CASE REPORT

Uncommon antenatal presentation of tuberous sclerosis

Eleni Paleologou,¹ Richard Nicholl²

¹Department of Neonates/ Paediatrics, Northwick Park Hospital, London, UK
²Department of Neonates, Northwick Park Hospital, London, UK

Correspondence to
 Dr Eleni Paleologou,
 eleni.paleologou@nhs.net

Accepted 3 June 2014

SUMMARY

This is a case of a newborn male who was diagnosed in the first month of life with tuberous sclerosis following an incidental ultrasound finding of unilateral ventriculomegaly at 36+6 weeks gestation. The antenatal ultrasound scan at 36+6 weeks was performed to establish fetal lie. Subsequent fetal brain MRI showed lesions that were initially thought to be haemorrhages, but turned out to be features of tuberous sclerosis. The baby also had five cardiac rhabdomyomas and multiple ash leaf macules. This was an unusual presentation of tuberous sclerosis, which on average is diagnosed later (mean age of diagnosis is 5 years). It also illustrates two important points: that subependymal nodules and haemorrhage can have a similar radiological appearance on antenatal MRI and cranial ultrasound and that routine antenatal ultrasound screening will miss the majority of cardiac rhabdomyomas.

BACKGROUND

This was an unusual presentation of tuberous sclerosis, which on average is diagnosed later (mean age of diagnosis is 5 years¹). It also illustrates two important points: that subependymal nodules and haemorrhage can have a similar radiological appearance on antenatal MRI and cranial ultrasound and that routine screening will miss the majority of cardiac rhabdomyomas.

CASE PRESENTATION

A mother of 37 years was pregnant with her fourth child. She had two late miscarriages at 17 and 22 weeks gestation. In the current pregnancy she was found to have cardiolipin antibodies at booking, so was started on aspirin until 34 weeks gestation. Routine antenatal scans were normal.

At 36+6 weeks, the mother expressed concerns regarding the fetal position and had an ultrasound to establish fetal lie. This showed incidental left ventriculomegaly.

A subsequent fetal MRI was provisionally reported as showing severe left hydrocephalus (20.2 mm) and bilateral germinal matrix haemorrhages.

Urgent delivery was advised due to concern about an evolving hydrocephalus.

A male infant was born by caesarean section at 37+3, weighing 2630 g (10th centile) with a head circumference of 35 cm (90th centile). He was born in good condition and no resuscitation was required. Clinical examination was unremarkable, apart from an ejection systolic murmur 3/6, loudest over the left sternal edge.

Echocardiography on day 6 showed multiple echogenic lesions arising from the left ventricle ([figure 1](#)).

Cranial ultrasound showed left ventriculomegaly and echogenic lesions bilaterally, which were felt to be germinal matrix haemorrhages.

He was referred for specialist cardiac opinion on day 7. This confirmed he had five echogenic masses in the left ventricle, of which two were causing dynamic left ventricular outflow tract obstruction. They were reported as typical of rhabdomyomas.

He was also noted to have six hypomelanotic patches, mostly on his trunk and one on his lower limb, consistent with ash leaf macules, as also seen under Wood's light ([figures 2 and 3](#)).

On day 11, the formal report of the antenatal MRI described dilation of the left lateral ventricle and abnormal foci along germinal matrices with a large lesion in the left caudothalamic notch ([figure 4](#)). There were two areas of abnormality in the right temporal lobe and the left sylvian fissure with multiple small foci of low signal intensity within the white matter. The differential diagnosis included acquired haemorrhagic lesions or a neurocutaneous disorder such as tuberous sclerosis. The postnatal MRI on day 28 confirmed lesions typical of tuberous sclerosis.

The infant's blood was tested for the TSC1 and TSC2 gene mutations, which are known to cause tuberous sclerosis, but no mutations were identified. However, he fulfils the clinical criteria for a definite diagnosis of tuberous sclerosis to be made (4 major criteria: (1) more than three ash leaf

Figure 1 Subcostal four-chamber view echogenic lesions seen in the left ventricle.

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To cite: Paleologou E, Nicholl R. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-201012

Figure 2 Ash leaf macule on trunk.

macules, (2) cardiac rhabdomyomas, (3) cortical tubers and (4) subependymal nodules).

INVESTIGATIONS

Antenatal fetal ultrasound and fetal MRI at 36+6 weeks, post-natal MRI on day 28 of life, cranial ultrasound on day 1 of life and echocardiogram on day 6 of life (please see previous section for the details of findings). His blood was tested for the TSC1 and TSC2 gene mutations; the results were negative.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included acquired haemorrhagic lesions or a neurocutaneous disorder such as tuberous sclerosis.

TREATMENT

The patient was discharged with multidisciplinary follow-up arranged. No medications were started at first; however, he later presented with seizures and required antiepileptic treatment.

Figure 3 Ash leaf macule on lower limb.

Figure 4 T2-weighted MRI: subependymal lesion in caudothalamic notch.

OUTCOME AND FOLLOW-UP

The patient fulfils the clinical criteria for a definite diagnosis of tuberous sclerosis to be made (4 major criteria: (1) More than three ash leaf macules, (2) cardiac rhabdomyomas, (3) cortical tubers, (4) subependymal nodules). His management is multidisciplinary, with neurology, neurosurgical, cardiology, general paediatric and ophthalmology follow-up arranged.

In terms of his cardiac rhabdomyomas, following the first echocardiogram the concern had been the dynamic left ventricular outflow tract obstruction caused by the two pedunculated rhabdomyomas. There was no haemodynamic compromise or cardiac arrhythmias at any time and no treatment was initiated. When he was reviewed by the paediatric cardiologist at 2 months of age the obstruction to the flow across the aortic valve had lessened, so he continued to be managed conservatively. The expectation is that these cardiac rhabdomyomas will spontaneously regress.

In terms of his neurological status, he presented with multiple seizure types to the emergency room at 4 months of age and antiepileptic treatment was initiated. There was no concern about his development at the time.

DISCUSSION

This case was unusual, as the initial findings were discovered incidentally on the ultrasound performed at 36+6 weeks to establish fetal lie. This allowed the diagnosis to be made in the first month of life, whereas on average, tuberous sclerosis is diagnosed later (mean age of diagnosis is 5 years¹).

In addition, the case further illustrates the point that cardiac rhabdomyomas are generally diagnosed at a later gestational age than the routine anomaly scan performed at 20 weeks, making their antenatal diagnosis difficult. Looking into published articles of antenatally diagnosed cardiac rhabdomyomas, the range of gestational ages at which they were detected ranged from 22.4 to 34.4 weeks in 20 fetuses,² 27 to 36 weeks in 9 fetuses³ and 21 to 38 weeks in 19 fetuses.⁴

Lastly, in this case the fetal brain MRI and the postnatal cranial ultrasound findings were initially reported as haemorrhages, drawing the inference that the appearance of

subependymal nodules and/or astrocytomas and haemorrhage antenatally and on cranial ultrasound can be similar.

Learning points

- ▶ The appearance of subependymal nodules and/or astrocytomas and haemorrhage antenatally and on cranial ultrasound can be similar.
- ▶ Echocardiogram and brain MRI are the most useful diagnostic tests for tuberous sclerosis prenatally and in early infancy.^{1 5}
- ▶ Routine antenatal screening will miss the majority of cardiac rhabdomyomas, which are detected later than the 20-week anomaly scan.^{2–4} This is significant, when the diagnosis is made prenatally, appropriate planning at delivery for the management of potential complications may prevent adverse neonatal outcomes.⁶

Acknowledgements Mary A Rutherford, MD FRCR MRCPCH, Professor of Perinatal Medicine, The Robert Steiner MR Unit, Imaging Sciences Department, London.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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