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FETAL PROCEDURES

Prenatal Embolisation of Giant Chorioangioma Using *n*-Butyl Cyanoacrylate: Technique, Clinical Course and Perinatal Outcome

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Abstract Giant Chorioangiomas, although rare, can be associated with serious fetal complications due to blood cell sequestration, shunt physiology or both. Prenatal treatment is aimed to counter the primary complication, usually an intrauterine transfusion to treat anemia or occlusion of the feeder artery to negate the shunt physiology. We describe a case of giant chorioangioma complicated by high output cardiac dysfunction with imminent hydrops that was treated with embolisation of the feeder artery using *n*-butyl cyanoacrylate and discuss how one modality may not fit all cases.

Keywords Giant chorioangioma · Fetal therapy · Fetal interventions · Embolisation · Enbucrilate · Fetal hydrops · Fetal procedure · Placental tumor

Introduction

Chorioangioma which is a benign neoplasm of the placenta consisting of varying proportions of capillary/sinusoidal vascularity, stromal tissue, and Wharton's Jelly is relatively common with frequency as high as 1% [1]. However, Giant Chorioangioma, defined as a diameter greater than 4–5 cm, is rare and complicates less than one in 10,000 pregnancies [2]. They are associated with significant perinatal morbidity and even mortality.

Large chorioangioma causes polyhydramnios, possibly due to secondary hyperdynamic fetal circulation and/or fetal anemia resulting in high-output cardiac failure, hydrops and fetal demise. Prenatal intervention can change the course of the disease and improve fetal outcome. Various strategies for management include early delivery, laser photocoagulation of feeder vessels by fetoscopic or interstitial approach and intravascular embolisation. Among the available modalities, no single intervention has been recognized as the best fit for all cases of chorioangiomas.

In this report, we present a case of giant chorioangioma causing imminent fetal cardiac failure treated prenatally by feeder-artery embolisation using enbucrilate.

Case Report

Thirty-year-old, second gravida presented at 29^{+6} weeks with polyhydramnios. The sonographic evaluation showed structurally normal fetus with appropriate growth; a giant chorioangioma with the largest diameter measuring 8 cm, fed through a single large artery and drained by a large vein that communicated to the umbilical vein at the placental cord insertion, 7 cm away (Fig. 1). The fetus had features

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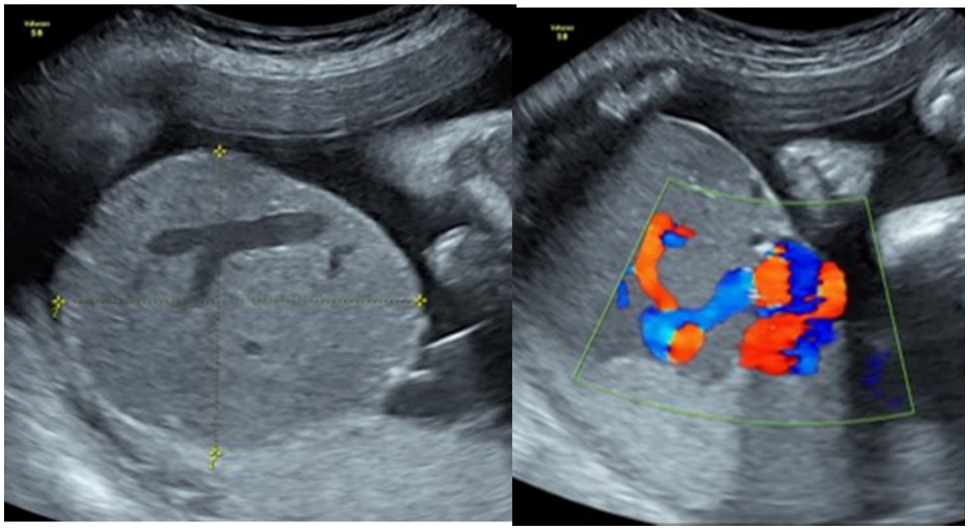

Fig. 1 B-mode and Color Doppler demonstrating the large tumor with a single large feeder vessel

of hyperdynamic circulation (MCA PSV 1.5 MoM, high PSV in ductus venosus, Tei Index of left ventricle 0.3, distended umbilical vein and polyhydramnios), with imminent cardiac failure (cardiomegaly, CC:TC ratio 0.56, tricuspid regurgitation). Delivery was considered unfavourable in view of prematurity and cardiac compromise. Laser photocoagulation by fetoscopy or interstitial technique was deemed too risky in view of the large vessel size. Therapy with intravascular embolisation with enbucrilate as described by Cheng et al. [3] was considered the optimal approach. Parents agreed for intravascular embolisation after the discussion about the procedure and its risk including the uncertain effect on portal circulation [4].

Under aseptic conditions, fetal analgesia and immobilisation were achieved with fentanyl (10 mg per kilogram) and atracurium (0.4 mg per kg) which was injected into the fetal gluteal region. A 15 cm long 22 g needle was introduced transamniotically and positioned into the feeder artery just as it entered the substance of the chorioangioma. Two ml of fetal blood was aspirated and sent for hemoglobin estimation. The needle was flushed with 5% dextrose, following which 1.5 mL of enbucrilate diluted with 4.5 mL of lipiodol was injected. The instantaneous echogenic coagulum was visible inside the artery with near total occlusion. The needle was withdrawn and about 1.5 litres of excessive liquor was removed using an 18-gauge spinal needle. About 10 min after the procedure, the blood flow in the feeder artery was reassessed which revealed persistent flow peripheral to the central tissue-glue coagulum. In view of the huge size of the tumor, 0.5 mL enbucrilate diluted with 2.5 mL of lipiodol was injected proximal to the first injection site and complete cessation of blood flow was noted (Fig. 2). The fetal heart remained stable throughout the procedure.

Reassessment after one week showed resolution of polyhydramnios, regression of dilatation of umbilical vein and normalisation of MCA flow. However, mild right ventricular dysfunction and tricuspid regurgitation persisted until delivery. In view of previous caesarean delivery and persistent right ventricular dysfunction, baby was delivered electively by caesarean section at 38 weeks.

Baby was born in good condition but had difficulty in breathing soon after birth. Non-invasive nasal ventilation was commenced shortly after birth. Chest X-ray showed bilateral reticulogranular opacities with contracted lung volume consistent with hyaline membrane disease. In addition, baby had features of pulmonary hypertension presenting as a significant difference between pre and post ductal oxygen saturation. Echo showed moderate pulmonary shunt with predominantly right to left shunt at atrial and ductal level. The baby was started on sildenafil and the difference between pre and post ductal oxygen saturation decreased over the next 96 h. Respiratory distress settled gradually over the next 4 days and baby was weaned to nasal oxygen and eventually to air. Repeat echo on day 5 showed mild pulmonary hypertension and with left to right shunt at the ductal level and bidirectional shunt at atrial level.

Baby was discharged on oral sildenafil on day 5 of life. Echo at 1 month showed resolution of pulmonary hypertension and sildenafil was discontinued. Follow up after 6 months showed normal infant with no residual morbidity.

Discussion

Although small chorioangioma is relatively common occurrences, giant chorioangioma that causes fetal compromise is quite rare. Giant chorioangioma is arbitrarily

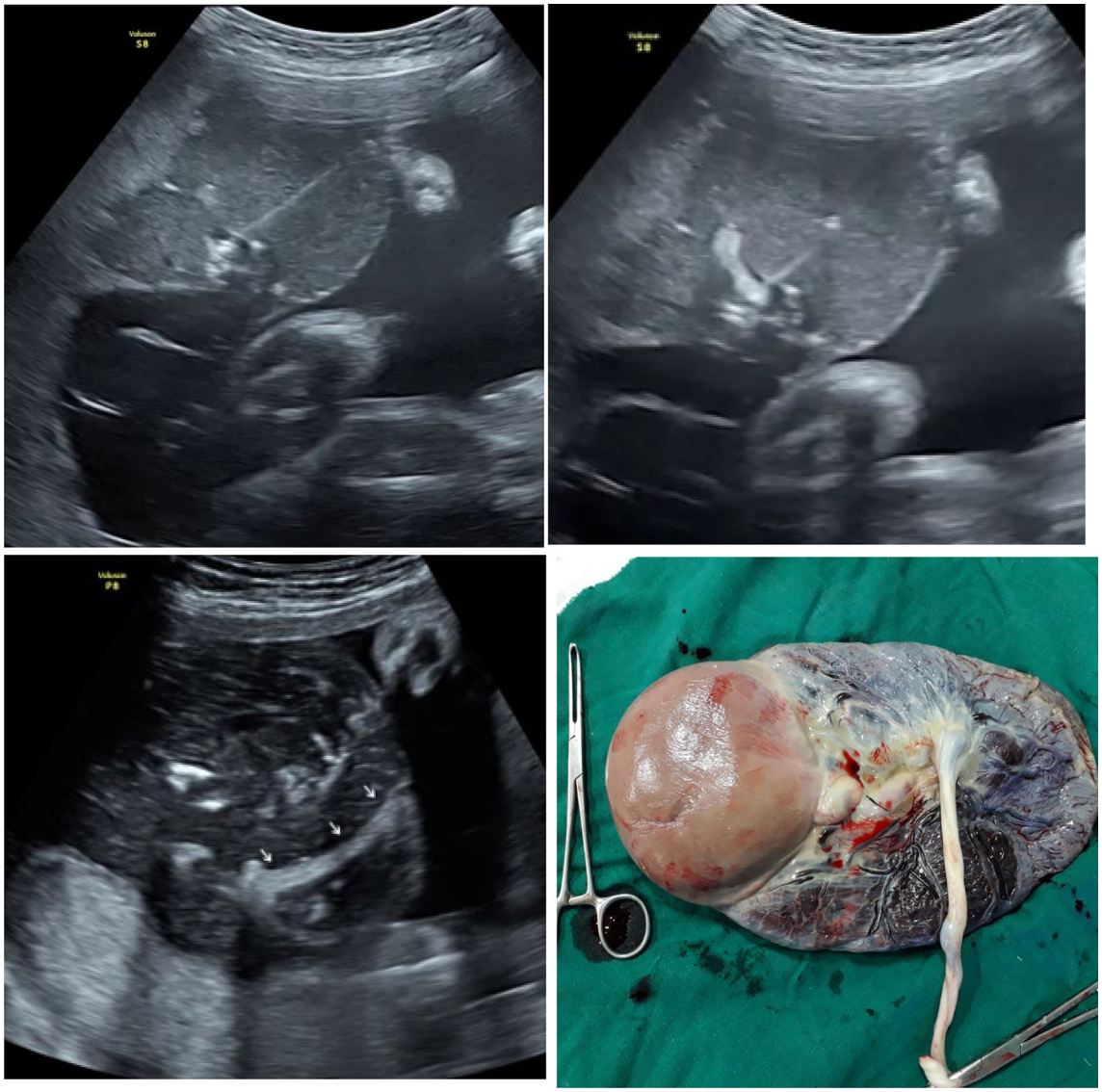

Fig. 2 Top left—needle inside the feeder artery; top right—instantaneous coagulum with injection; bottom left—stable, echogenic coagulum filling the arterial lumen 2 days later; bottom right—appearance of tumor at delivery

defined as measuring > 4–5 cm in its largest dimension [2]. Factors other than the size that may impact fetal outcome may include the degree of vascularity within the tumor, distance of the tumor from the placental site of cord insertion and the number of tumors.

Fetal compromise in giant chorioangiomas can be classified into sequestration related sequelae and shunt related sequelae. The former is characterised by fetal anemia and thrombocytopenia, and the latter by cardiac volume overload. Both sequelae may co-exist, and may have secondary effects such as high-cardiac output state superimposed on the primary features. Polyhydramnios, placental edema, and hydrops may complicate in both categories. From a therapeutic point of view, it may be useful to know the primary category of the fetal compromise—a sequestration based fetal compromise can often be managed by simple transfusion while a shunt based fetal compromise requires aggressive therapy directed at the tumor itself.

Tumor therapy is primarily aimed at depriving the tumour of its blood supply. Several modalities have been attempted in the past. Key factors that determine the choice of modality include the site of tumor, accessibility, size and number of feeder vessels, operator expertise with modality and risk of iatrogenic pre-labour rupture of membranes (iPROM).

Obliteration of the feeder vessels can be achieved by extrinsic energy induced coagulation of vessels or by intrinsic endoluminal occlusion by mechanical methods. Operator's expertise is of paramount importance in judging

Table 1 Literature review of prenatal interventions for giant chorioangioma

Intervention	Authors and years	Number of cases	Size (mm)	Complications	GA at diagnosis/ procedure	Supportive therapy	GA at delivery	Outcome
Vasoobliteration using extrinsic energy/device								
Fetoscopic laser	Quarello et al. (2005)	1	44		23/25	AD	39	Livebirth
	Bermudez et al. (2007)	1	61	Hydrops	24/24	IUT twice, AD	26	IUFD (autopsy—UV thrombosis)
	Sepulveda et al. (2009)	2	67	CHF	–/26	AD	37	Livebirth
			58	CHF	–/27	IUT (due to intra-op bleeding)	28	Livebirth; died at 1 year of age due to CRF
	Zanardini et al. (2010)	1	42		24/24		36	Livebirth
	Jones et al. (2012)	1	56	Tumour enlargement and HCOS following AD	14/27	AD	38	Livebirth
	Hosseinzadeh et al. (2015)	1	60	HCOS	16/21 Laparoscopy assisted fetoscopic laser due to anterior placenta		39	Livebirth
	Jhun et al. (2015)	1	156		28/29		33	Livebirth
Interstitial laser	Zanardini et al. (2010)	3	45		24/25		32	Livebirth
			35		25/32		39	Livebirth
			54		28/29	AD, IUT	37	Livebirth
	Papaioannou et al. (2018)	1	140		24/24	AD	31	Livebirth
	Bhide et al. (2003)	1	53		23/24 and 26		32	Livebirth Post-procedure developed FGR
Fetoscopic bipolar coagulation	Foong Yen Lim et al. (2015)	1	125	Hydrops	26/26		34	Livebirth (PPROM, chorioamnionitis)
Fetoscopic surgical clipping	Foong Yen Lim et al. (2015)	1	88	HCOS	20/20		29	Livebirth (PTL, IVH)
Combination of above								
Fetoscopic laser/ interstitial laser	Sepulveda et al. (2009)	1	85	Hydrops	–/28		28	IUFD (? due to bleeding into tumour)
Fetoscopic laser/bipolar coagulation	Mendez-Figueroa (2009)	1	80	Hydrops following AD	25/25	AD, IUT	25	IUFD
	Foong Yen Lim et al. (2015)	2	69	HCOS	23/24		38	Livebirth
			71	Hydrops	24/24		39	Livebirth
Fetoscopic laser/bipolar coagulation/ RFA	Foong Yen Lim et al. (2015)	1	97	Hydrops	24/24		24	IUFD (due to vessel rupture)
Fetoscopic ligation and bipolar cautery	Quintero et al. (1996)	1	85	Hydrops	24/24		24	IUFD (increased placental resistance post procedure)

Table 1 continued

Intervention	Authors and years	Number of cases	Size (mm)	Complications	GA at diagnosis/ procedure	Supportive therapy	GA at delivery	Outcome
Intratumoral injection of sclerosants								
Alcohol	Ercan et al. (2012)	1	55		25/25	AD, IUT	29	Livebirth
Intravascular occlusive techniques								
Alcohol injection	Nicolini et al. (1999)	2	60		25/27	AD	Term	Livebirth
			50		18/24 and 25		Term	Livebirth
	Jauniaux et al. (2000)	1	100	Hydrops	–/32		32	NND
	Wanapirak et al. (2002)	1	80	Hydrops	27/27		32	Livebirth
	Sepulveda et al. (2003)	1	75	Hydrops	23/26		26	IUFD
	Deren et al. (2007)	1	83		24/25 and 26	IUT	28	Livebirth
Microcoil embolisation	Lau et al. (2003)	1	100		24/24 and 25	IUT	29	NND
	Emery et al. (2018)	2	112	Hydrops	25/26		26	IUFD
			92		22/22	IUT	39	Livebirth
Enbucrilate embolisation	Lau et al. (2005)	1	90	Hydrops	24/24		26	NND
	Babic et al. (2012)	1	58		22/22	AD, IUT	30	Livebirth
	Haddad et al. (2010)	2	57		22/27		39	Livebirth
			76		20/29		41	Livebirth
	Perrotin et al. (2004)	1	80	Hydrops	26/26		40	Livebirth
	Voon H Y et al. (2018)	1	58		20/24	AD	36	Livebirth (right portal vein thrombosis)
	Cheng et al. (2017)	1	80		21/22		34	Livebirth
	Bolla et al. (2014)	1	62		22/22		37	Livebirth
Tissue glue injection (Glubran)	Gajeswka et al. (2010)	1	80		22/23	IUT	38	Livebirth

HCOS high cardiac output state, *AD* amniodrainage, *CHF* congestive heart failure, *IUT* intrauterine transfusion, *IUFD* intrauterine fetal demise, *NND* neonatal death

the applicability of a particular method apart from the feasibility, advantages and potential limitations of each method. Since a multitude of factors dictate the suitability of each modality, and the tumor anatomy is variable, our opinion is that no single modality is suitable in all cases. A summary of the different interventions reported in prenatally treated chorioangioma cases is presented in Table 1 [2–29].

Pros and cons exist for each of the available modality and the choice needs to be individualised. Table 2 illustrates the different characteristics of the treatment options that need to be considered by the stakeholders before deciding a therapy.

This case also illustrates the course of recovery taken by the fetus after elimination of the cause of impending hydrops. Cardiomegaly and umbilical vein distention were the first to regress, indicating that the volume overload was the primary pathology. Persistence of tricuspid regurgitation and right ventricular dysfunction point to long standing strain on the right heart even after treatment.

This case is unique for the successful use of intravascular embolisation with enbucrilate, a scarcely used

Table 2 Summary characteristics of different interventional options in chorioangioma

Modality	Equipment, device/drug	Cost	Maternal morbidity	iPPROM	Fetal risks	Efficacy	Expertise	Remarks
Fetoscopic laser	Fetoscope, laser generator and fibre	++++	+++	+++	+	++++	++++	High rate of preterm birth
Fetoscopic bipolar coagulation	Fetoscope, electrosurgical unit, bipolar forceps	++	+++	+++	+	+++	++++	Rarely performed
Fetoscopic surgical clipping	Fetoscope, miniature instruments, clips	+++	+++	+++	+	++	++++	
Interstitial laser	18G needle, laser generator and fibre	+++	+	++	++	+++	+++	Risk of vessel rupture if superficial and large caliber
Radio frequency ablation	RF electrode (17G), RF generator	+++	+	++	++	++	+++	Risk of collateral thermal damage
Alcohol injection	20 G needle, alcohol	+	+	+	+++	++	++	Unsuitable for multiple, small feeder vessels; non-target embolisation risk medium to high
Microcoil embolisation	20 or 21 G needle, microcoils	+++	+	+	+	+++	+++	Unsuitable for multiple, small feeder vessels; non-target embolisation risk low
Tisue glue embolisation	Needle 20 or 22G, enbucrilate or glubran, lipiodol	++	+	+	+	++++	++	

intervention for chorioangioma. One of the potentials, albeit unproven adverse events reported in the literature with enbucrilate therapy is neonatal portal vein thrombosis. Post-procedure followup of portal sinus calibre measurement and flow pattern of the fetus did not show any abnormality.

We conclude that in selected conditions, endovascular embolisation with enbucrilate (*n*-butyl cyanoacrylate) provides a safe and minimally invasive means of treating a giant chorioangioma that acts as a peripheral arterio-venous shunt. It must be considered as one of the therapeutic options since it is a percutaneous procedure with a negligible adverse effect on the mother and the pregnancy.

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