Congenital cervical teratoma in association with neuronal migration disorder

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Abstract

Congenital cervical teratoma is a rare congenital malformation with an estimated incidence of one in 20,000-40,000 live births. Due to its mass effect it has a potential to cause significant fetal airway obstruction, while its hyper-vascularity may result in fetal heart failure and hydrops fetalis. An association with intracranial abnormalities has been previously described but is extremely rare and no cases of postnatal survival have previously been reported. In this study we report the first case of congenital cervical teratoma with neuronal migration disorder in a live-born infant and the role of in-utero cyst drainage as an airway salvage intervention. We also present a literature review on etiology, diagnosis, management options and prognosis of congenital cervical teratoma with and without intracranial abnormalities.

Key words: cervical teratoma, neuronal migration disorder, congenital malformation, antenatal counseling, postnatal palliative care.

Introduction

Accurate antenatal counseling for complex fetal malformations when parents wish to continue with the pregnancy is frequently limited by the availability of literature on possible outcomes. As termination of pregnancy and postnatal palliative care are both viable options for many women and families in this context, clinicians must ensure that the full range of management plans and postnatal outcomes are adequately discussed.
In this article, we report the first case of a prenatally diagnosed cervical teratoma in association with extensive neuronal migration disorder in a live-born infant. We also review the literature on cervical teratomas, their association with structural brain abnormalities, management options and prognosis.

Case report

Ms A, a primiparous 30-year-old woman with an IVF pregnancy was referred to our regional maternal-fetal medicine (MFM) service following an abnormal morphology scan at 20 weeks gestation. Two-dimensional ultrasound scan at 23 weeks gestation revealed a right-sided neck mass, clenched hands, agenesis of the corpus callosum (ACC), absent Cavum Septum Pellucidum and colpocephaly (Figure 1). The neck mass measured 35x18x23mm, was largely cystic with a solid central component, and there was an associated superior displacement of the right mandible. The ultrasound appearance raised a strong suspicion of a congenital cervical teratoma. An amniotic fluid sample was taken at 23 weeks gestation and analyzed by array Comparative Genomic Hybridization (aCGH) using the Agilent ISCA (v2) 60K oligonucleotide array platform. The result was a normal female hybridization pattern with no abnormality detected. Maternal cell contamination was excluded by multiplex QF-PCR (quantitative fluorescent) analysis.

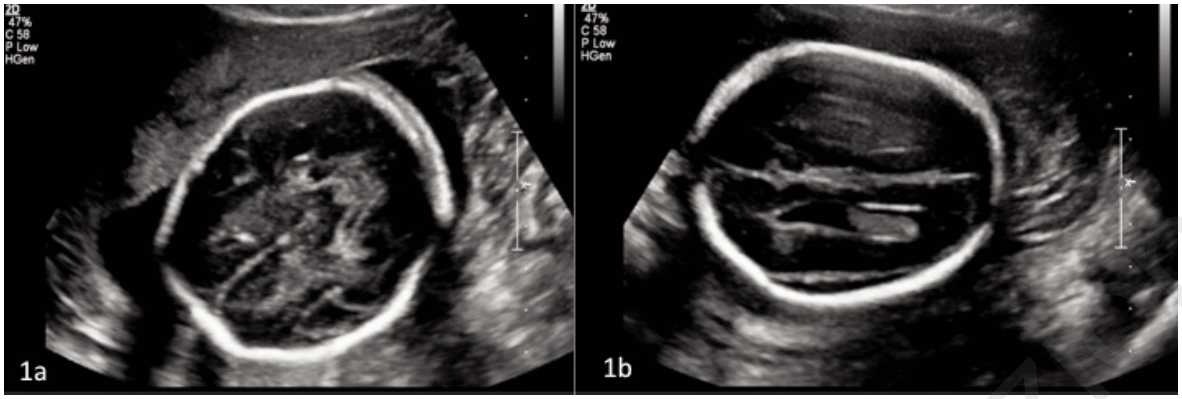

Figure 1. Ultrasound demonstrating absent Cavum Septum Pellucidum (a) and colpocephaly (b).

A multidisciplinary team comprising of quaternary maternal-fetal medicine, neonatology, ENT, pediatric surgery, pediatric radiology and clinical genetics were consulted to determine the optimal antenatal and perinatal management.

Fetal MRI (Phillips Achieva 1.5T) was performed at 25 weeks gestation, to assess the degree of airway compromise and anatomy of the tumor in relation to surrounding tissues (Figure 2a). It revealed compression and displacement of the oropharynx and hypopharynx by a predominantly cystic lesion extending from the right parapharyngeal region. Diffuse cortical abnormality of the frontal lobes and grey matter heterotopia was suspected in addition to the known ACC. In view of the additional intracranial findings and persistently clenched hands, parents were counseled of the high risk of a long-term and severe neurological impairment. However, as there was no similar case in the literature to guide accurate prognostication, the parents opted to continue with pregnancy.

The mass progressively enlarged to 79x64x53mm by 34 weeks gestation, with associated polyhydramnios from 31 weeks. There was no significant vascularity within the mass nor development of hydrops fetalis. Due to the development of polyhydramnios there was concern about adequacy and safety of the postnatal airway. Thoracic volumes consistently appeared to be adequate with no evidence of pulmonary hypoplasia. The possibility of the Ex-utero Intrapartum Treatment (EXIT) procedure was discussed with the parents. Following extensive multidisciplinary team discussion a decision was made to aspirate the cystic component to assess reversibility of the airway obstruction. At 35 weeks gestation, 140ml of straw-colored fluid was aspirated under ultrasound guidance from the presumed cervical teratoma. Amniodrainage of 1000ml was additionally performed. Post-aspiration fetal MRI demonstrated successful decompression of the cystic component of the mass and complete resolution of the airway obstruction. Fetal ultrasound scan 2 days later showed some re-accumulation of fluid within the cystic component of the mass although it remained significantly smaller compared to pre-drainage.

Cytology of the cystic aspirate showed abundant macrophages and epithelioid cells. It was also noted to contain beta-2 transferrin, a sensitive and specific marker of cerebrospinal fluid (CSF) (1). However, the immunohistochemistry did not assist with diagnosis of cervical teratoma.

Ms A developed spontaneous late preterm labor at 36 weeks and 2 days gestation. Bedside ultrasound scan showed significant re-accumulation of fluid within the cyst, similar to the pre-drainage volume. A further 130ml of fluid was therefore successfully aspirated from the cyst immediately prior to delivery to optimize neonatal airway management. A paired theatre set-up was coordinated whereby the lower segment caesarean section was performed in one theatre and the baby was then immediately transferred to the adjacent ENT theatre for airway management. The delivery was attended by the maternal-fetal medicine specialist, pediatric anesthetist, pediatric ENT surgeon and neonatologist. Baby A was born in good condition; however, despite adequate respiratory effort, due to concerns about airway adequacy was electively intubated at birth with an uncuffed oral 3.5 mm endotracheal tube.

Baby A was transferred to Neonatal Intensive Care Unit (NICU), and was stable on minimal ventilation settings with no supplementary oxygen requirement. The decompressed cyst re-accumulated quickly with a visible change in size within the first few hours of life.

Postnatal examination revealed short palpebral fissures with micro-ophthalmia, a large neck mass that supero-posteriorly displaced the right ear and mild finger contractures on all digits, but no other dysmorphic features.

Baby A was noted to be hypotonic with reduced spontaneous movement but with regular breathing effort, stable heart rate and blood pressure. She was unable to suckle feed, in part due to the presence of the neck mass, but tolerated full milk feeds via naso-gastric tube.

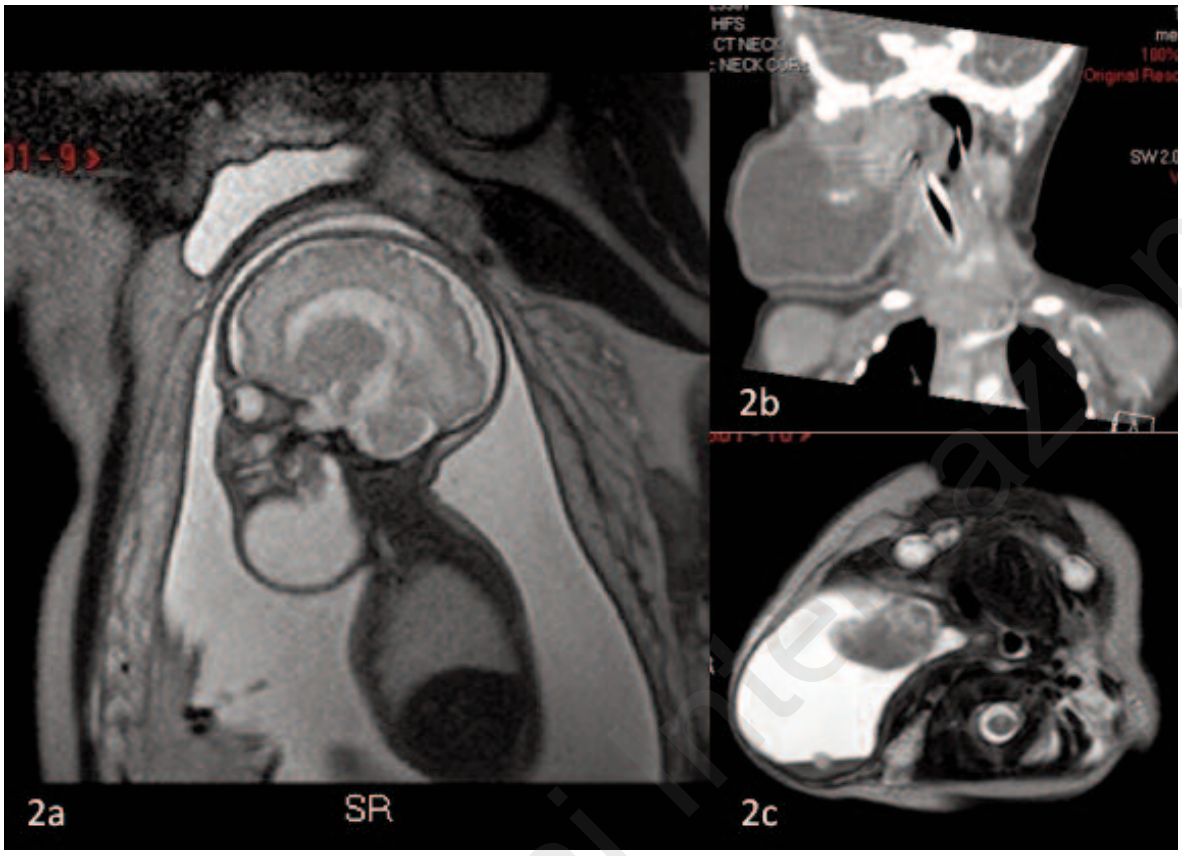

Figure 2. Ante- and post-natal MRI demonstrating location and mass effect of neck lesion; (a) Fetal MRI at 25 weeks gestation demonstrating the large solid-cystic mass intimately associated with the skull base; (2b) Postnatal contrast CT on day 2 of life demonstrating the complex solid-cystic mass with foci of calcification; (2c) Postnatal MRI on day 2 of life demonstrating fluid/fluid level in the peripheral cystic component of the mass, with a more central, solid portion of the mass causing mass effect on the hypopharynx.

There was no clinical seizure activity, but conventional and amplitude-integrated electroencephalograms (EEG) were performed to assess the background cortical activity. Both were significantly abnormal with discontinuous activity patterns suggestive of a significant abnormality of brain maturation.

Postnatal CT and MRI of the brain and neck on day 2 of life allowed more detailed anatomical assessment of the mass and intracranial abnormality. The large complex solid-cystic mass within the right neck contained fat and calcium (Figure 2b). There was involvement of the right middle and inner ear and significant effacement of the pharynx (Figure 2c). The mass was intimately associated with the right internal jugular vein and internal carotid arteries at the skull base. The mass was felt to be most in keeping with the presumed diagnosis of a teratoma. The intracranial abnormality seen on the postnatal MRI was more extensive than antenatal imaging had suggested, and confirmed extensive diffuse polymicrogyria throughout the cortex, grey matter heterotopia, ACC and dysmorphic lateral ventricles.

The intimacy of the tumor with major blood vessels and extension into the temporal bone limited surgical options; complete resection was extremely unlikely to be achievable, with a high risk of peri-operative mortality due to tumor placement and degree of invasion. Additionally, the extensive neuronal migration disorder alone posed a bleak prognosis with a high likelihood of severe neurodevelopmental disability and major seizure disorder. The MDT team, following an extensive discussion with parents over a course of two weeks, came to a conclusion that palliative comfort care rather than extensive surgical intervention would be in baby A's best interest.

Baby A was extubated successfully on day 8 and remained well saturated in room air without respiratory support or supplemental oxygen. The patency of her airway post-extubation was maintained by needle aspiration of the cyst, under sucrose analgesia, every 2-3 days, whenever the fluid reaccumulation caused tense swelling of the cyst with resultant airway compromise and stridor.

Baby A was therefore discharged home on day 18 of life with support from the community palliative care team, neonatal nursing team and a consultant neona-

tologist. The decision had been made not to re-aspirate the cyst and she died peacefully on day 20 of life from the inevitable airway obstruction.

Post-mortem examination confirmed the diagnoses of congenital cervical teratoma and severe neuronal migration disorder. Infiltration of surrounding connective tissues by the tumor was confirmed. No macroscopic defect in the skull base or dura was found to account for the presence of CSF within the tumor, however a microscopic defect could not be excluded. Histologically the teratoma contained mature cells of mesodermal and endodermal origins, with abundant choroid plexus tissue. The presence of choroid plexus could account for beta-2 transferrin in the cystic aspirate, although it does not exclude intracranial extension of the tumor. There was no yolk sac tumor present within the teratoma.

The parents and the wider family were extremely grateful to have had the opportunity for postnatal care and time with their baby. For them, termination of pregnancy had not been an option, in part due to the paucity of information available to inform likely postnatal outcomes. The decision to transition to palliative care was collaborative, had full consensus from the family and their medical team and underpinned by the recognition that all possible medical and surgical options had been explored.

Discussion

We report the first published case of postnatal survival in a neonate with a complex cervical teratoma complicated by neuronal migration disorder. These data add to the informational available for parents making informed choices about pregnancy termination *versus* postnatal palliative care.

Neonatal tumors are rare and account for approximately 2% of childhood cancer (2). Congenital teratomas represent 20-40% of all neonatal tumors, and have an estimated incidence of 1/20,000-40,000 births (2-4). The majority of congenital teratomas occur in sacrococcygeal and gonadal sites, while head and neck teratomas are much rarer and only represent 5 to 15% of all congenital teratomas. Intracranial extension of a cervical teratoma is uncommon (5,6) and the combination of a cervical teratoma and a structural brain abnormality is extremely rare. Of the three cases previously described over the last 22 years (Table 1), two ended in fetal demise and one case resulted in termination of pregnancy. No live births have previously been reported, limiting parental and medical access to information about possible postnatal care options.

Etiology

The most accepted theory on the pathogenesis of congenital teratoma is that of abnormal proliferation of pluripotent cells sequestered during early embryonic development. A number of genetic abnormalities have been reported in association with congenital or childhood teratomas, including aneuploidies, marker chromosomes, ring chromosomes, and copy number variants (3, 7, 8, 10). Sacrococcygeal teratomas are well described in Currarino syndrome (MIM:176450) caused by pathogenic variants in MNX1, however there are no well described single gene causes of congenital cervical teratomas (7-9).

Prenatal diagnosis

Congenital cervical teratomas are rare but an important differential diagnosis to consider in a fetus or a neonate presenting with a neck mass. The commonest cause of fetal cervicofacial tumors is lymphatic malformation (75%) followed by teratoma/epignathus (21%), haemangioma (2%) and thyroid tumor (2%) (10).

With advances in technology it is now possible to identify congenital cervical teratomas by 2D ultrasound scan as early as 15-17 weeks gestation (3). Cervical teratomas may be cystic or solid but frequently contain calcification, which helps differentiate them from other causes of a fetal neck mass. Absence of calcification, however, does not exclude the diagnosis of teratoma (11,12). Classically cervical teratomas are found anteriorly and close to the midline. In contrast, lymphangioma, haemangioma and branchial cysts are typically found more posteriorly and laterally. Based on the location, echogenicity and vascularity of lesions, ultrasound examination is usually sufficient to reliably diagnose congenital cervical teratomas (10).

Beta-2-transferrin is a product of neuraminidase activity and is found in CSF and perilymph. While it has high sensitivity and specificity for CSF and is useful in identifying a breach of intracranial space (1), it has a limited value in congenital cervical teratomas because of the relatively common finding of mature CSF-secreting tissue within the tumor itself (40-100%) (13).

Accurate early diagnosis of congenital cervical teratoma enables clinicians to inform parents of the potential prognosis and optimize prenatal and perinatal management. Once the diagnosis is suspected, close monitoring is mandatory to enable early identification of clinically significant airway narrowing and/or polyhydramnios. Antenatal 3D ultrasound and fetal MRI are strongly recommended for further assessment of the tumor extent, airway patency, and associated abnormalities (5, 6, 14, 15).

Association with intracranial abnormalities

In the absence of an underlying genetic abnormality, congenital cervical teratomas are usually isolated phenomena (16). While intracranial extensions of cervical teratomas have been described, true associations of intracranial pathology with extracranial teratomas are extremely rare (Table 1). The pathophysiological mechanism underpinning these associations is currently not understood.

Table 1. Previously reported head and neck teratomas with associated intracranial abnormality.

Author (reference)	Year of publication	Location of teratoma	Intracranial abnormality	Outcome
Shipp et al. (17)	1995	Palatal	Dandy-Walker malformation	Fetal demise
Goldstein et al. (18)	2005	Cervical	Agenesis of corpus callosum and subarachnoid cyst	Termination of pregnancy
Zielinski et al. (10)	2015	Cervical	Cerebellar and rhombencephalon anomalies	Fetal demise
Present study	-	Cervical	Agenesis of corpus callosum and neuronal migration disorder	Postnatal demise on day 20

To the Authors' best knowledge, this is the first report of a congenital cervical teratoma with ACC and extensive neuronal migration disorder.

Prenatal and perinatal intervention

In all cases, early prenatal involvement of a multidisciplinary team, including maternal-fetal medicine, geneticists, neonatologists, and pediatric ENT surgeons, is strongly recommended.

De Backer et al. (19) and Hirose et al. (20) have proposed treatment algorithms for prenatally diagnosed cervical teratomas. It is generally recommended that prenatally identified airway obstruction should be managed by Ex-utero Intrapartum Treatment (EXIT) at or close to term with the facility to perform Operation On Placental Support (OOPS). If polyhydramnios poses a risk of preterm labor amniodrainage should be performed.

In the presence of significant fetal compromise, Hirose et al. (20) recommend fetal intervention below 28 weeks gestation and delivery thereafter. In-utero surgical resection of the cervical teratoma has successfully been performed at around 24 weeks gestation (13, 20). However, fetal surgery poses a significant risk of intraoperative mortality, and such intervention should be reserved as a 'life-saving' measure when the risk of fetal demise from cardiovascular compromise and/or hydrops fetalis outweighs the risk of fetal intervention.

We propose that in-utero aspiration of cervical teratomas can be a beneficial adjunct to the conventional amniodrainage/EXIT procedure approach when the teratoma contains a large cystic component. In-utero aspiration has a number of advantages. First, management of fetal airway obstruction by tumor reduction is likely to promote normal lung development and avoid potentially life-threatening pulmonary hypoplasia. Second, oral intubation during the EXIT procedure is more likely to be successful if the tumor is reduced in size prior to delivery, avoiding the need for a more invasive surgical airway.

In the current case, repeated in-utero aspiration clearly demonstrated the reversibility of the airway obstruction and obviated the need for an EXIT procedure.

While the EXIT procedure has been shown to benefit infants with prenatal airway compromise, it is not without risks to the mothers (21-23). The EXIT procedure requires mothers to receive general anesthesia and agents to promote uterine relaxation in order to maintain placental support for the fetus. Consequently, significant intrapartum blood loss may require management in the forms of volume replacement, blood transfusion and use of inotropic support. Additionally, Noah et al. found an increased risk of postoperative wound infection following the EXIT procedure compared with conventional caesarean section (24). Determining the optimal timing of the EXIT procedure is challenging as the risk of preterm labor in a center without necessary expertise should be weighed against the socio-economic and financial costs of relocating family to a quaternary center (25).

More recently, novel therapeutic techniques such as fetal endoscopic tracheal intubation (26) and fetal airway reconstruction (14) have been proposed as potential future treatment options in management of fetal neck mass but are not yet part of routine clinical practice.

Prognosis and follow-up

Overall, congenital teratomas have the highest risks of fetal and neonatal deaths among prenatally diagnosed fetal tumors (27). For congenital cervical teratomas, the degree of airway obstruction is the single most significant prognostic factor (19). If an adequate airway cannot be secured shortly after birth, neonatal hypoxia, anoxic brain injury and death ensue rapidly. Additionally, cervical teratomas, compared with similarly sized neck tumors of other origin, are more likely to cause pulmonary hypoplasia in the fetus due to their relatively solid, incompressible nature (14). Currently, the reported mortality rate for congenital cervical teratomas with airway obstruction is 30-50% (19, 28, 29). However, it is plausible that with increasing accessibility to more advanced perinatal airway management, this figure may improve.

For isolated congenital cervical teratomas, prognosis beyond the immediate perinatal period is determined by whether or not the tumor can be completely re-

sected. Although malignancy is uncommon in congenital teratomas (16) the risk of malignant transformation increases with age (28). Complete resection shortly after birth is therefore strongly recommended.
When congenital cervical teratomas are associated with intracranial extension, mortality and morbidity rates are significantly higher. In a review of 31 cases of head and neck teratomas with intracranial extension, only 4 children survived without complications following a complete resection of tumor (5).
Long-term complications are contingent on the degree of disruption to normal tissue that results from surgical resection of the tumor; complications include recurrence of disease and possible malignant transformation, cranial nerve dysfunctions, facial disfigurement and thyroid dysfunction. Poor prognostic factors include intracranial extension of the teratoma, presence of other anomalies and underlying genetic abnormalities (5, 30). Clinical, radiological (MRI or CT) and biochemical (AFP) follow-up are recommended to monitor for recurrence of tumor (6) and management of any post-operative complications. Multidisciplinary approach is therefore crucial in optimizing functional and neurocognitive outcomes of infants with congenital cervical teratomas.

Conclusion

There is a paucity of literature available to assist parental decision-making when an antenatal diagnosis of cervical teratoma with cortical abnormality is made. To date, no post-natal outcomes have been described, limiting the ability of parents and their medical teams to make informed decisions about termination of pregnancy versus postnatal intervention and/or palliative care. In selected cases such as this, careful maternal, fetal and postnatal management may enable short-duration but high-quality survival in the neonatal period.
Although the mainstay perinatal management of cervical teratomas complicated by airway obstruction is the EXIT procedure with or without OOPT, we report successful in-utero decompression of cervical teratoma with resolution of the airway obstruction obviating the need for the EXIT procedure. As this approach also enables lung maturation, preventing the development of pulmonary hypoplasia, it should be considered when the tumor is largely cystic.
In all cases early diagnosis and involvement of a wider multidisciplinary team is crucial to enable individualized care and achieving optimal short and long-term outcomes for these infants and their family. Decisions about the risks and benefits to the family of pregnancy continuance are challenging and highly emotive. Adequately informing these discussions with medical literature that explores the full range of potential outcomes is an essential part of antenatal counseling for these high-risk babies and their families.

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Disclosure of interest

The Authors report no conflict of interest.

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