Case series of prenatal diagnosis of fetal intrahepatic lesions and postnatal outcome

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Abstract

With advancing technology, it is becoming common for antenatal ultrasound to detect echogenic lesions in fetal abdomen. Paucity of data in this field, however, makes it difficult to counsel patients. We report four cases of fetal liver echogenic lesions, postnatal outcome (delivered during 2015–2016) and a literature review to increase awareness. Intrahepatic calcification is relatively common with an incidence of approximately 5–10 in 10,000 pregnancies. Prenatal detection of echogenic lesions in fetal abdomen causes huge anxiety and stress to parents; therefore, it is important for the ultrasonographers to be up to date with the evidence-based management of these lesions. Most lesions would carry no or little risk to neonate; however, few cases may require careful planning to optimise the time and place of delivery. We describe four cases between February 2015 and December 2016 using machine Voluson S6 and E8.

Keywords

Prenatal ultrasound, fetal intrahepatic calcification

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Case Series

Case 1

A 21-year-old nulliparous woman had a normal dating and anomaly scan. She had declined for combined screening. A scan at 30 weeks of gestation for reduced fetal movements showed fetus on 10th centile, echogenic bowel and an echogenic intra-abdominal lesions measuring approximately $6 \times 5 \times 1$ mm (Figure 1). The rest of the scan findings such as amniotic fluid (AFI) and umbilical artery, and middle cerebral artery Dopplers were normal. Couple was counselled for the possibility of chromosomal abnormalities, infections such as TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes simplex), and cystic fibrosis (CF). Repeat scan at 35 weeks showed persistent fetal hepatic lesion; however, fetal bowel appeared normal. TORCH and CF screening were negative. Induction of labour was planned at 37 weeks due to the baby on 10th centile and ongoing concerns with fetal movements after discussion with neonatal team. She delivered as a spontaneous vaginal delivery (SVD) a male baby weighing 3005 g. A neonatal examination after delivery otherwise was unremarkable. A paediatric review at eight weeks

with abdominal scan showed that the hepatic lesions had completely resolved and baby was appropriately growing with no concerns. The child is now 3 years old with no ongoing concerns.

Case 2

A 34-year-old woman, smoker, with two previous small-for-gestational-age babies had low risk on combined screening (risk of Down's syndrome 1 in 8419). Her growth scan at 28 weeks showed an echogenic hepatic lesion measuring $10 \times 12 \times 12$ mm (Figure 2). Rest of the scan findings, AFI and Dopplers, were normal. TORCH screening was negative. Further advice from Fetal Medicine tertiary Centre was sought, and a possible differential diagnosis of sub-diaphragmatic sequestration

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Figure 1. Fetal echogenic intra-abdominal lesion.

Figure 3. Fetal echogenic hepatic lesion.

Figure 2. Fetal echogenic hepatic lesion.

was made. Regular growth fetal scans showed persistent similar sized hepatic lesion with fetus on 10th centile growth and no other concerns. The woman delivered a healthy baby at 38 weeks by emergency caesarean section for fetal distress. A neonatal abdominal scan at two days of age suggested the diagnosis of liver haemangioma. The lesion resolved spontaneously on eight weeks postnatal follow-up. The child is two years and six months old now without any concerns.

Case 3

A 21-year-old nulliparous woman with low risk on quadruple (risk of Down's syndrome less than 1 in 10,000) screening showed an echogenic focus in the left ventricle of the heart, echogenic bowel and an avascular echogenic hepatic lesion (Figure 3). She was counselled for possible chromosomal disorder, CF and infections. She declined amniocentesis. TORCH and

CF screening were negative. On regular growth scans, these lesions remained small with no other fetal concerns. She had a vaginal delivery of a healthy baby at 40+4 weeks. The lesions completely resolved at a follow-up scan at four weeks of age. The child is now two years and four months old without any concerns.

Case 4

A 39-years, para 1, in vitro fertilization pregnancy and an early dating scan revealed dichorionic diamniotic twins. She had history of aggressive breast cancer and unilateral mastectomy five years ago. She had anti-Ro and anti-La antibodies positive prior to her pregnancy. Her combined screening results showed as risk of Down's syndrome (T21) as 1 in 311 for twin 1 and 1 in 384 for twin 2 with risks of Edwards (T18) and Patau's (T13) as less than 1 in 10,000 for both twins. She declined invasive test but had non-invasive prenatal testing which showed low risk for all three trisomy (less than 1 in 10,000). Regular scans from 28 weeks showed normal growth for twins but also reported the multiple liver echogenic avascular lesions (Figure 4) less than 1 cm each in first twin. AFI and Dopplers were normal for both twins. TORCH screening was negative.

She had SVD of twins at 35 weeks weighing 1.8 kg and 2.5 kg. Twin 1 had a normal liver function test and no clinical concerns. An abdominal scan at two days of age for twin 1 showed calcifications clustered around the right lobe of the liver measuring 5.1 mm, 6.7 mm, 4.4 mm and 4.7 mm. The liver otherwise appeared normal, and all the other abdominal organs were reported normal. These lesions were considered to be of uncertain clinical significance. Multiple paediatric reviews of the baby until one year of age showed the persistence of these lesions; however, the liver function tests remained normal.

Figure 4. Fetal hepatic calcifications in twin 1.

Discussion

Improved imaging equipment and techniques have resulted in an increased detection of intra-hepatic calcification in the fetus during pregnancy with an incidence of 5-10 in 10,000.^{1,2} Based on the appearance, echogenicity, calcification, size, number, presence of vascularity or calcification and any additional abnormalities, causes for these echogenic lesions could be:

- infections
- ischaemic causes
- portal and hepatic vein thrombosis
- tumours
- chromosomal abnormalities
- CF

These echogenic lesions can also be classified based on its locations:

- peritoneal
- parenchymal
- vascular

Infections such as TORCH can often cause multi-organ calcifications but can sometimes cause focal hepatic calcified lesions.

Ischaemic causes determine calcifications with diffuse distribution throughout the liver. The mechanism of ischaemic hepatic calcification is not clear; it could be related to vascular insufficiency in the fetal liver leading to infarction without secondary venous thrombosis.³

Portal and hepatic vein thromboembolism results in abnormal hepatic blood flow with infarction, fibrosis and calcifications appearing as multiple nodules or branching lines mainly subcapsular.⁴

Tumours: Benign and malignant liver tumours may have similar ultrasound features, making the diagnosis challenging. These lesions on scan can present with change in size, calcification, vascularity and signs of hydrops.

Haemangioma is the commonest benign tumour of infancy, usually in liver, lung and gastrointestinal tract (GIT). It is usually a non-calcified, single, well-defined avascular echogenic lesion with spontaneous regression over time in majority of cases. However, large haemangioma associated with high morbidity and mortality have also been reported.⁵

Mesenchymal hamartoma is a typically cystic avascular tumour which may enlarge rapidly. Usually they have a benign course, but large lesions may require surgical resection in infants and usually carry good prognosis.⁶

Hepatoblastoma is the commonest congenital hepatic malignancy. It is a well-defined echogenic mass, very vascular with a spoke-wheel appearance, with calcifications and pseudo-capsule. The five-year survival rate has increased to $\geq 75\%$ with appropriate chemotherapy.^{7,8}

Chromosomal abnormalities such as trisomy 21, trisomy 18 and 13 and monosomy X have been associated with intrahepatic echogenic lesion. The chances of chromosomal abnormalities are higher if more abnormalities detected on the scan.

CF: Literature reports good association with ultrasound markers: echogenic bowel, bowel obstruction and polyhydramnios, meconium peritonitis and non-visualisation of fetal gallbladder.⁹

Peritoneal calcification

Meconium peritonitis is a sterile chemical peritonitis due to in utero small bowel perforation with spillage of meconium intraperitoneally. The ultrasound shows multiple calcifications throughout the peritoneal surface of liver. It may be associated with CF, ileal or jejunal atresia, volvulus, micro-colon, Meckel's diverticulum and imperforate anus.^{9,10} In such cases, usual recommendation is for tertiary centre referral and delivery. Its complication, meconium pseudocyst has a high mortality rate up to 25%.¹¹

The other causes of echogenic lesion in fetal abdomen could be as follows: echogenic bowel, gallstones and sludge, enteroliths and echogenicity in fetal adrenal area including adrenal haemorrhage, neuroblastoma and mesoblastic nephroma.

Echogenic bowel remains the commonest aetiology of echogenic lesions identified in fetal abdomen in the second trimester with an incidence of 0.5% to 1%. It may be associated with chromosomal abnormalities, CF, intra-amniotic bleeding, congenital infections, gastrointestinal atresia, intrauterine growth restriction

and fetal demise. It resolves spontaneously in majority of cases if there are no underlying causes.¹²

Gallstones and sludge is an incidental finding and can present an echogenic area in fetal abdomen in third trimester ultrasound. They usually regress spontaneously and require no further intervention.

Echogenicity in fetal adrenal area: This can be caused by adrenal haemorrhage, neuroblastoma, other adrenal gland tumours and lesions from renal fossa such as mesoblastic nephroma and dysplastic kidneys. Tumours may have association with hydrops, polyhydramnios, and metastases to liver and other organs, which leads to a poorer prognosis.

Conclusions

The identification of echogenic lesion in the fetal liver should prompt a careful and detailed anomaly survey for any other structural abnormality. These women should be referred to fetal medicine specialist for further evaluation and counselling. These lesions should be carefully and regularly explored for their number, sites, size, vascularity and presence of fetal hydrops or other structural abnormality. Invasive testing such as amniocentesis should be recommended if chromosomal abnormalities are suspected. If after careful evaluation they appear to be 'isolated', a positive prognosis can be assured to parents. All cases should still be followed by further imaging and appropriate investigations in neonatal period.

The evidence present in literature is consistent with our findings for simple lesions but clearly emphasises the need to refer for further investigations in a fetal medicine centre if the lesions have a significant increase in size, change in vascularity or findings of hydrops, as in these conditions, the diagnosis and management may involve higher perinatal morbidity and mortality. However, most pregnancies will have a good outcome if there are no other structural abnormalities, no evidence of intrauterine infection and karyotype is normal.

In our cases, the differential diagnosis of echogenic lesions in fetal liver was discussed in detail, but the prognosis was considered good in view of no other associated fetal abnormalities. The diagnosis of echogenic lesions in fetal abdomen created a huge degree of anxiety in parents. We acknowledge the limitations of such a small case series and consider that a larger series may provide more guidance especially if non-isolated fetal hepatic lesions are identified.

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Contributors

SP scanned all these women and managed them antenatally. SP conceived the idea of publishing this case series due to paucity of data in this field. LG performed literature search and wrote first version of this case report. All authors reviewed and approved the final version of the manuscript.

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