Arachnoid cyst and chronic subdural haematoma in a child with osteogenesis imperfecta type III resulting from the substitution of glycine 1006 by alanine in the pro $\alpha 2(I)$ chain of type I procollagen

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Abstract

The features of a child with osteogenesis imperfecta type III (OI III) resulting from the heterozygous substitution of glycine 1006 by alanine in the pro $\alpha 2(I)$ chain of type I procollagen were studied. He was born at term with the clinical features of severe OI, including deep grey-blue sclerae. He had severe osteopenia and all long bones were smaller than normal with cortical thinning, metaphyseal expansion, poor metaphyseal modelling, and multiple fractures. However, the vertebrae, pelvis, and shoulder girdle were of normal shape and there were few rib fractures. Histological examination of the calvarium and tibial shaft showed woven bone without lamellar bone or Haversian systems. The shafts of the long bones were widened owing to repeated fractures. Progressive enlargement of the calvarium occurred between 3 and 4.5 months of age owing to bilateral chronic subdural haematomata and a large arachnoid cyst in the Sylvian fissure. The cyst was probably developmental in origin while the subdural collections were probably the result of perinatal skull trauma. The cyst and the subdural collections resolved following drainage but ventricular dilatation with normal cerebrospinal fluid pressure followed. The proband is the first reported case of OI with a glycine substitution by alanine in the pro $\alpha 2(I)$ chain of type I procollagen.

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Key words: arachnoid cyst; subdural haematoma; osteogenesis imperfecta type III.

Osteogenesis imperfecta type III (OI III) is usually caused by dominant negative mutations of the COL1A1 or COL1A2 genes that encode the $\alpha 1(I)$ and $\alpha 2(I)$ chains of type I collagen, respectively.¹⁻³ We previously reported the biochemical findings in the first case of OI resulting from a Gly substitution by Ala in the $\alpha 2(I)$ chain of type I collagen.⁴ The proband was heterozygous for a transversion of G-3287 to C in $\alpha 2(I)$ cDNA, which converted the GGC codon for Gly 1006 to GCC for Ala. The point mutation was located in exon 49 of COL1A2.

Figure 1 Clinical appearance at 6 months of age.

In this paper we describe the clinical, radiographical, and pathological features of this child with OI III.

Case report

CLINICAL HISTORY

The male proband was the first child of an unrelated 33 year old father and 28 year old mother. Both parents were healthy and neither had any clinical or biochemical features of OI. The proband was born by caesarian section with a birth weight of 3045 g which was on the 15th centile for the period of gestation. He had the typical clinical features of OI III (fig 1).^{1,2} His sclerae were deep grey-blue. Crepitus, as a result of fresh fractures, was present in most of the long bones of the limbs.

RADIOGRAPHICAL FEATURES

The skeleton was poorly ossified. At birth all the long bones were smaller than normal with cortical thinning, metaphyseal expansion, and

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Figure 2 Anteroposterior radiograph of the chest at 1 month of age. The chest is narrow proximally. The ribs are narrow with expanded metaphyses. The vertebrae and shoulder girdle are well formed.

multiple fresh and healing fractures (figs 2 and 3). The calvarium was poorly mineralised but the occiput, base of the skull, and orbits were better ossified (fig 4). There were numerous Wormian bones in the occipital sutures. The midface was hypoplastic.

PROGRESS

His respiratory function was satisfactory at birth as there were few rib fractures. The mobile fresh fractures of the femora, tibiae, and one forearm healed rapidly, but multiple new fractures occurred with normal handling of the baby.

At 1 month of age, his head circumference was 39 cm (75th centile). Between 3 and 4.5 months of age, his mother noted that his calvarium was progressively enlarging. The head circumference of 48 cm was beyond the 98th centile of 45 cm and he had the clinical features of raised intracranial pressure.

A CT scan of the head showed bilateral subdural haematomata, a large arachnoid cyst

Figure 3 Radiograph of the pelvis at 1 month of age. The pelvic shape is normal. The femoral metaphyses are expanded. There are fractures of the femoral shafts and metaphyses.

Figure 4 Lateral radiograph of the skull at 1 month of age. The base of the skull, orbits, and face are better ossified than the calvarium.

Figure 5 CT scan of the head at 4.5 months of age. The chronic subdural haematomata (SDH) and the right sided arachnoid cyst (AC) are labelled. The ventricles are enlarged. Contrast enhanced the membrane between the subdural collections and the subarachnoid space.

arising from the right Sylvian fissure, and ventricular dilatation (fig 5). A right temporal craniotomy was undertaken to treat these disorders. The temporal bone was extremely thin. The dura mater was expanded and bluish. The subdural collections contained xanthochromic fluid and were, therefore, classified as chronic subdural haematoma. The lining membrane of the right subdural haematoma was adherent to the membrane surrounding the arachnoid cyst. There was no obvious communication between them. The arachnoid cyst contained clear fluid without any evidence of haemorrhage. The surrounding neural anatomy was normal. The cyst wall was laid open. A catheter drained the cyst, subdural space, and basal cistern into the peritoneum. The subdural haematoma and the arachnoid cyst resolved but the ventricular sizes increased without increased cerebrospinal fluid pressure (fig 6). The shunt was revised to a ventriculoperitoneal shunt. There were no neurological signs at any time.

When last reviewed at 3 years of age he was having few fractures. The long bones of the limbs were abnormally wide and their cortices were abnormally thin. His head circumference

Figure 6 CT scan of the head at 13 months of age. The subdural haematoma and the arachnoid cyst have resolved. The ventricles are dilated.

had stabilised. He had delayed gross motor development but no other neurological abnormalities. He had gained head control and some trunk control but showed no signs of wishing to stand. He had ligamentary laxity and muscle hypotonia. He also had severe dentinogenesis imperfecta.

PATHOLOGICAL FEATURES

The calvarial bone removed during the temporal craniotomy was very thin and the inner and outer tables were fused. Histological examination showed woven bone without any trabecular bone. The cortex of the tibial shaft also consisted of woven bone with numerous plump osteoblasts and little intervening bone matrix. There was no trabecular bone and no Haversian systems.

The membrane surrounding the subdural haematoma contained dense collagenous connective tissue with focal areas of granulation tissue. The membrane surrounding the arachnoid cyst was lined with typical spindle shaped arachnoid cells.

Discussion

The proband was born at term as is usual for babies with OI III.¹ Radiographs of neonates with OI III may show thin or thick long bones although none of them resembles the broad crumpled long bones of OI II.¹² In the proband, most of the shafts of the long bones were abnormally wide owing to poor metaphyseal modelling and to thickening of the bone from external fracture callus. Thickening of the tibiae and femora was more marked at 2.5 years than at birth. It is uncertain whether the shafts of the proband's long bones will progressively narrow during childhood as reported in other cases with OI III.¹

Cephalhaematoma, subdural haematoma, and intracranial haemorrhage are recognised complications of trauma to the skull during the latter part of the pregnancy and during delivery.⁵ These anomalies are usually evident at birth or in the neonatal period. The prob-

and's chronic subdural collections are unusual in OI but were probably the result of shearing injuries to the skull in the perinatal period.⁶

Arachnoid cysts have not previously been reported in OI. They are usually developmental in origin and can be familial.^{7,8} Subarachnoid cysts and subdural haematoma may also co-exist.⁹ We propose that the proband's cyst was developmental rather than traumatic in origin as it did not contain xanthochromic fluid. Babies with developmental arachnoid cysts often present at a later age than the proband.⁷ It is likely that his early presentation was because of the added chronic subdural collections. Although the subdural collections and the cyst resolved with treatment, ventricular dilatation and cerebral atrophy remained.

There is only one other report of the bone histology in patients with OI III and defined type I collagen mutations.¹⁰ Our findings of severe osteopenia, woven bone, plump osteoblasts with minimal intervening matrix, and lack of lamellar bone and Haversian systems were also reported in a case of OI III resulting from the substitution of Gly 427 by Arg in the triple helical domain of the $\alpha 2(I)$ chain.¹⁰ However, these changes are not specific for OI III as they are also shared by babies with lethal perinatal OI II resulting from the substitutions of Gly by Arg at residues 391, 667, and 976, Gly by Val at residues 256, 973, and 1006 of the $\alpha 1(I)$ chain, and Gly 700 by Asp in the $\alpha 2(I)$ chain.¹¹⁻¹³

There are no other reported glycine substitutions at residue 1006 of the $\alpha 2(I)$ chain. However, a substitution of Gly 1006 by Val in the $\alpha 1(I)$ chain produces lethal perinatal OI II.^{12,14} Only two Gly to Ala substitutions have been reported in the $\alpha 1(I)$ chain, at residues 910 and 928, and both produced the OI II phenotype.^{14,15}

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