutation in *COL1A1*, the gene encoding the alpha-1 chain of type 1 collagen, was found in the familial cases.[9]

The inflammatory nature of infantile cortical hyperostosis has led to treatment trials with anti-inflammatory agents, and resolution of symptoms have been reported with the use of glucocorticoid and indomethacin.[10,11] Couper et al[10] reported their unsuccessful experience of treating twins with infantile cortical hyperostosis with prednisolone, as the infants had many side-effects. Subsequently, the treatment was switched to indomethacin 3 mg/kg/day with good response. Non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen have also been reported to provide symptomatic relief to patients with hyperostosis.[11] The rationale for NSAIDs is based on their prostaglandin synthetase–inhibiting action. Prolonged prostaglandin infusion in neonates with congenital heart disease has been shown to be associated with cortical hyperostosis.[12,13] Awareness of the similarities between periostosis produced by prostaglandin infusion and that seen in infantile cortical hyperostosis has enabled successful use of indomethacin for these patients. For the patient in this report, indomethacin provided symptomatic relief and successful resolution of the cortical thickening. The drug was well tolerated without significant side-effects.

The clinical course of the disease is highly variable. It is usually self-limiting with resolution of bony deformity without treatment in 6 to 9 months.[7,14] Kamoun-Goldrat and le Merrer[8] reported an infant with spontaneous resolution of all cortical lesions in 5 months. The condition may flare up and remit spontaneously and repeatedly, however.[7,10] There are reports of late recurrence with or without persistent bony deformities.[6,14,15]

This patient illustrates the importance of considering rare alternative diagnosis when assessing a patient with suspected NAI. The symmetrical distribution of hyperostosis involving the diaphysis of the long bones and the involvement of the mandible before the age of 5 months, together with the fluctuating disease course, assist the differentiation of this condition from physical abuse.

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