J. Fetal Med. (March 2022) 9:23–27
https://doi.org/10.1007/s40556-022-00339-5

CASE REPORTS

Prenatal 2-D and 3-D Ultrasound Characteristics of a Case of Fetal Orofacial Macrocystic Lymphatic Malformation and its Postnatal Management with Intralesional Bleomycin

Nithya Elango[1] · Seneesh Kumar Vikraman[2,4] · A. C. Saranyadevi[3] · Chithra Sengodan[4] · Kumar Athapanur Sengottiyan[4]

Received: 31 October 2021 / Accepted: 19 April 2022 / Published online: 6 June 2022

Abstract Fetal lymphatic malformations (FLM) are benign hamartomatous lesions of the lymphatic vasculature usually localized in the cervicofacial and axillary regions and less frequently in the abdomen or inguinal areas, with an overall incidence of 1:6000 to 1:16,000 live births. FLM has a potential association with chromosomal aneuploidies such as Trisomy 21,18,13, Turner syndrome and genetic conditions such as Noonan syndrome, and with an excess risk for co-existing structural defects. A progressive increase in the dimensions of FLM's may result in polyhydramnios, hydrops, intrauterine fetal demise, airway obstruction and neonatal respiratory distress. We report a case of fetal orofacial lymphatic malformation detected in the mid-trimester anomaly scan with details of two- and three-dimensional imaging, prenatal counseling, cytogenetic workup, serial ultrasound surveillance, postnatal magnetic resonance imaging, and management with an intra-lesional sclerosing agent. The case depicts the strategic importance of multidisciplinary inputs in managing cases of prenatally diagnosed oral-cervical masses for optimizing perinatal outcome.

Keywords Fetal tumors · Oro-facial lymphangioma · Bleomycin · Sclerosing agents · Prenatal diagnosis · 3D ultrasound

✉ Seneesh Kumar Vikraman
drseneeshkv@gmail.com

[1] ARMC Salem, Salem, Tamil Nadu, India

[2] ARMC AEGIS Hospital Perinthalmana, Malappuram, Kerala, India

[3] ACR Clinic, Metturdam, Salem, India

[4] SIMS Chellum Hospital, Salem, India

Background

Fetal lymphatic malformations (FLM) are benign hamartomatous lesions of the lymphatic vasculature [1]. They are typically localized in the cervicofacial and axillary regions and less frequently in the abdomen or inguinal areas, with an overall incidence of 1:6000 to 1:16,000 live births. About 50% of the FLMs present at birth and up to 90% are usually evident later by the age of two years [2]. The use of overlapping nomenclatures such as cystic hygroma, lymphangioma, nuchal thickening, nuchal translucency and lymphatic malformation without standard definitions and differentiating aspects has led to the ambiguity concerning their prevalence, prognostic significance and potential sequelae [3, 4].

We report a case of orofacial FLM detected in the mid-trimester anomaly scan with details of two-dimensional and three-dimensional (2D-3D) imaging characteristics and neonatal management.

Case report

An 18 year old South Indian woman, primigravida, spontaneous conception from a third degree consanguineous marriage, was referred to our fetal medicine unit at 22 weeks of gestation for evaluation of an abnormal cystic swelling in the fetal face. The obstetric, medical and family history were unremarkable. Ultrasound examination performed with a GE Voluson S10 Expert, C1-5 convex transabdominal transducer, revealed a single live intrauterine fetus with an anechoic cyst which measured 7 × 6.8 cm seen with thin septations located in the right cheek near the right mandible (Fig. 1). Another cyst measuring 2 × 1.6 cm was noted in the anterior part of the neck with fine septations. The two cysts were observed

communicating with each other. There were no vascular signals on Doppler interrogation. Fetal growth and amniotic fluid volume were normal. No additional structural abnormalities were noted. 3D ultrasonography confirmed the origin of the mass from the right cheek and presence of another small cyst in the anterior part of the neck. A diagnosis of FLM was made.

Multidisciplinary counseling of the couple with the obstetrician, fetal medicine specialist, clinical geneticist and pediatric surgeon was performed. The couple were informed about the condition in detail, the need for prenatal chromosomal analysis, and a plan regarding postnatal management. They denied the offer of prenatal invasive genetic testing and opted to continue the pregnancy.

Serial four-weekly ultrasound surveillance was done to detect any increase in the dimensions of the mass, development of hydrops, assess the risk of airway obstruction and need for EXIT (ex utero intrapartum procedure). On a follow-up scan at 33 weeks of gestation, the previously noted cyst size had reduced to 4.9 × 4.2 cm and 2 × 1 cm respectively. Amniotic fluid volume was normal suggesting the absence of upper airway obstruction. Elective cesarean delivery was performed at 39 weeks of gestation. An active male baby weighing 3500 g with no signs of respiratory distress was born.

Postnatal MRI showed a large cyst of 5 × 5 × 4 cm in the right cheek with thin septations and another cyst of 1.3 × 1 cm along infratemporal fossa (Fig. 2). MRI of the brain and spine were unremarkable.

As the cysts were communicating with each other and located in the neck, surgical excision was considered not feasible, and a decision was made for postnatal cyst aspiration. Cytological examination confirmed cells of lymphatic origin and absence of malignancy. Management was done with the instillation of intralesional Bleomycin, an anti-tumor antibiotic, with a dose of 1.5 mg (0.5 mg/kg). Evaluation after three weeks showed reaccumulation of fluid. Re-aspiration was done and a second dose of the sclerosing agent was instilled. Meanwhile, peripheral blood of the neonate was sent for Karyotype which revealed a balanced translocation involving chromosomes 5 and 8 (Fig. 1). A chromosomal microarray of the neonate (to look for sub-Karyotypic genomic losses) and a parental Karyotype (to ascertain the origin of the balanced translocation) was offered which was declined by the couple. The baby is in a regular pediatric follow up and is doing well with attainment of normal milestones.

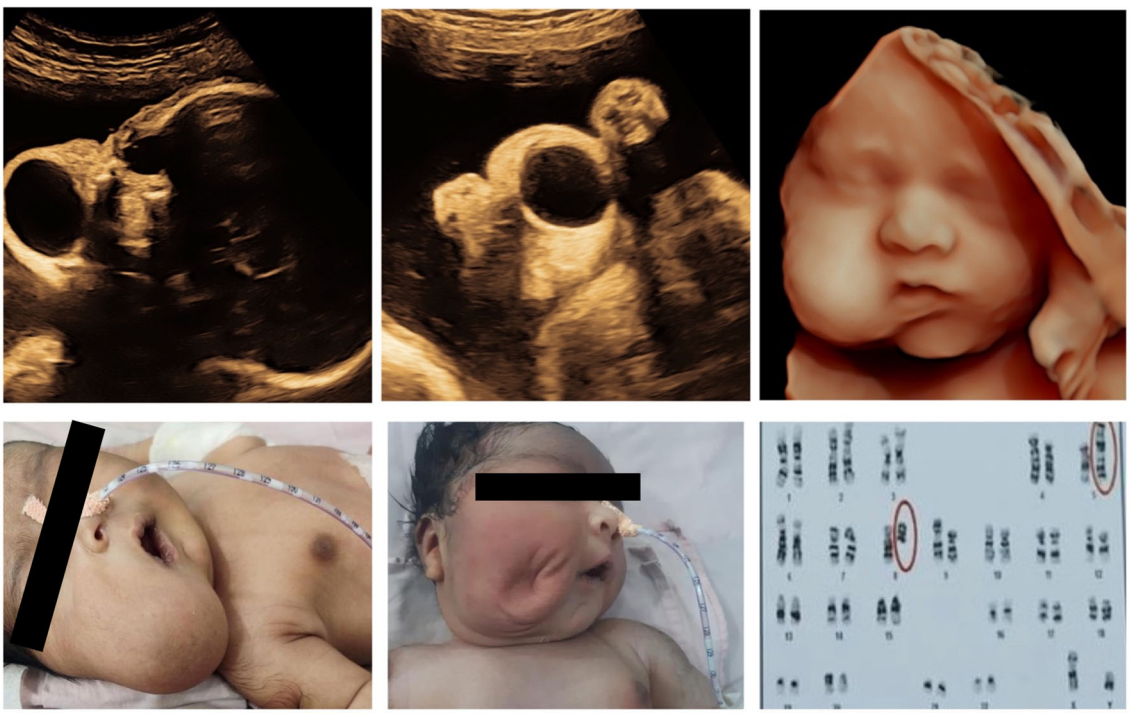

Fig. 1 Ultrasound examination at 22 weeks of gestations showing **a** Gray scale 2D image of the right parasagittal fetal face with a cystic mass projecting from the site of the right cheek, apparently from the subcutaneous plane, **b** Gray scale 2D coronal image of the fetal face showing the cystic mass, **c** 3D surface rendering of the fetal face depicting surface features of the mass, **d** Neonate at birth showing the mass in the right cheek, **e** The mass reduced in size after aspiration and Bleomycin instillation, **f** High resolution Karyotype after G-banding of peripheral lymphocytes showing a balanced translocation 46, XY, t(5;8) (q35;q12)

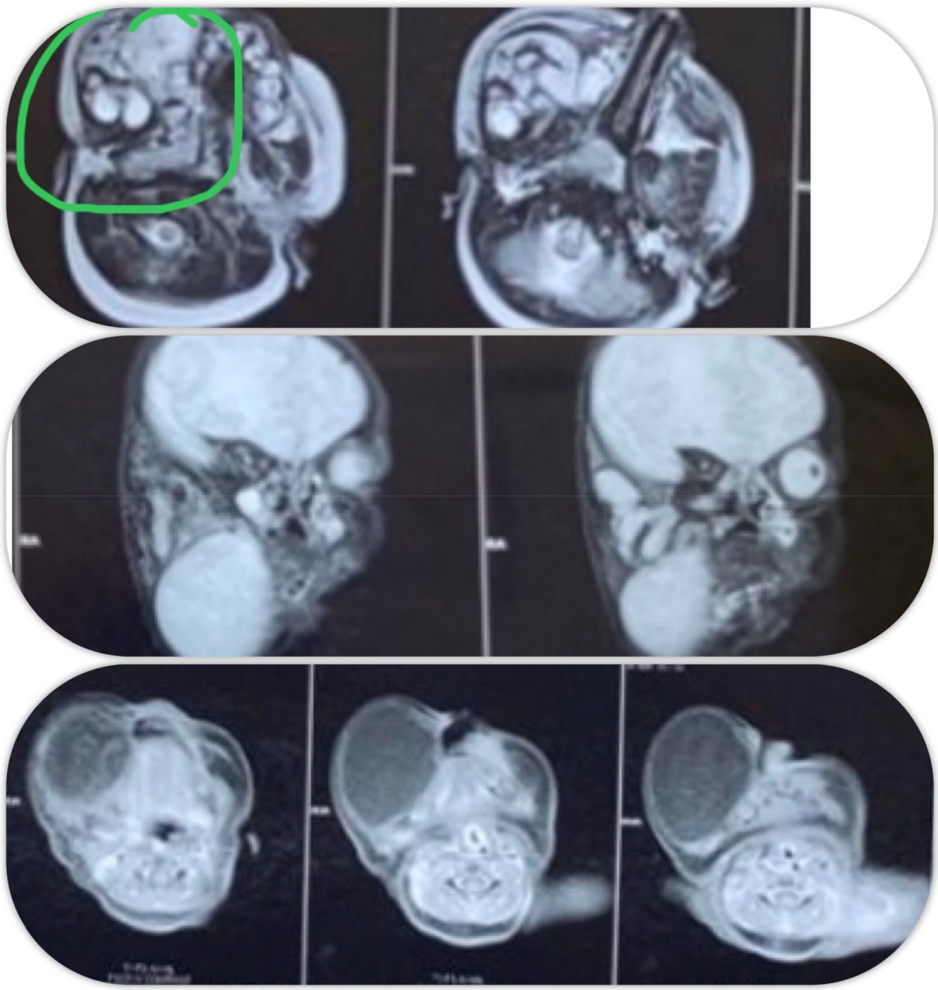

Fig. 2 MRI image showing the features of the fetal oro-cervical mass in the neonate

Discussion

Lymphatic anomalies of the fetal neck are categorized into three groups based on their sonographic anatomy: nuchal thickening (NT), dorsal lymphatic malformation (DLM), and ventral lymphatic malformation (VLM) [5]. The DLMs are more commonly affected by chromosomal aberrations such as Turner syndrome and structural abnormalities such as cardiac, renal and skeletal defects. Nuchal thickening is likely to resolve but has a significant association with Trisomy 21. On the other hand, VLMs usually do not spontaneously resolve and have generally low association with aneuploidies [6].

Histologically, FLM can be classified into three main types: (1) simple lymphangiomas, consisting of lymphatic capillaries; (2) cavernous lymphangiomas, consisting of larger lymphatic vessels with a fibrous adventitia; (3) cystic lymphangiomas or cystic hygromas, consisting of multiple cysts ranges from a few millimetres to several centimetres [7]. All these histological subtypes may coexist within the same lesion. FLMs are also classified as macrocystic, microcystic or mixed, depending on their size, with radiologically discernible lesions termed as macrocystic [8].

The differential diagnosis of oro-cervical masses includes teratoma, ranula, palatal cysts, epidermoid cysts, congenital epulides, dermoid cysts, lymphatic malformation and haemangiomas [9] (Table 1). Though all lesions are benign, their location can have different effects on the clinical course and outcome.

Fetal cystic lymphangiomas appear on ultrasound as well defined, unilocular or multilocular cystic masses, with or without septations and may be anechoic, or with internal echoes due to bleeding and fibrin deposition [10]. In our case, 2D ultrasound and 3D surface rendering accurately delineated the mass, its anatomical location and extent. This facilitated parental counseling and planning postnatal management.

MRI is often used as a complementary technique to ultrasound in prenatal diagnosis. In the context of an oro-cervical mass, it is useful to assess the nature of these lesions, their extension, and, mechanical compression of

Table 1 Differential diagnosis of common fetal oro-cervical facial tumors

Type	Key ultrasound Imaging features
Foregut duplication cyst	Hypoechoic lesion with a heterogenous internal echotexture and regular margins
Frontal encephalocele	Pure cystic mass or may contain internal echoes from herniated brain tissues. A cystic mass indicates the predominant component as a meningocele
Myoblastoma	Cystic mass with internal echoes; Colour Doppler shows marked vascularity within the tumor
Cystic hygroma	Complex cystic mass with septations and may present as a nuchal cyst; associated with fetal hydrops and anasarca
Haemangioma	Well-defined echogenic mass with prominent internal vascularity on Colour Doppler imaging
Ranula	Thin-walled cystic lesion. Infected cysts have a thicker wall and internal echoes
Neurofibroma	Well defined round to oval shaped mass with homogenous hypoechoic appearance and through transmission and internal vascularity
Rhabdomyosarcoma	Heterogenous well defined irregular mass of low to medium echogenicity

adjacent organs [11]. In our case, the couple denied prenatal MRI.

Fetal lymphangiomas can have a variable course including spontaneous regression or progression due to lymphangiogenesis, excessive fluid accumulation, poor drainage, lymphatic aggregation, and cellulitis [12]. Management options for large lymphangiomas include prenatal cyst aspiration and/or elective cesarean section followed by postnatal management [13]. The preferred postnatal treatment of lymphangioma is surgical excision, with careful preservation of adjacent structures. Large but localized lymphangiomas can be excised completely, but the surgical treatment of diffuse and multiple lesions is extremely difficult and is associated with high morbidity and mortality [14].

In cases of FLM which are surgically unresectable, the injection of a sclerosing agent may be considered appropriate. Successful outcomes have been reported following the use of intralesional Bleomycin, OK-432, or percutaneous embolization with Ethibloc [15, 16]. In our case, Bleomycin, an anti-tumor antibiotic was used postnatally. Aspiration and instillation of Bleomycin was repeated after reaccumulation in three weeks time. An adverse reaction like immune suppression and fibrosis are the main adverse drug reactions of Bleomycin. Other oral medications used for the resolution of the lesion include sirolimus, propranolol and sildenafil [17–19]. Prenatal treatment of a cystic hygroma with OK-432 has also been reported successfully [20].

Our case depicts the importance of multidisciplinary inputs in managing a case of a fetal oro-cervical mass. The important considerations are a detailed anatomical survey, ruling out chromosomal aberrations, serial ultrasound assessment and planning the mode of delivery and need for immediate interventions such as EXIT. Red flags for immediate postnatal intervention include polyhydramnios, protrusion of the tongue and lack of to and fro motion of tracheal fluid.

Conclusion

Precise prenatal diagnosis and multidisciplinary counseling is effective in the perinatal management of oro-cervical masses. The use of sclerosing therapy needs introspection for prenatal use, as this has the potential of reducing the size of the mass and averting potential dystocia and respiratory distress.

Data availability statement Data sharing is not applicable as this article as no new data were created or analyzed in this study.

Declarations

Conflict of interest The authors declare no conflict of interest.

References

1. Bloom DC, Perkins JA, Manning SC. Management of lymphatic malformations and macroglossia: results of a national treatment survey. Int J Pediatr Otorhinolaryngol. 2009;73:1114–8.
2. Marches C, Savin E, Dragone E, et al. Cystic hygroma: prenatal diagnosis and genetic counseling. Prenat Diagn. 1985;5:221–7.
3. Bloom DC, Perkins JA, Manning SC. Management of lymphatic malformations. Curr Opin Otolaryngol Head Neck Surg. 2004;12:500–4.
4. Malone FD, Canick JA, Ball RH, et al. First-trimester or second-trimester screening, or both, for Down's syndrome. N Engl J Med. 2005;353:2001–11.
5. Longstreet B, Balakrishnan K, Saltzman B, et al. Prognostic value of a simplified anatomically based nomenclature for fetal nuchal lymphatic anomalies. Otolaryngol Head Neck Surg. 2015;152(2):342–7.

6. Dighe MK, Peterson SE, Dubinsky TJ, et al. EXIT procedure: technique and indications with prenatal imaging parameters for assessment of airway patency. Radiographics. 2011;31:511–26.
7. Rha SE, Byun JY, Kim HH, et al. Prenatal sonographic and mr imaging findings of extensive fetal lymphangioma: a case report. Korean J Radiol. 2003;4(4):260–3.
8. Choi DJ, Alomari AI, Chaudry G, et al. Neurointerventional management of low-flow vascular malformations of the head and neck. Neuroimaging Clin N Am. 2009;19:199–218.
9. Ercan F, Sarikaya M, Toprak E, et al. Prenatal diagnosis and intrapartum management of congenital ranula. Z Geburtshilfe Neonatol. 2018;222(6):262–5.
10. Lee SH, Cho JY, Song MJ, et al. Prenatal ultrasound findings of fetal neoplasms. Korean J Radiol. 2002;3:64–73.
11. Peiro JL, Sbragia L, Scorletti F, et al. Management of fetal teratomas. Pediatr Surg Int. 2016;32:635–47.
12. Hassanein AH, Mulliken JB, Fishman SJ, et al. Lymphatic malformation: risk of progression during childhood and adolescence. J Craniofac Surg. 2012;23:149–52.
13. Suzuki N, Tsuchida Y, Takahashi A, et al. Prenatally diagnosed cystic lymphangioma in infants. J Pediatr Surg. 1998;33:1599–604.
14. Kosir MA, Sonnino RE, Gauderer MW. Pediatric abdominal lymphangiomas: a plea for early recognition. J Pediatr Surg. 1991;26:1309–13.
15. Deshpande P, Twining P, O'Neill D. Prenatal diagnosis of fetal abdominal lymphangioma by ultrasonography. Ultrasound Obstet Gynecol. 2001;17:445–8.
16. Dubois J, Garel L, Abela A, et al. Lymphangiomas in children: percutaneous sclerotherapy with an alcoholic solution of zein. Radiology. 1997;204:651–4.
17. Reinglas J, Ramphal R, Bromwich M. The successful management of diffuse lymphangiomatosis using sirolimus: a case report. Laryngoscope. 2011;121:1851–4.
18. Maruani A, Brown S, Lorette G, et al. Lack of effect of propranolol in the treatment of lymphangioma in two children. Pediatr Dermatol. 2013;30:383–5.
19. Swetman GL, Berk DR, Vasanawala SS, et al. Sildenafil for severe lymphatic malformations. N Engl J Med. 2012;366:384–6.
20. Watari H, Yamada H, Fujino T, et al. A case of intrauterine medical treatment for cystic hygroma. Eur J Obstet Gynecol Reprod Biol. 1996;70:201–3.