Congenital Vitamin C Deficiency or Fractures Due to Non-Accidental Injury?

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Abstract: It has long been recognised that much of the symptomatology associated with severe vitamin C deficiency in adults and children can be related to the essential role of ascorbic acid in collagen formation. The fractures and the bleeding disorders including bruises, sub-periosteal bleeding and intracranial bleeding can all be explained in this way.

This paper reports an infant boy who at the age of nine weeks was found to have multiple fractures and fracture-like lesions. A confident diagnosis of non-accidental injury was made. However it was later revealed that throughout her pregnancy the mother had prolonged severe nausea and a very limited diet. She had developed sore limbs, swollen bleeding gums and, later, multiple bruises. A diagnosis of severe scurvy was eventually made when the infant was 13 weeks old. She responded to vitamin C supplements.

The paediatricians did not recognise any relevance of the mother's overt scurvy to the infant's fractures. It is likely that the mother suffered severe vitamin C deficiency during her pregnancy, adversely affecting fetal bone formation and leading to fractures. Scurvy is now seldom diagnosed but surveys indicate that vitamin C sub nutrition is not uncommon even in western countries. The laboratory investigation of vitamin C status is demanding and not widely available. This paper highlights the need for maternal vitamin C deficiency to be considered in the differential diagnosis of unexplained fractures in infants.

Keywords: Scurvy, ascorbic acid, vitamin C, fractures in infancy, non-accidental injury, nausea in pregnancy.

1. INTRODUCTION

Scurvy has been recognised since at least the sixteenth century, particularly in seamen after long voyages. In the eighteenth century James Lind, a surgeon's mate in the Royal Navy and later a physician, demonstrated that a likely cause at sea was the '…want of fresh vegetables and greens' [1]. He showed that citrus fruits were curative.

In the 1930s it was recognised that the anti-scorbutic property of fresh vegetables and of citrus fruits was related to their content of ascorbic acid, which became known as vitamin C. It has since become clear that ascorbic acid is essential as a co-factor in the hydroxylation of lysine to hydroxylysine and of proline to hydroxyproline, essential for collagen formation. In addition ascorbic acid is important for the control of collagen synthesis [2].

It is not surprising, therefore, that the classical symptoms of adults with scurvy can be related to collagen defects, particularly tender and bleeding gums, subcutaneous bruises and pain in the limbs (generally due to sub-periosteal bleeding). In young children the classical symptoms of scurvy were described by Barlow in 1883 and the condition has often been known as Barlow's disease [1]. Features included screaming when limbs were handled, due to sub-periosteal bleeding and to fractures, and often a pseudo-paralysis. As in adults spongy gums could be found where teeth had erupted. As early as 1894 Sutherland described intracranial haemorrhages associated with scurvy in children [3]. Subdural bleeding continued to be described [4].

Spontaneous fractures have been recognised in children with scurvy. Barlow's original description mentioned fractures near the epiphyses. One of Sutherland's cases included transverse fractures of the shafts of one femur and one humerus [3]. The fractures sometimes led to long-term deformity [5]. Metaphyseal fractures were also recognised [6]. Spontaneous metaphyseal fractures as well as diaphyseal fractures were also seen in rhesus monkeys with vitamin C deficiency [7].

It is not surprising, therefore, that the bone changes of vitamin C deficiency have sometimes been misdiagnosed as non-accidental injury [8 - 10]. The current review was stimulated by the case of an infant with fractures ascribed to non-accidental injury whose mother had overt scurvy.

2. CASE REPORT

A baby boy was born at 37 weeks' gestation after induction of labour because of fetal growth restriction. The mother was a 20-year-old primigravida. The baby was noted to have a sub-conjunctival haemorrhage at

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birth but did well. He was visited daily by the health visitor for ten days and thereafter weekly when he was weighed naked. Weight gain was initially poor but he seemed well on breast-feeding and some supplementary formula feeds.

At the age of nine weeks his mother noticed that he was holding his left leg in an odd position and sought medical advice. There was some swelling but no bruising at the lower part of this leg. Initial radiographs were described as showing classical metaphyseal lesions of proximal and distal left tibia, the distal left femur and the distal right femur. There was sub-periosteal new bone formation on the left tibia and an irregularity of the left fifth rib anteriorly. The serum 25-hydroxyvtiamin D was reported to be 46 nmol/L. Two weeks later two of the metaphyseal lesions were no longer visible but there was callus at the left fifth rib anteriorly. In addition probable recent fractures were noted on the left 10th and 11th ribs. Each of the lesions was 'reported to have a high specificity for non-accidental injury'. Following reports to the social work department, the child was permanently removed from the parents, taken into foster care and eventually placed with his grandmother.

The parents strenuously denied causing any injuries, pointing out that at no time were there any bruises. They asked for further tests to be undertaken but were told that the evidence from the radiographs was sufficient to make a confident diagnosis. However further history from the mother may be relevant. She had had severe nausea throughout the pregnancy and her weight had only increased from 58 kg to 63 kg. Her diet was very limited and contained no fruit. She took no vitamin supplements. From about the fifth month of the pregnancy she noticed that her limbs were tender and that her gums were swollen and bled easily. About nine weeks post-partum she noticed small bruise-like lesions all over her body. She consulted a general practitioner a month later. She was initially told that her symptoms reflected stress from the recent diagnosis of non-accidental injury. A second general practitioner made a diagnosis of scurvy and started treatment with ascorbic acid. Within six weeks the bruise-like lesions ceased to occur. The gum symptoms and limb pain improved slowly over several months.

The nausea that had blighted her pregnancy was relieved as soon as the child was born.

3. DISCUSSION

It seems likely that the mother had severe malnutrition throughout her pregnancy. The paediatricians were told about the maternal scurvy but did not recognise its relevance to the fractures and fracture-like lesions in her son. The bones affected would have been formed *in utero*; the vitamin C deficiency could well have contributed to bone fragility in the child. The finding of probable rib fractures occurring in hospital should have given additional grounds to question the accuracy of the diagnosis of non-accidental injury.

A wide range of disorders in infancy can cause unexplained fractures including fractures said to be characteristic of abuse. These are summarised in Table **1** and include osteogenesis imperfecta, osteopathy of prematurity, vitamin D deficiency, copper deficiency, and Menkes' syndrome [11 - 14]. There is little evidence in this case that any effort was made to consider or exclude these disorders. For more than 25 years we have published reports on a group of patients in whom unexplained fractures, attributed to non-accidental injury, were more likely to have been the result of a temporary brittle bone disease for which we could not identify the metabolic cause. These infants had many features in common, including a gross discrepancy between the clinical and radiological evidence of trauma [15]. Similar cases were found in which all or most of the fractures took place in hospital [16]. When 65 infants with this syndrome were returned to their parents there was no subsequent evidence of abuse [17].

Table 1: Metabolic Causes of Unexplained Fractures in Infancy

Osteogenesis imperfecta.
Osteopathy of prematuriy.
Vitamin D deficiency, particularly healing rickets.
Copper deficiency and Menkes' syndrome.
Vitamin C deficiency.
Myofibromatosis.
De Toni-Debré-Fanconi syndrome (cysitinosis).
Congenital syphilis.
Temporary brittle bone disease

This case also shows typical features of temporary brittle bone disease. Although vitamin D deficiency cannot be excluded, there is strong evidence that the major factor here was maternal malnutrition and vitamin C deficiency in pregnancy. One difficulty was that, as in other cases, a confident diagnosis of non-accidental injury inhibited significant effort to look for alternative causes of the fractures. One feature seen in all the metabolic disorders mentioned is that fractures take place spontaneously or with normal handling. As with conventional osteogenesis imperfecta, fractures

are often not associated with evidence of the significant external force needed to fracture normal bone. This discrepancy is even more striking with large numbers of fractures and fracture-like lesions.

Overt scurvy is uncommon in many countries and individual case reports are still published. They often reflect severe and prolonged dietary deficiency. However surveys of vitamin C nutritional status in western countries indicate that deficiency is not uncommon [18, 19]. Unfortunately all the methods for the assessment of vitamin C status call for close attention to detail because of the instability of ascorbic acid. The older literature regarded as best various forms of saturation tests, with collections of urine after loading doses of ascorbic acid. Others have advised assays of leucocyte ascorbic acid as a fair reflection of body stores, but the assays are technically demanding. Measurements of ascorbic acid in plasma are now used in surveys but, while low values may reflect sub-nutrition, they also occur in inflammatory episodes. Accurate results depend on very careful sample handling. For example Robitaille and Hoffer [20] placed their blood samples immediately into crushed ice, delivered them to the laboratory within one hour, separated them in a refrigerated centrifuge and added metaphosphoric acid to the plasma. It is not surprising that few clinical laboratories are equipped to deal confidently with requests for vitamin C assays.

Because of these difficulties it is likely that the condition is seriously under-diagnosed [20]. Most reported cases of scurvy are identified because of the severity of their symptoms. An additional problem in infants with unexplained fractures is that the fractures occur in bones laid down *in utero*. By the time the fractures are identified in post-natal life the child's own vitamin C status may be normal as a result, for example, of formula feeding. A similar concern applies to vitamin D status in early infancy [21]. In both situations investigation of the mother is needed.

In the current case it is clear that severe symptoms attributable to scurvy were present during the mother's pregnancy. It is probable that maternal vitamin C deficiency was the most significant cause of the infant's fractures. Maternal vitamin C deficiency needs to be added to the long list of metabolic causes of unexplained fractures in infants.

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REFERENCES

[1] Evans PR. Infantile scurvy: the centenary of Barlow's disease. Br Med J 1983; 287: 1862-3. https://doi.org/10.1136/bmj.287.6408.1862

[2] Pinnell SR. Regulation of collagen synthesis. J Invest Dermatol 1982; 79: 73s-6s. https://doi.org/10.1111/1523-1747.ep12545835

[3] Sutherland GA. On haematoma of the dura mater associated with scurvy in children. Brain 1894; 17: 27-36. https://doi.org/10.1093/brain/17.1.27

[4] Gilman BB, Tanzer RC. Subdural hematoma in infantile scurvy. JAMA 1932; 99: 989-91. https://doi.org/10.1001/jama.1932.02740640031009

[5] Silverman FN. An unusual osseous sequel to infantile scurvy. J Bone Joint Surg Am 1953; 35: 215-20. https://doi.org/10.2106/00004623-195335010-00022

[6] Fain O. Musculoskeletal manifestations of scurvy. Joint Bone Spine 2005; 72: 124-8. https://doi.org/10.1016/j.jbspin.2004.01.007

[7] Eisele PH, Morgan JP, Line AS and Anderson JH. Skeletal lesions and anemia associated with ascorbic acid deficiency in juvenile rhesus macaques. Lab Animal Sci 1992; 42: 245-9.

[8] Berant M and Jacobs J. A "pseudo" battered child. Clin Pediatr 1966; 5: 230-7. https://doi.org/10.1177/000992286600500408

[9] Lewis D, Carpenter C, Evans A and Thomas P. Rickets and scurvy presenting in a child as apparent non accidental injury. Internet J Orthop Surg 2007; 4 (2).

[10] Paterson CR. Multiple fractures in infancy: scurvy or nonaccidental injury? Orthop Res Rev 2010; 2: 45-8. https://doi.org/10.2147/ORR.S13043

[11] Paterson CR. Bone disease and fractures in early childhood. In Turner RA, Rogers HO, editors. Child Abuse pp 27-52 New York: Nova 2012.

[12] Ayoub DM, Hyman C, Cohen M and Miller M. A critical review of the classic metaphyseal lesion: traumatic or metabolic? AJR 2014; 202: 185-96. https://doi.org/10.2214/AJR.13.10540

[13] Miller M, Ward T, Stolfi A and Ayoub D. Overrepresentation of multiple birth pregnancies in young infants with four metabolic bone disorders: further evidence that fetal bone loading is a critical determinant of fetal and young infant bone strength. Osteoporos Int 2014; 25: 1861-73. https://doi.org/10.1007/s00198-014-2690-9

[14] Cannell JJ and Holick MF. Multiple unexplained fractures in infants and child physical abuse. J Steroid Biochem Mol Biol 2018; 175: 18-22. https://doi.org/10.1016/j.jsbmb.2016.09.012

[15] Paterson CR and Monk EA. Clinical and laboratory features of temporary brittle bone disease. J Pediatr Endocr Metab 2014; 27: 37-45. https://doi.org/10.1515/jpem-2013-0120

[16] Paterson CR. Temporary brittle bone disease: fractures in medical care. Acta Paediatr 2009; 98: 1935-8. https://doi.org/10.1111/j.1651-2227.2009.01388.x

[17] Paterson CR and Monk EA. Long-term follow-up of children thought to have temporary brittle bone disease. Pediatr Health Med Therap 2011; 2: 55-8. https://doi.org/10.2147/PHMT.S21449

[18] Schleicher RL, Carroll MD, Ford ES and Lacher DA. Serum vitamin C and the prevalence of vitamin C deficiency in the United States: 2003-2004 National Health and Nutrition Examination Survey (NHANES). Am J Clin Nutr 2009; 90: 1252-63. https://doi.org/10.3945/ajcn.2008.27016

[19] Hagel AF, Albrecht H, Dauth W, Hagel W, *et al*. Plasma concentrations of ascorbic acid in a cross section of the German population. J Internat Med Res 2017; 46: 168-74. https://doi.org/10.1177/0300060517714387

[20] Robitaille L and Hoffer LJ. A simple method for plasma total vitamin C analysis suitable for routine clinical laboratory use. Nutr J 2016; 15: 40. https://doi.org/10.1186/s12937-016-0158-9

[21] Paterson CR and Ayoub D. Congenital rickets due to vitamin D deficiency in the mothers. Clin Nutr 2015; 34: 793-8. https://doi.org/10.1016/j.clnu.2014.12.006

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