Caffey disease – an unusual neonatal presentation

A male infant was noted at birth to be fractious and have deformity of his distal limbs. A diagnosis of Caffey disease was made based on radiological appearances of hyperostosis. This usually benign, self-limiting condition should be considered as a diagnosis in a neonate with bony swelling. Early imaging and multidisciplinary team discussion may aid prompt diagnosis.

Gillian Campbell
MBChB, MRCPCH
Paediatric Registrar, Royal Hospital for Children, Glasgow

Thomas Kendrew-Jones
MBChB, MRCPCH
Paediatric Registrar, Wishaw General Hospital, Lanarkshire

Kerry Kasem
MBChB, MRCPCH
Neonatal Consultant, Princess Royal Maternity Hospital, Glasgow

Christopher Allan
MBChB, MRCS
Orthopaedic Registrar, Queen Elizabeth University Hospital, Glasgow

Keywords

neonatal; bone; Caffey disease; cortical hyperostosis

Key points

Campbell G., Kendrew-Jones T., Kasem K., Allan C. Caffey disease – an unusual neonatal presentation. *Infant* 2017; 13(3): 105-06.

1. Caffey disease is a rare genetic condition that can present with bony swelling in the neonatal period and should be considered in the clinician's differential diagnosis.
2. Early imaging and discussion with a multidisciplinary team, including radiologists, clinical geneticists and endocrinologists, may aid prompt diagnosis.
3. Caffey disease has a much more favourable outcome than skeletal dysplasia and this should be considered when having early discussions with parents of a neonate with limb abnormalities.

The case history

A male infant was delivered at 36 weeks' gestation following spontaneous onset of labour. There was a history of polyhydramnios, however, no abnormalities were detected on routine antenatal scanning and there was no family history of bone disease. He was born in good condition by caesarean section and did not require resuscitation.

At delivery he was noted to have a deformed right forearm (**FIGURE 1**) along with marked bowing and swelling of both lower legs (**FIGURE 2**). He was fractious and appeared distressed when handled.

Initial X-rays showed irregularity and dense periosteal reaction of the right radial shaft with associated bowing of the distal radius. The ulna and humerus were spared (**FIGURE 1**). Lower limb X-rays showed bowing with a thick irregular periosteal reaction along both tibia. The fibulae and femora were unaffected (**FIGURE 2**). There were no definite fractures identified. Bone biochemistry was normal.

The baby was nursed gently in case of bone fragility and given appropriate analgesia. The family were initially counselled on the possible diagnosis of skeletal dysplasia and the case was discussed with specialists at the tertiary children's hospital.

The consensus from the tertiary centre was that skeletal dysplasia was not likely and, based on the radiological appearances of hyperostosis (excessive bone growth), a diagnosis of Caffey disease was made.

Sequencing of genomic DNA of the *COL1A1* (collagen type I, alpha-1 chain) gene showed that the patient was heterozygous for a mutation predicted to result in an amino acid change associated with autosomal dominant Caffey disease. Predictive and diagnostic testing is available for this family.

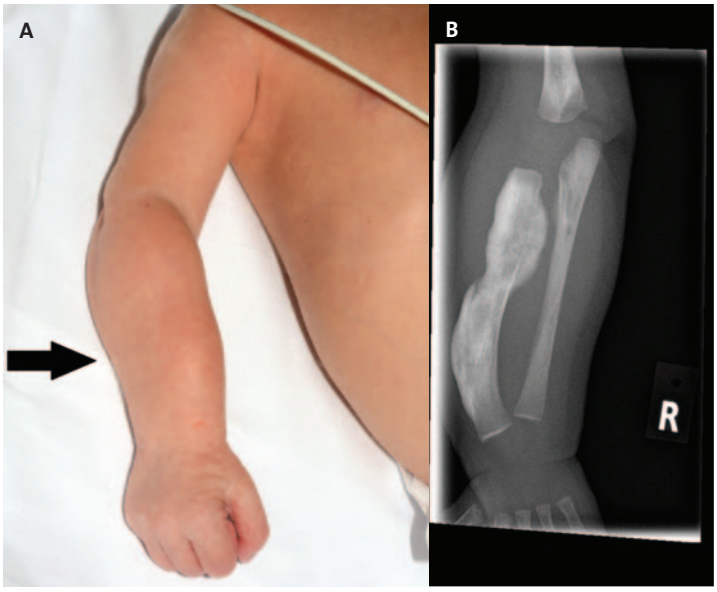

FIGURE 1
(A) The right forearm. There is firm swelling and apparent angulation of the midshaft radius. (B) An X-ray of the right forearm demonstrating irregularity and dense thick periosteal reaction of the radius. The ulna and distal humerus appear spared.

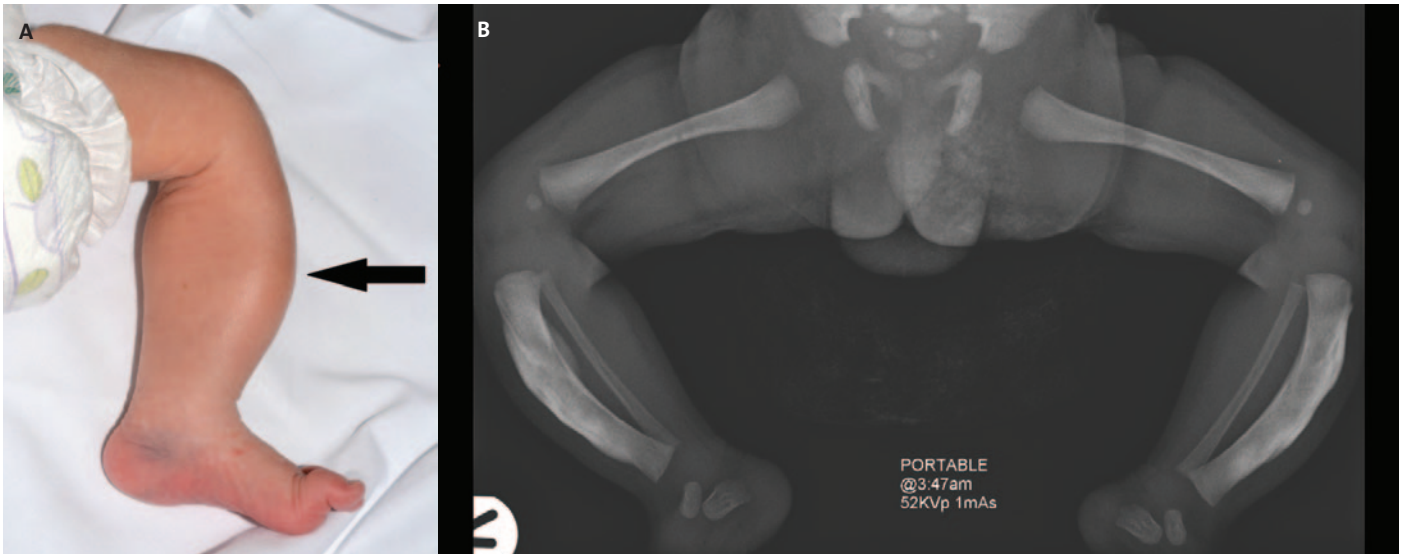

FIGURE 2 (A) The left leg demonstrating firm swelling on the tibial shaft. (B) A lower limb X-ray demonstrating bowing and hyperostosis with a thick irregular periosteal reaction along both right and left tibia.

Management

The baby was discharged home after three days. His initial distress on handling settled over the first few days of life. No orthopaedic intervention was required.

Conservative management has been adopted in this case but steroids and non-steroidal anti-inflammatory agents may be considered. He continues to attend a joint clinic with the endocrine and genetic teams at the tertiary children's hospital where his disease progress is monitored.

Background

Caffey disease – also called cortical hyperostosis – is a rare autosomal dominant genetic disorder that has been described in two different forms.[1] The identified mutation in the *COL1A1* gene leads to the production of collagen molecules that vary in size and shape. The exact mechanism by which this produces the deformities of Caffey disease is not fully understood.[2] Although genetic testing may identify a parent with the gene mutation, there may be no family history of the condition because of failure to recognise the disease or reduced penetrance. Alternatively patients may have a *de novo* pathogenic variant of the mutation.

The classical form of the disease (infantile cortical hyperostosis) is characterised by excessive new bone formation within the first six months of life and typically presents with a triad of fever, soft tissue swelling and irritability. Abnormalities mainly affect the mandible, scapulae, clavicles, ribs and the diaphyses of long bones.[2] Adjacent bones (eg radius and ulna) may fuse together due to the hyperostosis.

The infantile form is usually benign, self-limiting and resolves in early childhood. In the majority of cases bone remodelling leads to resolution of the deformities so that they are undetectable on radiographs by two years of age[3]. This is not the case in instances of bony fusions that do not resolve spontaneously and can lead to complications, for example, rib fusions leading to ventilation problems or scoliosis of the spine.[4] In some cases individuals can go on to develop connective tissue disorders in later life producing joint laxity and hyperelasticity of the skin.[2]

In contrast, cases with prenatal onset of disease have historically been described as taking a more severe, often lethal course, presenting with extensive hyperostotic bone involvement, marked polyhydramnios, fetal hydrops, hepatomegaly, pulmonary hypoplasia and prematurity.[5] However, there have been reports of a milder form of prenatal cortical hyperostosis with a more favourable outcome.[5] This patient differs slightly from the milder prenatal cases previously reported in the literature due to the presence of polyhydramnios, normally associated with the severe form. Mandibular involvement is usually expected at the time of presentation and its absence in this case is notable.

Caffey disease is widely quoted as having an estimated incidence of three per 1,000 infants worldwide.[2] This statistic was surprising to staff in our department who agree that this condition is rarely encountered in clinical practice. It is thought that many of these infants remain undiagnosed due to mild symptoms and the fact that the condition resolves itself in early childhood.

Prognosis

This is a favourable outcome for a family who were initially counselled on the possibility of a life-long diagnosis of skeletal dysplasia. The disease spontaneously regresses in the first few years of life and prognosis is excellent.

Summary

Caffey disease should be considered in the diagnosis of neonates with bony swelling. This case is an example of the more rarely seen form of the disease with 'mild' prenatal onset. Radiologic findings are diagnostic and genetic testing is available.

Parental consent

The authors received written consent to publish this report from the patient's parents.

References

1. **Nemec S.F., Rimoin D.L., Lachman R.S.** Radiological aspects of prenatal-onset cortical hyperostosis. *Eur J Radiol* 2012;81:565-72.
2. **Guerin A., Dupuis L., Mendoza-Londono R.** *Caffey Disease.* Gene Reviews. 2012 [Online] Available from: www.ncbi.nlm.nih.gov/books/NBK99168 [Accessed 16 February 2017].
3. **Kamoun-Goldrat A., Le Merrer M.** Infantile cortical hyperostosis (Caffey disease): a review. *J Oral Maxillofac Surg* 2008;66:2145-50.
4. **Genetics home reference.** *Caffey Disease.* 2013 [Online] Available from: https://ghr.nlm.nih.gov/condition/caffey-disease [Accessed 16/2/17].
5. **Schweiger S., Chaoui R., Tennstedt C. at al.** Antenatal onset of cortical hyperostosis (Caffey disease): case report and review. *Am J Med Genet* 2003;120A:547-52.