Prenatal diagnosis in X-linked lissencephaly
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Objective
X-linked lissencephaly (MIM 300067) is a rare genetic disorder caused by mutations in the DCX (double-cortin) or ARX genes. Affected males have a ‘smooth brain’ caused by arrest of cortical neuronal migration resulting in intractable seizures and severe intellectual disability. Carrier females are mildly affected and have the typical double cortex appearance on MRI. Few publications of prenatal diagnosis of this condition have been reported.

Methods
A consanguineous southern Indian couple had two male children with severe global delay, intractable seizures and lissencephaly. No dysmorphic features or genital ambiguity were noted. Routine karyotyping and FISH testing for Miller-Dieker syndrome (MDS) were normal. The mother, a graduate of normal intelligence reported a single generalized seizure at age 13yrs. CT brain was normal. Repeat MRI brain revealed typical sub-cortical band heterotopias associated with heterozygous carriers of DCX mutations. DCX gene testing in mother and sons identified a novel causative mutation, absent in maternal grandparents. The couple proceeded with a planned pregnancy.

Results
Chorion villus sampling (CVS) was done at 11 weeks after detailed counselling. CVS DNA tests confirmed the fetus did not have the familial mutation. Subsequent anomaly and growth scans were normal.

Conclusion
In recurrent, syndromic lissencephaly FISH testing for chromosome 17p13 micro-deletion (MDS) and LIS1 gene mutations are usually tested for. Lissencephaly affecting males should also prompt testing DCX or ARX genes and include maternal neuro-imaging. Antenatal ultrasound scans / fetal MRI identify lissencephaly in 3rd trimester whereas genetic testing by CVS offers definitive, early diagnosis in this very rare disorder.