Temporary brittle bone disease versus suspected non-accidental skeletal injury

Alan Sprigg

Temporary brittle bone disease has been proposed again as an alternative explanation for suspected non-accidental injury. This is still not considered a real entity by mainstream opinion. The recent publications remind us to look carefully for alternative explanations and to investigate for predisposing bone disorders thoroughly.

INTRODUCTION

When a child presents with unexplained skeletal injury, the age, history of presentation and level of mobility of the child is important. The absence of a clear history to explain an injury raises the issue of non-accidental skeletal injury (NASI). It is also important to consider any underlying bone disorder that might predispose a bone fracturing with normal handling force.

NASI has medicolegal implications for children and parents. In the UK, experts must provide balanced and impartial evidence to assist the court. Lawyers are instructed by the various parties but the expert is independent. Against this background the judge balances contrary medical expert evidence and opinion. Many alternative explanations have to be considered. Courts are faced with issues of scientific hypothesis, leading edge research and epidemiological data but court is not the best arena for scientific discussion.

Paterson first proposed the concept of temporary brittle bone disease (TBBD) in 1993.[1] He described a personal series of 39 children who had unexplained fractures in the first year of life. He proposed TBBD as a transient predisposition to fracture with normal handling force, without any bruising, proven medical diagnosis or biochemical abnormality. They suggested this was due to temporary immaturity or fragility of collagen related to trace element deficiency (eg, copper) or transient osteogenesis imperfecta (OI). They provided no specific test to confirm TBBD. There was no complete data table on their 39 cases and there was a lack of comprehensive bone biochemistry results. TBBD presented a theoretical and attractively benign explanation for suspected NASI but this was based on association rather than causality. TBBD is not generally accepted by the main stream of paediatric or radiological opinion.[2 3] Many considered most of his original cases to be NASI.

Paterson's expert testimony was subject to censure by several judges – Singer and Wall.[4 5] His registration was erased by the General medical council in 2004.[6]

Recently he published again on TBBD[7] and rickets[8] which rallied further support[9] and critique of his theory.[10–12] He published five cases as TBBD. His dating of healing rib fractures meant that some may have happened in hospital. On review these cases were considered due to birth trauma, metabolic bone disease, forceful handling or NASI rather than supporting TBBD. Although TBBD is still not accepted as a specific diagnostic entity, his latest publications serve to remind us that other transient disorders (including nutritional rickets) may mimic NASI.

NASI is itself a time-limited disorder, occurring mainly in premobile infants. Pending judgement the infant may be removed from the care of those under suspicion and placed in a different environment with different patterns of handling and possibly feeding. If the court returns the child to the same carers months later following judgement, the factors leading to an injury may have passed and there may be no further fractures. Paterson considered that the absence of fractures on clinical follow supported TBBD.

WHAT PREDISPOSES A BONE TO FRACTURE?

A bone fractures when the stress applied exceeds it mechanical limit. This may be due to excessive applied force or reduced bone strength. Bone strength may be influenced by antenatal or postnatal dietary deficiency and drug treatment. When considering NASI we should exclude any underlying medical disorders. Live bone has a complex structure and mechanical properties. Biomechanical data confirm there are multiple factors that affect bone strength including bone diameter, cortical thickness and collagen structure.

WHICH MEDICAL DISORDERS PREDISPOSE TO FRACTURING?

We recognise osteopathy of prematurity as a predisposition to fracturing while in hospital. Fractures may be diagnosed coincidentally on radiographs taken for clinical reasons. There is evidence of osteopaenia or associated biochemical abnormalities which respond to appropriate supplementation. This transient bone disease is different to proposed TBBD.

Koo *et al* used photon absorptiometry in a research setting to confirm that infants born <28 weeks and weighing <1550 g had low bone mineral content and that this persisted for many months.[13]

In a similar group of infants of very low birth weight (VLBW), Dabezies and Warren identified hepatobiliary disease, total parental nutrition and diuretic therapy, physiotherapy with passive motion and chest percussion therapy associated with rickets (39%) and fracturing (10%) in VLBW infants.[14] Others emphasise the benefit of daily movement of all extremities (physical activity against passive resistance) in promoting growth and improving bone mineral content in pre-term infants.[15]

These studies remind us of the complex factors that affect bone strength and development. If a VLBW infant presents with unexplained fractures, it should be appropriately investigated for predisposing factors.

OI has an increased fracture risk and occasionally may present in infancy with a fracture from normal handling force. The number of affected children who fracture with minimal trauma, who have absent family history, clinical features and radiographic changes are small. If a child develops new fractures in care, without significant trauma, then this raises the possibility of a permanent bone disorder (eg, OI) and collagen culture may be needed for confirmation. Collagen disorders were mentioned by the early TBBD paper, but as a transient event rather than a permanent predisposition to fracturing.

Correspondence to Alan Sprigg, Radiology Department, Sheffield Children's Hospital, Western Bank, Sheffield S10 2TH, UK; alan.sprigg@sch.nhs.uk

It is rare to have multiple long bone or metaphyseal fractures without other radiographic evidence of OI. Similarly it is exceptionally unusual to have multiple rib fractures without a clear history of the causative event in a child with OI.

Copper deficiency may mimic metaphyseal fractures and was included as one of Paterson's factors. Copper deficiency and scurvy are rare in term infants fed with current formula milk. We recognise that treatment with steroids, diuretics or prolonged parenteral nutrition may lead to reduced bone strength but this does not always result in fractures. Metaphyseal fractures are similarly rare in osteopathy of prematurity.

Other authors propose antenatal factors as a predisposition – oligohydramnios or reduced fetal movement in pregnancy being translated into a fracturing tendency secondary to decreased limb movement in utero.[16 17] This is also difficult to assess objectively as premature delivery may occur secondary to intrauterine growth restriction (IUGR) and a retrospective history of decreased fetal movements can be subjective.

As there are so many risk factors predisposing bones to fracturing in the early months of life then we should see a high incidence of fracturing happening with normal handling, especially in infants who are growth retarded or premature. In clinical practice the incidence of detected fractures is much lower than these papers infer, but it is difficult for a court to unravel the issues unless each infant is assessed individually and thoroughly.

Vitamin D deficiency also affects bone strength. Keller and Barnes propose that mothers in northern latitudes who have a poor diet, dark skin or low exposure to sunlight may have low maternal vitamin D stores. This may influence fetal vitamin D status which they refer to as congenital rickets and hence potential fracturing predisposition. This was described as an 'epidemic' occurring in up to 40% of mothers[18] provoking further debate on transient neonatal vitamin D deficiency as a predisposition to fracture.[19] Rickets has specific changes on x-ray (apart from osteopaenia) but it is unclear how 'biochemical rickets' or poor maternal vitamin D levels alter infantile bone strength and hence fracture risk in the absence of radiographic changes.[20] True rickets can produce pseudo-fractures or metaphyseal changes on x-ray in older children but these are different than fractures or classic metaphyseal lesions.

A recent retrospective, clinico-radiological study reviewed 45 children aged under 24 months with rickets and fractures.[21] All fractures occurred exclusively in children with severe, radiographically evident rickets. Senniappan *et al*[22] published two case reports of infants under 6 months of age who presented with fractures associated with nutritional rickets. Both were dark skinned and exclusively breast fed from birth without the recommended vitamin D supplementation (http://www.healthystart.nhs.uk). Bone biochemistry was abnormal in both infants. Neither mother had the recommended vitamin D supplements in pregnancy.[23] This emphasises the need for bone biochemistry investigations when a child presents with suspected NASI, especially when there are risk factors from the nutritional history.

These papers remind us of the complex factors that may affect bone strength. Some of these factors may be transient until catch-up growth occurs or the infant establishes normal nutrition. This provides a 'pot pouri' of potential factors as alternative explanation for NASI in court to a non-medical judiciary.

HOW CAN WE ASSESS BONE STRENGTH IN INFANTS?

The tools we have for assessing bone strength in infants have limitations. While there is a set series of investigations that are performed to exclude medical disorders in infants with unexplained subdural haemorrhage[24] or bruising, there is no national agreement regarding investigating unexplained fractures.[25 26]

In all cases of suspected NASI, standard bone biochemistry tests should be performed as a minimum. More extensive testing should be performed if there are nutritional factors, prematurity or IUGR, including vitamin D levels, parathyroid and trace elements if indicated. These tests should be taken at first assessment as they may be irrelevant if suggested after expert review several months later.

The cost of tests needs consideration (relative UK clinical laboratory costs): calcium, fasting phosphate and alkaline phosphatase costs under £10; copper, caeruloplasmin, PTH, 25OH-vitamin D assay cost under £20 each. A low fasting phosphate level is preferred as a more reliable indicator of mineral deficiency. Collagen culture and analysis for legal rather than clinical considerations may cost well over £1000. The monetary cost of basic screening (fasting Ca/P/ALP and PTH plus 25-OHVit D) is minimal compared with missing a predisposing disorder.

Imaging assists but also has limitations.[27] A skeletal survey is performed to exclude dysplasia, identify clinically unsuspected fractures and assess bone quality, including bone size, modelling and cortical thickness.

In laboratory studies osteopaenia is not detectable radiographically until 50% of calcium is lost from the bone (range 20–70%), but this depends on radiographic factors and technique.[28] However, this does not translate into a proportional loss of bone strength, since live bone has considerable physiological reserve. Dual energy x-ray absorptiometry (DXA) is used to assess bone density in older children but infant data are limited for standard commercial DXA scanners.

Not all patients with reduced bone density will fracture. When there is a predisposition shaft fractures are still painful and should have a clear history of when it happened, even if it was with reduced force. We recognise that metaphyseal and rib fractures may be clinically asymptomatic to paediatricians after the event and may be diagnosed on a skeletal survey or on radiographs taken for clinical management.

We cannot determine the true number of infants who might have asymptomatic fractures, since it would be unethical to perform full skeletal surveys on all infants routinely. Neither can we determine precisely how much force is needed to cause fractures in live infants. We have nature's experience from autopsy, clinical radiographs and clinical experience but this cannot be assessed in a scientifically controlled way as an ethical study.

WHERE DOES THIS LEAVE US?

TBBD is not generally accepted as a specific medical disorder predisposing to fracture with normal handling force. Paterson's 1993 paper suggests that TBBD is a specific entity which is not confirmed. His latest publications remind us to investigate all infants with suspected NASI for predisposing bone disorder and alternative explanations thoroughly. This involves taking an accurate history of how the injury happened, family history of fracturing, a careful clinical examination and appropriate biochemical tests routinely.

The effect of possible maternal vitamin D insufficiency on infant bones and other hypotheses need continuing evaluation. We must investigate predisposing medical, therapeutic and nutritional factors.

Recent research reminds us of the complex factors that predispose to fractures

in infants. We need to continue ethical scientific research and agree on appropriate investigations to exclude bone disorders in suspected NASI. It is important to take a thorough family and nutritional history to consider factors that may predispose to fracturing with normal handling and to request appropriate bone biochemical testing in all children presenting with unexplained fractures.

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Alleged Chinese saying: 'May you live in interesting times.'

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