Prenatal Diagnosis of WAGR Syndrome

Berrin Tezcan, Philip Rich, Amarnath Bhide

Introduction

Wilm’s tumour, aniridia, genitourinary abnormalities and mental retardation (WAGR) syndrome is a rare genetic disorder with an estimated prevalence of 1 in 500,000 to 1 million. It is a contiguous gene syndrome due to deletion at chromosome 11p13 in a region containing WT1 and PAX6 genes. Children with WAGR syndrome mostly present in the newborn/infancy period with sporadic aniridia. The genotypic defects in WAGR syndrome have been well established. However, antenatal ultrasonographic presentation of this syndrome has never been reported. Prenatal diagnosis of this condition is possible in some cases with careful ultrasound examination of classical and non-classical manifestations of this syndrome. We were able to diagnose this rare genetic syndrome from the antenatal features, and offer parents information regarding the syndrome.

Case Report

We report a case of a 30 years old fit and well Asian (Indian ethnicity) woman in her second pregnancy, with a BMI of 26. The couple were non-consanguinous.

In the current pregnancy, her 11-14 weeks’ scan revealed no major structural abnormalities in the fetus and the risk for Down syndrome was low (1:50000) on combined screening. A routine anomaly scan at 20 weeks was also reported as normal. She was diagnosed with gestational diabetes at 16 weeks that was diet controlled and was offered serial growth scans from 28 weeks. A growth scan at 29 weeks showed reduced growth, and in view of this the woman was referred to the Fetal Medicine Unit. Scan performed by the fetal medicine specialist showed borderline bilateral ventriculomegaly, absent corpus callosum and absent cavum septum pellucidum. The amniotic fluid volume was mildly reduced. All the other systems appeared normal (Figure 1).

The couple were counselled regarding the possibility of genetic or chromosomal causes, and they opted for an amniocentesis. A fetal MRI was also organised for further assessment of the brain. Microarray result indicated a copy number loss for the short arm of chromosome 11 with break points between 11p12 and 11p14.1. Deletion of this region indicates WAGR 11p13 deletion syndrome.

Another detailed ultrasound scan was performed before the late termination. In addition to the above findings, large kidneys visualised. Measurements of both kidneys’ volumes were above the 97th centile for gestational age. There was no evidence of hydronephrosis (Figure 1).

MRI

Agenesis of corpus callosum was confirmed. There was associated colpocephaly causing widening of the lateral ventricles posteriorly. Elsewhere the brain was normal in appearance. Sulcation and linear measurements were within expected limits for gestational age (Figure 2). Midsagittal MRI scan confirmed absence of the corpus callosum. Coronal MRI scan at the level of the third ventricle showed agenesis of the corpus callosum. The bodies of the lateral ventricles had a lateral convexity in the coronal plane and a medial concavity due to the presence of Probst's white matter bundles. This was in keeping with the typical appearance in callosal agenesis. Axial scans at the level of the atria and bodies of the lateral ventricles showed bilateral posterior ventriculomegaly. Anteriorly the lateral ventricles were narrow and parallel. This was the appearance of colpocephaly which is characteristically associated with ACC (Figure 1).

Outcome

In view of the microarray result showing a deletion in the short arm of chromosome 11 associated with WAGR syndrome and the MRI brain confirming ultrasound findings, the parents were counselled regarding the outcome and parents decided to terminate the pregnancy. A fetocide procedure was performed at 31 weeks and this was followed by medical termination of pregnancy. The parents were offered a post-mortem examination but it was declined.

There were no obvious external structural anomalies on postnatal examination (Figure 1). An appointment with the clinical geneticist was organised. Both parents agreed to cytogenetic testing and qPCR and FISH analysis showed normal results indicating that there was no evidence of copy number change, deletion or rearrangement of this region of chromosome 11 suggesting that this genetic change was de-novo in origin. Hence, the risk of recurrence of deletion seen in this fetus in a subsequent pregnancy was deemed to be low.