Foetal pelvic and left lower extremity lymphatic malformation

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SUMMARY

We report a case of foetal pelvic and lower limb lymphatic malformation that resulted in a fatal complication. At 31 weeks 4 days, an antenatal ultrasound revealed an isolated left lower limb swelling with no other abnormalities, which was possibly a haemangioma. At 38 weeks, a baby boy weighing 4.59 kg was delivered via elective caesarean section. Postnatal magnetic resonance imaging at 2 months revealed features consistent with a lymphatic malformation with both micro and macro-cystic components involving the pelvis, left thigh and left lower limb. He was planning for sirolimus therapy but was not executed due to his parents' indecision. Soon after, he developed an acute deterioration due to an intra-lymphatic bleed, which resulted in bowel ischaemia and perforation, which resulted in metabolic acidosis, renal failure and death.

INTRODUCTION

Vascular anomalies are classified as vascular tumours which include proliferative changes of endothelial cells (EC) and vascular malformations, which are structural vascular abnormalities without EC proliferation. Lymphatic malformation is one of the vascular malformations, and it is a congenital lymphatic dysplasia. It can be categorised as macrocystic, microcystic and mixed type.[1] After venous malformations, lymphatic malformations are the most common type of vascular. They are commonly found in the neck (70–80%) or in the axillary region (20%) and are hardly seen in the pelvis or extremities.[2] Approximately half of these lesions are discovered at birth and up to 90% become visible by the age of 2 years.[3] There have been few reports of neonatal lower limb lymphatic malformation that were diagnosed in the antenatal period and had various outcomes including termination of pregnancy, resolution after sclerotherapy or surgical resection.[4] We present a case of newborn with pelvic and left lower limb lymphatic malformation that resulted in a lethal complication.

CASE PRESENTATION

Madam S, the mother of Baby A is a 31-years-old, chemotherapy staff nurse and this is her third pregnancy. Her previous two pregnancies took place seven and three years ago. Both babies were born at full term via spontaneous vertex deliveries. They are currently in good health. There was no family history of congenital anomalies. Both parents had no prior medical illness. Early booking was done at 11 weeks and 1 day period of amenorrhoea (POA). A viable foetus was seen on transabdominal sonography (TAS). The crown rump length was 49.8 mm and the revised expected date of delivery corresponded with her last menstrual period. As for her antenatal history, Madam S was treated for vulvovaginal candidiasis with Clotrimazole pessary at 12 weeks POA. She also had iron deficiency anaemia which was treated with oral haematinics and parenteral iron at 33 weeks POA. Madam S has also admitted at 27 weeks POA for premature contraction and received dexamethasone in ward. During admission, her TAS revealed no abnormalities. At 29 weeks POA, Madam S developed herpes zoster and was treated successfully with oral Acyclovir.

Madam S was admitted for contraction pain and reduced foetal movement at 31 weeks and 4 days POA. Her vital signs were stable and her physical examination in the hospital was unremarkable. However, her TAS revealed that the foetus had left lower limb swelling. She was referred to the maternal-foetal medicine (MFM) specialist for confirmation of scan findings. Upon review by the MFM specialist, the left lower limb swelling was thought to possibly be a left lower limb haemangioma. Subsequent TAS showed that the foetus was growing, and there was no sign of hydrops. The parents were counselled regarding the potential outcome. Due to the foetal left lower limb swelling, Madam S underwent an elective lower segment caesarean section at 38 weeks POA. Baby A was born with a good Apgar score. The birth weight was 4.59 kg, the height was 55 cm and the head circumference was 36 cm.

Baby A was admitted shortly after birth for transient tachypnoea of newborn and left lower limb swelling. He did not have any syndromic features and his cardiorespiratory examination was normal. His left lower limb was enlarged from the groin to ankle with normal overlying skin (Figure 1). The swelling had the same soft consistency as the opposite side. He could move his left lower limb. There were no other birthmarks or skin abnormalities. Ultrasound of the left lower limb showed a low-flow vascular anomaly that may be a congenital haemangioma. On his second day of life, he was discharged with an outpatient magnetic resonance imaging (MRI) appointment.

MRI at 2 months old (Figure 2) showed multilobulated cystic lesions seen in the pelvis, deep intermuscular left gluteal, left

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Fig. 1: Photography of Baby A demonstrating the left lower limb swelling

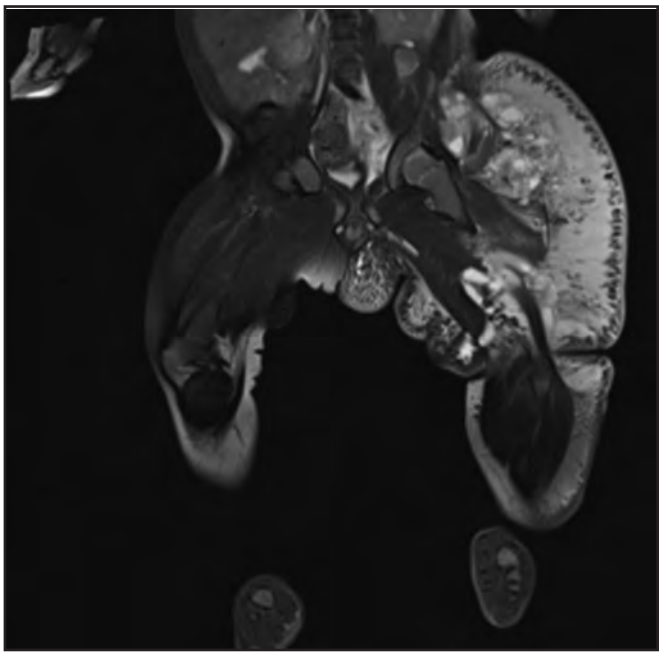

Fig. 2: MRI of pelvis and lower limbs of Baby A.

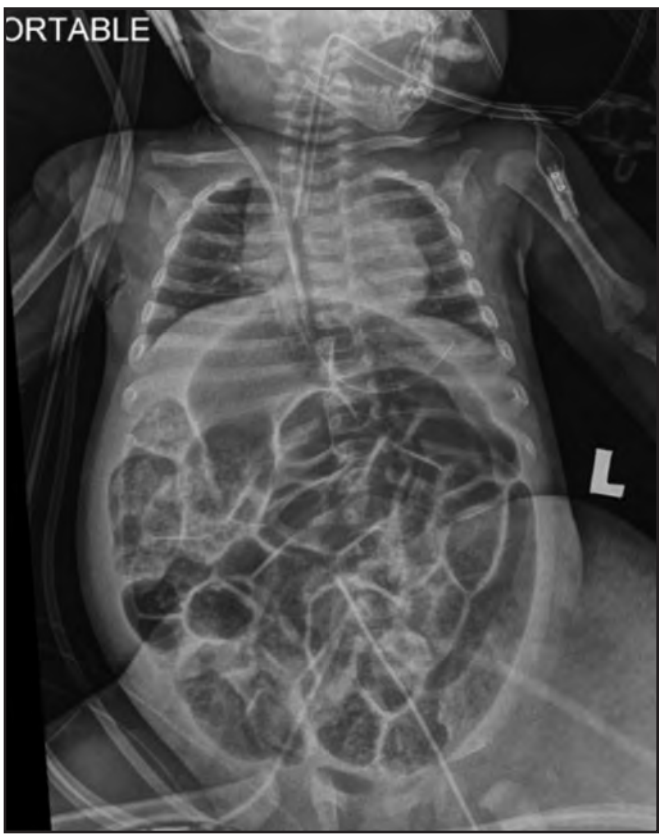

Fig. 3: Plain radiograph of Baby A when he deteriorated

thigh and deep subcutaneous layer of the lateral aspect of the left knee. The largest cystic component in the pelvis and thigh measures 1.2 cm and 1.8 cm, respectively. These cysts show peripheral rim enhancement post gadolinium. The overlying subcutaneous layer of the left thigh and distal left lower limb is thickened with a mass-like appearance, with no significant enhancement post gadolinium. It may represent the microcystic component. Overall, the MRI features suggest a lymphatic malformation with both micro and macro-cystic components affecting the pelvis, left thigh and left lower limb. Following consultation with the paediatric surgeon, it was planned to begin with Sirolimus for 6 months, followed by sclerotherapy if Sirolimus was futile. His parents needed more time to think about the treatment because they were not sure about it.

The day following the MRI, Baby A developed fever and did not urinate for 12 hours. He could still breastfeed normally and had normal bowel movement. Following morning, Baby A developed abdominal distension and became more lethargic with laboured breathing. He was rushed to emergency unit for resuscitation. He had poor perfusion. His abdomen was grossly distended and firm on palpation. Additionally, the left lower limb had increased swelling. Blood investigation revealed the metabolic acidosis and hypoglycaemia, along with a haemoglobin level of 7.1 g/dL. Plain radiograph of the abdomen showed dilated small and large bowels with a loss of polygonal shape. There was no bowel wall thickening or intramural gas (Figure 3). An ultrasound of the abdomen and left lower limb showed free fluid with echogenic debris seen predominantly in the perihepatic, subhepatic and perisplenic regions, raising the

Table I: Difference between congenital haemangioma and lymphatic malformation in ultrasound

	Vascular tumors: Congenital haemangioma	Vascular malformation: Lymphatic malformation
Sonogram	Heterogeneous subcutaneous mass Might contain a large visible vessel	Macrocystic component appears as multiple cystic formations of variable sizes with liquid content separated by thin hyperechogenic septa, compressible with ultrasound probe Microcystic component appears as solid formations with scattered cysts
Colour Doppler	Very high vascular density	Slow flow lesion Vascular signals are generally absent

suspicion of a perforated hollow viscus. Baby A required multiple inotropic supports and renal replacement therapy. Due to his declining condition, he was ineligible for exploratory laparotomy. Baby A deteriorated and succumbed to death the following day. An intra-lymphatic bleed that led to intestinal ischaemia and perforation was considered to be his cause of death.

DISCUSSION

We present a rare case of foetal lymphatic malformation that originated from the pelvic region to the left lower limb. Lymphatic malformations are benign masses containing fluid-filled channels or spaces that may be caused by abnormal lymphatic system development. They are rare, not cancerous and there is no known risk of malignant transformation. The prevalence of lymphatic malformations in the general population is estimated to be around 1:4000 live births.[5] Most are discovered at birth or during antenatal period, but they are rarely found in pelvic and extremities.[2,6]

The exact aetiology of lymphatic malformations is unknown. Lymphatic malformation is caused by abnormalities in the development of the lymphatic vascular system during embryonic growth.[5] Vascular endothelial growth factor (VEGF)-C and VEGF receptor type3 (VEGFR3), PIK3CA mutations have been detected in the lymphatic EC of the lymphatic malformation.[1,7] Madam S has worked as a staff nurse at a haematology day-care facility for the past three years and handled chemotherapy medications daily while she was pregnant. Study showed that the risk of congenital anomalies of the eye was significantly higher among the babies of nurses working in oncology unit. The risk of other congenital anomalies including circulatory system was also increased but they were limited by small number of cases and were not statistically significant.[8]

In this case, the swelling of the lower limb was discovered at 31 weeks POA, but it was initially thought to be a haemangioma. Ultrasound can be a useful imaging technique to differentiate between haemangioma and lymphatic malformation, as shown in Table I. However, there is a limitation if the lesion was extensive and deep-seated. Also, it is not always possible to come to a diagnosis with colour doppler alone. Therefore, MRI will be needed in certain situations.[9] Lymphangiomas detected in the second and early third trimesters had a worse prognosis as they have a stronger association with karyotypic abnormalities. Those detected in the middle to late third trimester however, have a decent prognosis.[4] Foetal karyotyping and antenatal foetal MRI were not done in this case due to a lack of resources. These tests can be offered to antenatal mothers since a normal karyotype and the lack of hydrops imply a good prognosis.[4] No complications from the vascular malformation, such as skin oedema, hydrops fetalis or polyhydramnios, were found during Baby A's subsequent TAS. TAS was essential to continuously monitor the development of the lesion and the emergence of complications. It is also essential for parental counseling and planning the mode of delivery. Termination of pregnancy was reported in other studies[4] but it was not permitted locally without proper indication.

Although cystic lymphangiomas are associated with genetic disorders such as Noonan syndrome, Turner syndrome, and Down syndrome, Baby A appeared normal without any syndromic features.[6] The baby's enlarged limb had the same soft consistency as his other normal limbs. It was incompressible, similar to venous malformations.[2] Features of macrocystic malformations include 1–3 large cystic lesions[1] with rim and septal enhancement[2] which are seen in this case. Cysts less than 2 cm, however, are classified as microcytic type.[2] The largest cyst, in this case, was only 1.8 cm. Besides that, the left thigh and distal left lower limb had a mass-like appearance at the subcutaneous layer with no significant enhancement post gadolinium which may indicate a microcystic component. This led to the conclusion that Baby A had a mixed kind of lymphatic malformation with a predominance of the microcystic type.

Sirolimus was offered as treatment in this case. Sirolimus is a mammalian target of rapaymycin (mTOR) inhibitor which is one of the most promising drugs for treating various vascular anomalies including lymphatic malformations.[1] However, Sirolimus should be administered at modest doses, after considering the risks and benefits, due to the high rate of adverse events, such as infections, blood or lymphatic problems, neutropenia, interstitial pneumonitis, or sirolimus hypersensitivity syndrome.[7] The risk of side effects made Baby A's parents unsure about starting Sirolimus. The lymphatic malformation complication led to Baby A's death. The clinical findings and imaging were suggestive of an intra-lymphatic bleed that led to bowel ischaemia and perforation. A foetal lymphangioma diagnosed during the prenatal period has a poor prognosis, with a mortality rate ranging from 50 to 100%. Because of this, all three reported cases of foetal abdominal lymphangioma that spread to an extremity resulted in the termination of the pregnancy.[10]

As primary care practitioners are often the first point of contact for antenatal mothers, it is critical that we detect

subtle findings on routine TAS and do not overlook measurements of all parameters and their correspondence to gestational age. Picking up a swelling could indicate fatal congenital malformations, necessitating immediate referral to the maternal foetal medicine specialist. Early detection may allow for better planning on the continuation of pregnancy, further evaluations as well as aid parental counseling and anticipation of the pregnancy. It was fortunate that Baby A was delivered via an elective caesarean section, avoiding the risk of birth trauma. Nonetheless, things did not turn out well because the lymphatic malformation eventually led to his death.

CONCLUSION

Foetal lymphatic malformation can be detected early during prenatal ultrasound and suspicious swellings should warrant urgent referral. If lymphatic malformation is detected early, treatment and delivery options, as well as the pregnancy's outcome, can all be planned for. Future cases of lymphatic malformations should be reported, and risk factors and causes for their occurrence may be researched. A multidisciplinary approach for cases of lymphatic malformation is preferred for the best perinatal outcome, including a comprehensive antenatal assessment and parental counseling with primary care practitioners, maternal foetal medicine specialists, neonatologists, and paediatric surgeons.

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DECLARATIONS

The authors declare they have no conflict of interest.

INFORMED CONSENT

Informed consent for the publishing of this case report was obtained from the patient's parents.

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