

# Prenatal ultrasound diagnosis of Leroy I cell disease

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## ABSTRACT

*Leroy I cell disease is a rare autosomal recessive disorder which progressively leads to death within the first decade of life. Invasive prenatal diagnosis is possible but is only undertaken in families who have previously had an affected child. We describe the antenatal ultrasound diagnosis of the disease in a case referred at 30 weeks' gestation for suspected polyhydramnios.*

## INTRODUCTION

Leroy I cell disease (mucopolipidosis type-2) is a rare autosomal recessive disorder characterized by progressive mental retardation, coarse facial features and skeletal abnormalities<sup>1</sup>. Invasive prenatal diagnosis is possible using enzyme or DNA analysis of chorionic villi or amniotic fluid<sup>2,3</sup>. However, invasive testing is only undertaken in families identified to be at risk of this condition because of the birth of a previously affected child. This report describes the antenatal ultrasound diagnosis of a case of Leroy I cell disease.

## CASE HISTORY

A 27-year-old multiparous Caucasian woman was referred by her local hospital to the fetal medicine unit at 30 weeks' gestation with suspected polyhydramnios. She had had five previous pregnancies: two full term healthy live births, two unexplained stillbirths at 24 and 28 weeks and one delivery at 36 weeks of a male infant who died at 8 months of age due to Leroy I cell disease.

The first ultrasound examination of this pregnancy at 20 weeks had been unremarkable with normal biometry and no obvious structural abnormalities noted. A further scan at 30 weeks was carried out because of clinical suspicion of polyhydramnios. This was confirmed and, in addition, the femora were below the 5th centile for gestation and there was an increase in echogenicity around the periosteum of both the humerus and the femur (Figure 1). There was no past or



**Figure 1** Ultrasound scan of the femur (length, 48.3 mm) taken at 32 weeks showing apparent periosteal 'cloaking'.

present history of maternal diabetes, nor was there any evidence of fetal upper gastrointestinal obstruction to account for the polyhydramnios.

The parents were counseled on the likely recurrence of Leroy I cell disease and were offered invasive prenatal diagnosis, which they declined. A male infant was born by spontaneous delivery at 34 weeks with a birth weight of 2.04 kg (50th centile) and an Apgar score of 9 at 5 min. He did not have any dysmorphic features at birth but his head circumference was on the 3rd centile. His neonatal course was complicated by mild respiratory distress syndrome but by day 8 he was breathing normally in air. He required phototherapy for jaundice for 3 days and was discharged home at 33 days.

In view of the antenatal findings and the previous family history, metabolic studies were performed at 1 day of age. These showed a gross elevation of plasma lysosomal enzymes (b-glucuronidase, b-mannosidase, a-mannosidase) consistent with the diagnosis of Leroy I cell disease.

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**Figure 2** X-ray of the pelvis and femur of an infant aged 6 months with Leroy I cell disease. The femoral periosteum shows the characteristic thickening. (Image courtesy of the Medical Genetics Department, St. George's Hospital, London, UK.)

## DISCUSSION

Leroy I cell disease is a rare autosomal recessive disorder<sup>1</sup> caused by a deficiency in the enzyme N-acetyl glucosamine-1-phosphotransferase<sup>4</sup> leading to low levels of intracellular lysosomal enzymes. Histological examination of cultured fibroblasts with a phase contrast microscope demonstrates the presence of numerous granular inclusions<sup>5</sup>. It is a progressive disorder leading to death at an average age of 5<sup>6,7</sup>. The characteristic features at birth include low birth weight, macrocephaly, congenital hernias in males, hirsutism, hypotonia and orthopedic problems such as club foot, dislocation of the hip and kyphosis. The skin is thick and the facial features become coarser with time. The gums are characteristically hypertrophic. Growth restriction is severe, often with antenatal onset. In this respect our case was unusual because the

birth weight was on the 50th centile and the head circumference on the 3rd.

The classic X-ray findings in the first few months of life are of general demineralization, coarse trabecular pattern and extensive periosteal cloaking of the long bones which is suggestive of excessive new bone formation (Figure 2). This latter feature disappears by about 10 months when the overgrowth becomes confluent with the underlying cortex. Skeletal changes after this age follow a pattern known as dysostosis multiplex; this is similar to the changes recognized in Hurlers syndrome although it tends to be more severe.

Leroy I cell disease is fatal within the first decade of life, and undoubtedly merits prenatal diagnosis. Up until now, this has relied on invasive testing in the first or second trimesters in families with a previously affected child. We made the diagnosis on the basis of the previous history and the ultrasound features of short femur and periosteal cloaking of the femur and humerus. However, it is uncertain as to whether the condition can be diagnosed in situations in which there is no family history at the routine 20-week ultrasound assessment; certainly in our case the femur length was normal at this scan.

## REFERENCES

- 1 Leroy JG, Demars RI, Opitz JMI. Cell disease. *BDOAS* 1969; 5: 174–84
- 2 Ben-Yoseph Y, Mitchell DA, Nadler HL. First trimester prenatal evaluation for I cell disease by N-acetyl-glucosamine 1-phosphotransferase assay. *Clin Genet* 1988; 33: 38–43
- 3 Owada M, Nishiya O, Sakiyama T, Kitegawa T. Prenatal diagnosis of I cell disease by measuring altered alpha-mannosidase activity in amniotic fluid. *J Inherit Metab Dis* 1980; 3: 117–21
- 4 Mueller OT, Honey NK, Little LE, Miller AL, Shows TB. Mucopolipidosis II & III. The genetic relationships between two disorders of lysosomal enzyme biosynthesis. *J Clin Invest* 1983; 72: 1016–23
- 5 Leroy JG, Demars RI. Mutant enzymatic and cytological phenotypes in cultured human fibroblasts. *Science* 1967; 157: 804–6
- 6 Okada S, Owada M, Sakiyama T, Yutaka T, Ogawa M. I-Cell disease: clinical studies of 21 Japanese cases. *Clin Genet* 1985; 28: 207–15
- 7 Beck M, Barone R, Kratzer W, Rakowsky T, Nigro F, Fiumara A. Inter and intrafamilial variability in mucopolipidosis II (I-cell disease). *Clin Genet* 1995; 47: 191–9