

# Boomerang Dysplasia in a Chinese Female Fetus

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## Abstract

Boomerang dysplasia (BD) was first described by Kozlowski et al in 1981; and is a form of neonatally lethal chondrodysplasia. The name itself vividly described its characteristic radiographic features, and the importance of recognising these features has major implication in genetic counselling. All, except two reported cases of BD were males. We here reported the third female case of Boomerang dysplasia in literature.

## Key words

Boomerang dysplasia; *FLNB* gene; Skeletal dysplasia

## Introduction

Boomerang dysplasia (BD) is a very rare perinatally lethal skeletal dysplasia that was first reported by Kozlowski et al in 1981,<sup>1</sup> and is characterised by decreased ossification of cranium and vertebral bodies, incomplete or absent ossification of long bones that are characteristically curved to give this condition its name. Vertebral ossification defect is most commonly found in the thoracic region, giving the appearance of 'hour glass' with associated wavy ribs. Histologically, it is characterised by the presence of multinucleated giant chondrocytes in resting cartilage.

Previously described Piepkorn type skeletal dysplasia is now thought to be a severe variant of BD,<sup>2</sup> and the oldest specimen suspected of BD was described in a 100-year-old specimen in a museum.<sup>3</sup> All cases reported have been

sporadic and the incidence of BD was estimated to be 1/1,222,698 live born infants.<sup>4</sup>

Autosomal recessive spondylocarpotarsal syndrome, atelosteogenesis type I and III, dominant form Larsen syndrome, and BD formed a spectrum of skeletal dysplasia with overlapping clinical phenotypes (Table 1). They shared a common pathogenesis in vertebral segmentation, joint formation and endochondral ossification.<sup>5</sup> In 2004, Krakow et al<sup>5</sup> identified mutations in the Filamin B (*FLNB*) gene in the first four conditions. In July 2005, Bicknell et al<sup>6</sup> reported *FLNB* gene mutations in two unrelated patients with BD. These findings confirmed the existence of a spectrum of disorders with varying degree of severity in clinical phenotype, but all sharing a common genetic abnormality which is mutations in the *FLNB* gene.

BD has an interesting male preponderance pattern and all except two reported cases were male.<sup>7,8</sup> We here reported the third case of female BD in literature. This report also emphasised the importance of recognising its radiological signs for proper diagnosis and genetic counselling.

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## Subject and Results

The fetus was the third conceptual product of a non-consanguineous Chinese couple with husband aged 32 years and wife aged 32 years at time of conception. The first pregnancy ended in termination for social reason, the second pregnancy resulted in a boy who subsequently developed

**Table 1** Phenotypic comparisons of skeletal dysplasia with mutations found in Filamin B gene

Disease	Vertebral fusion	Vertebral abnormalities	Joint dislocation	Tubular bones ossification
Spondylocarpotarsal syndrome	+	-	-	++
Atelosteogenesis type I	+/-	++	+	+/-
Atelosteogenesis type III	+/-	++	+	+
Larsen syndrome	-	+	+	++
Boomerang dysplasia	-	++	Joints poorly formed	+/- Fan-shaped

mental retardation and autism. Mother's height was 146 cm and father's height was 175 cm. Antenatal ultrasound detected micromelia and polyhydramnios at 25 weeks gestation and the couple elected to have termination of pregnancy in same week.

Post-mortem examination revealed a hydropic fetus with disproportionate body proportion (Figure 1). There was macrocephaly with frontal prominence, marked hypertelorism, flat broad nasal bridge, and nasal hypoplasia with central longitudinal depression that extended down philtrum to upper lip that resembles a cleft, mid-face hypoplasia, low set ears, down-turned mouth, micrognathia, severe micromelia, narrowed chest, protuberant abdomen and normal female genitalia. Hands and feet were short and broad. Fingers and toes were short with wide gap between the right second and third fingers but all digits were present in appropriate numbers. Elbow joints could not be seen and both knees were flexed. Left talipes equinovarus and right talipes equinovarus deformity were



**Figure 1** Hydropic fetus with disproportionated body proportion.

noted. There was no clefting of palate or any other internal organs anomalies.

Babygram showed relative macrocephaly with poorly ossified calvaria, apparent long trunk with short limbs (Figure 2). Twelves ribs were present but were short and wavy. The clavicles appeared long and bowed. Shortened, fan-shaped femori and unossified long tubular bones in humeri, radii, ulnae, tibiae and fibulae were noted. Few phalanges, in particular distal phalanges, of the hands were ossified and majority of metacarpal, metatarsal, and phalanges of hands and feet were unossified. Defective ossification of vertebral bodies at all level, together with narrowing of pedicles in mid-lower thoracic region,



**Figure 2** Babygram of fetus showed triangular shaped femori resembling a Boomerang.

resulting in the "Hour glass" appearance. Scapulae were well modeled but poorly ossified. Hypoplastic lower ilia formed the handle of a "table-tennis bat" configuration. The ischia were thick and broad. Some ossification was seen in superior pubic rami.

Since tissues were not saved, further protein and molecular analysis was not possible. Informed consent for publication that included photos and radiographs was kindly signed by her parents.

## Discussion

Phenotypic overlap between Boomerang dysplasia and Atelosteogenesis I was well described by Sillence et al 1987<sup>9</sup> and Greally et al 1993;<sup>10</sup> and was suggested by Hunter and Carpenter 1991<sup>11</sup> to have a common aetiology. This view was supported by radiology and histopathology findings.<sup>4</sup> Recent report by Krakow et al 2004<sup>5</sup> on mutations in the filamin B gene on a spectrum of disorders range from the severe end of atelosteogenesis I to a milder end of Larsen syndrome and spondylocarpotarsal syndrome. These findings sparked new insights into the role of filamin B in vertebral segmentation, joint formation, and endochondral ossification.

Sillence et al 1997<sup>8</sup> reported seven cases of BD with only one female case amongst their cohort. Krakow et al 2004<sup>5</sup> found no mutations in the *FLNB* gene in their only case of Boomerang dysplasia tested, and as Odent et al 1999<sup>7</sup> reported the second case of female BD, pointed out that majority of reported cases of Boomerang dysplasia were male. Together with the well recognised phenotypic overlap between skeletal dysplasia caused by mutations in *FLNA* and *FLNB*, the possibility of genetic heterogeneity in Boomerang dysplasia was postulated. In 2005, Bicknell et al<sup>6</sup> reported mutations in *FLNB* causing BD in two male subjects. This confirmed BD as part of the spectrum of Filamin B disorder and excluded BD as an X-linked disorder. It seems that male reported cases have a more severe dysmorphic phenotype<sup>1,2,4,8</sup> than females.<sup>7,8</sup> The frontal bone hyperostosis in reported male BD resembles that of Frontometaphyseal dysplasia. Sheen et al 2002<sup>12</sup> showed that Filamin A and Filamin B are co-expressed within neurons during periods of neuronal migration and can physically interact. The frequent report of associated omphalocele in Filamin A disorders also occurs in male BD. The link between the overlapping clinical phenotype and the reason for apparent male preponderance of BD will have to be solved in the future. Whether this condition is

genetically heterogeneous or whether other epigenetic factors may affect the phenotype await future clarification. More detailed examination and descriptions of clinical features with genetic correlation are needed to help in delineating the clinical heterogeneity in the future.

Achondrogenesis, being the most frequently made differential diagnosis in BD,<sup>1</sup> is a genetically heterogeneous group with type 1B being a recessive condition; and type II a dominant condition. The importance of recognising the radiological features of Boomerang dysplasia is apparent because it is often mistaken as Achondrogenesis. The occurrence of BD is mostly sporadic though with a dominant nature. Fortunately, the recurrence risk of BD is small, and this is significant as our index couple was keen to have further children.

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