Course:  Nuchal Cystic Lesions

Faculty:  Tu T.T. Le, MD, Philippe Jeanty, MD, PhD
Nuchal cystic lesions:

Although slightly arbitrary, it is convenient to divide the cystic lesions of the neck in 3 categories:

1. Mostly cystic masses:
   - Lymphangioma
   - Cystic hygroma
   - Meningocele
   - Epidermal scalp cyst

2. Mixed cystic and solid:
   - Hemangiolymphangioma

3. Mosty solid lesions with included cystic components:
   - Hemangioma
   - Teratoma
   - Neuroblastoma

1. Mostly cystic cyst:
   1.1. Lymphangioma:

Adapted and updated from Adrian Clavelli, MD.

1.1.1. Definition:

Lymphangiomas are a group of various abnormalities whose etiology is developmental defects of the lymphatic vessels.

Lymphangiomas are made up of lymphatic vessels and are, fundamentally, endothelial cells limiting spaces and supporting connective tissue. There are three groups:

- simple lymphangioma, formed by lymphatic capillaries;
- cavernous lymphangioma, formed by bigger lymphatic vessels with a fibrous adventitia;
- cystic lymphangioma, commonly called cystic hygroma
Histopathologic specimen of lymphangioma, multiple thin walled cystic spaces (lymphatic channels) are lined with thin endothelia (see arrow) and filled with proteinaceous fluid (see *). Surrounding stroma contains lymphocytes.

Most of these lesions are present at birth, and 90% are recognized before 3 years of age. The incidence of cystic hygroma is approximately 1.6:10,000 pregnancies or 0.8% of pregnancies at risk for a structural anomaly. Small phlebotoliths inside the lesion may appear as the bright echoes. They have been found in many areas including the nose, mouth, breast, chest, abdomen, retroperitoneum, skin, genitalia and a few prenatal diagnoses have been made. These slow growing lesions usually infiltrate adjacent tissues and may thus be difficult to extirpate. The local recurrence rate is 6% for incomplete excision in cases of complicated surgery. Yet surgical treatment is the best.

1.1.2. Ultrasound findings

The ultrasound appearance is that of an irregular mass varying from hypo- to hyperechoic. They can have thin- or thick-walled septa, be unicameral, or multilocular and cystic. They can also contain scattered low-level echoes, a solid component, or fluid/fluid levels. The borders of lymphangiomas are indistinct. Some may have intrathoracic extension.

On color Doppler, there is little or no flow detected within the mass.

Any large neck masses may compress the esophagus (causing polyhydramnios prenatally) and the airways (causing respiratory distress at birth). Lymphangiomas can also be part of Klippel-Trenaunay syndrome.

1.1.3. Prognosis:

When the whole lesion can be extracted, the prognosis is good. Complete resection is, however, not always possible, as the masses tend to be infiltrative. The lesion does not need to be totally removed if dissection is impossible, since it is not malignant. Large cysts can be sclerosed.

Of course, if the chromosomes are abnormal, the prognosis is poor.

1.1.4. Case report:

This is a case of cervical lymphangioma diagnosed at 25 weeks. The lymphangioma grew progressively during the gestation. The patient opted to continue the pregnancy. The baby was delivered at 38 weeks (cesarean section). The baby was hospitalized immediately in neonatology unit and intubated. He died after few hours from respiratory insufficiency.

1.1.4.1. Case 1:

Cervical view at 33 weeks showing cystic lymphangioma

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3D view at 33 week

Postnatal view
1.1.4.2. Case 2: The following images show a case of cervical lymphangioma of a fetus

A 37-year-old woman (G6P4), with negative family history of congenital diseases, attended the antenatal unit at 11+6 weeks of her pregnancy. No fetal abnormalities were found at that time. The patient did not take any medication. She presented again at 34 weeks of the pregnancy and the ultrasound examination revealed a large cystic mass protruding to the right of the fetal neck and extending over the right fetal shoulder, suggestive of the lymphangioma. The finding was accompanied by polyhydramnios. The newborn was delivered by cesarean section (3800 g, boy, Apgar scores 8, 10) and the diagnosis was confirmed. No other anomalies were found.

Images 1, 2, 3, 4, and 5: 34 week of pregnancy; the images show several scans of the fetal cervical region with a cystic mass concordant with cervical lymphangioma.
Images 6, 7: 3D images showing the fetal head and neck with a mass of lymphangioma.

Images 8, 9, 10: Postnatal appearance of the baby with the cervical lymphangioma.

Image 11: Diaphanoscopic image of the cervical lymphangioma.
1.2. **Cystic hygroma:**

Adapted and updated from Vincenzo Suma, MD, Eleni Tzachrista, MD

1.2.1. **Synonyms:** Lymphatic hamartomas, (cystic) lymphangioma, hygroma colli cysticum and jugular lymphatic obstructive sequence.

1.2.2. **Etiology:** Variable, probably multigenic.

1.2.3. **Recurrence risk:** Not increased.

1.2.4. **Pathogenesis:**

Cystic hygroma is thought to arise from an early sequestration of embryonic lymphatic channels, as suggested by Dowd in 1913 and expanded on by Goetch in 1938. This sequestration apparently occurs more commonly in the developing jugular lymph sack pair than in the other four embryonic sites of the lymphatic system. From this location, the sequestered site follows the path of the surrounding mesenchyme destined for either the neck or the developing mediastinum. This accounts for the propensity of these lesions to occur in the lower neck, axilla, and upper mediastinum. Alternatively, a cystic hygroma may arise from a failure of the juguloaxillary lymphatic sac to drain into the internal jugular vein, producing a congenital obstruction of lymphatic drainage. Some authors have proposed that involution of a cystic hygroma in utero produces the “web neck” of Turner syndrome.

Cystic hygroma are often isolated malformations with the remainder of the lymphatic system remaining normal. No communication exists between the lymphatic system and a cystic hygroma.

Cystic hygromas result from the blockage of the lymphatic vessels. They are located in the regions which contain lymphatic tissue. Most common location for cystic hygroma is a neck region, head and axilla.

1.2.5. **Location:**

In most cases, cystic hygromas are localized in the neck. The biggest masses can be so large as to reach the floor of the mouth and the tongue. They can also reach the cheek, parotid, axilla and mediastinum. In their descent toward the mediastinum, they follow the phrenic nerve between the subclavian vessels. Cystic hygromas confined to the mediastinum are rare; they usually represent mediastinal invasion by cervical hygroma and are found in about 2-3% of cases.

Distribution of cystic hygromas:

<table>
<thead>
<tr>
<th>Neck: 75%</th>
<th>Axilla: 20%</th>
<th>Retroperitoneum, abdominal viscera: 2%</th>
<th>Limbs, bones, chest wall, groin, scrotum, mesentry, parotid: 2%</th>
<th>Cervico-mediastinal: 1%</th>
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The most common region is the neck (75%) followed by the axillary region (20%). Other distributions are much less common.

1.2.6. Incidence:

It is not well defined. The incidence of cystic hygroma is approximately 1.6:10,000 pregnancies or 0.8% of pregnancies at risk for a structural anomaly.17,18,19

1.2.7. Associated anomalies

Cystic hygroma may be isolated; in many cases it is associated with hydrops fetalis. Chromosomal defects, particularly monosomy X (Turner’s syndrome) and a wide variety of anatomic abnormalities (Table below) are found in more than 80% of the fetuses.20,21,22

<table>
<thead>
<tr>
<th>Chromosomal anomalies</th>
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<tr>
<td>• Turner’s syndrome (45, X0 or mosaic 46, XX/45, X); 45-50% of cases</td>
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<tr>
<td>• Trisomy 21</td>
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<td>• Trisomy 18 15 % of cases</td>
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<td>• Trisomy 13</td>
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<td>• Trisomy 22 mosaicism</td>
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<tr>
<td>• Partial trisomy 11q/22q</td>
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<td>• 13q-syndrome</td>
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<td>• 18p-syndrome</td>
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<td>• balanced translocation t (6q; 12q)</td>
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<th>Single gene anomalies</th>
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<td>• Familiar pterygium colli</td>
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<td>• Multiple pterygium syndrome</td>
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<td>• Cowchowk syndrome</td>
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<td>• Roberts syndrome</td>
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<th>Syndromes from unknown origin</th>
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<tr>
<td>• Noonan’s syndrome</td>
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<td>• Polysplenia</td>
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<td>• Gonadal dysgenesis</td>
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In our this patient, who has a normal female karyotype and no morphological anomalies, ultrasound probing of the axillary cystic hygroma showed the top of a larger lymphangiomatosis that extended to the neck, chest and mediastinum.

1.2.8. Ultrasound findings
Cystic hygroma formed by multiple cysts ranging from a few millimeters to several centimeters in size. These cysts are filled with a lymph-like clear or sometimes echogenic fluid. The diagnostic clues of cystic hygroma include: asymmetric, thin-walled multiseptate, cystic masses of the posterolateral aspects of the neck with absence of meningocele, cephalocele, and calvarial defects.

1.2.9. Differential diagnosis
Thyroglossal duct cyst, branchial cleft cyst, (dermoid and epidermoid cyst), bronchogenic (visceral) cyst, hamartoma of the mandible and cervical thymic cyst are all differential diagnoses for cystic hygroma of the anterior neck. Encephalocele and meningocele should be added for lesions of the posterior neck.

1.2.10. Prognosis
The prognosis depends on the presence or absence of associated hydrops, chromosomal aberrations and anatomic defects. Spontaneous resolution of a cystic hygroma of the neck in a fetus affected by Turner's syndrome and a fetus with normal karyotype have been described.

The presence of hydrops fetalis or lymphangectasia indicates a poor prognosis, with a mortality rate of 100 percent within a few weeks from diagnosis.

Two reports suggest that isolated cystic hygroma in a typical location in the neck or axilla may have a better prognosis.

In the literature, 32 cases of cystic hygroma in children are reported. In 12 cases the hygroma was localized in the neck, while in the remaining cases it was in rare sites. Of these, six had hygromas in the axilla and chest wall, five in the mesentery and nine had lymphangiomas localized in various uncommon sites such as cervico-mediastinum, retroperitoneum, scrotum and multiple sites.

The complete excision of the cystic mass was possible in 23 cases. In another seven cases, only partial removal was possible because of the size of the cystic mass. Two of the twenty-three patients who underwent complete excision died during the postoperative period. It appears that the prognosis for these babies depends largely on the anatomical location and size of the tumors and on the ability of the pediatric surgeon to remove the masses.

1.2.11. Management: Standard obstetrical care.

1.2.12. Case report:

1.2.12.1. Case 1:

Images at 13 weeks and 2 days: The sonographic findings were: septated cystic hygroma

- pleural effusion
- hydrothorax
- suspicion of a cardiac defect
- ascites
- edema
1.2.12.2. Case 2:
This second trimester fetus demonstrates a very thick nuchal edema with **cystic hygroma**:

The cystic hygroma extends down the back of the fetus and pleural effusions are visible:
Postnatal Images:

This baby had several other associated anomalies, and diagnosis was **Muliple Pterygium syndrome**.

1.2.12.3. Case 3:

This is a 17-year-old woman scanned at 15 weeks of pregnancy. The ultrasound revealed massive septate cystic hygroma and subcutaneous edema of the fetus.
Images 1-6: 2D scans of the fetal neck with massive septate cystic hygroma.

1.2.12.4. Case 4:

These are some images of a 15-week-old fetus with cystic hygroma.

Image 1 and 2: 15 weeks of pregnancy. Coronal (Image 1) and transverse (image 2) scans showing cystic hygroma.
Image 3 and 4: 15 weeks of pregnancy. Transverse planes showing axillary lymphedema.

Image 5 and 6: 15 weeks of pregnancy. 3D images showing cystic hygroma.

1.2.12.5. Case 5:
This is a 26-year-old woman scanned at 15 weeks of pregnancy. The ultrasound findings were: septated cystic hygroma, pleural effusion, and ascites. These are some of the images obtained.

Images 1, 2. 2D scans showing transverse (left) and sagittal (right) planes through the fetal neck with septate cystic hygroma.
1.3. Epidermal scalp cysts:

Adapted and updated from Cheryl D. Turner, RDMS.

1.3.1. Definition:

An epidermal scalp cyst is an extracranial cystic mass with no intracranial extension and no calvarial defect. The mass is filled with laminated keratin and is lined with differentiated cornified squamous epithelium. Epidermal scalp cysts are benign in nature.

1.3.2. Prevalence:

There are few cases of epidermal scalp cysts reported prenatally. Dermoid and epidermoid cysts account for 23 percent of all scalp lesions and there is a 2:1 female

preponderance. The ethnic distribution is equal\textsuperscript{34,35}. The newest case report by Dr Sepulveda case in 2011\textsuperscript{33}.

1.3.3. **Etiology:** Unknown.

1.3.4. **Pathogenesis:**
Epidermal cysts are congenital tumors formed from pockets of ectoderm sequestered between the third and fifth week of embryonic life as the neural groove closes. This mechanism explains why most lesions are midline. They are typically found in the occipital region and over the anterior fontanelle \textsuperscript{34,36}. Recently, giant epidermal cysts (9x10 cm) has been reported in adults.\textsuperscript{37}

1.3.5. **Sonographic findings:**
An epidermal scalp cysts presents as an extracranial cystic or heterogenous mass with no associated defect in the calvarium. Recognition of the absence of a defect in the calvarium is perhaps the most reliable aid in making the diagnosis. The mass is mobile and not attached to the underlying structures. The mass tends to remain cystic during the pregnancy, however, there is one reported case where the original cystic lesion regressed to a dense tissue mass\textsuperscript{38}. Prenatal three-dimensional ultrasound can be a useful adjunct in the prenatal differentiation between small meningoceles and epidermal cysts.\textsuperscript{33}
A careful search for a defect in the calvarium, normal intracranial contents, and associated anomalies is warranted.

1.3.6. **Differential diagnosis:**
The differential diagnosis would include a cephalocele, meningocele, cystic hygroma, subcutaneous edema, cervical teratoma, lipoma, mesenchymal sarcoma, or hemangioma.

1.3.7. **Associated anomalies:**
There are no reported associated malformations prenatally.\textsuperscript{39} Multi epidermal cyst has been described in Lowe syndrome and Gardner syndrome in children.\textsuperscript{40,41}


\textsuperscript{32} Ferrim EL, McCormack J. An epidermal scalp cyst simulating an encephalocele. 1995 15,981-984.

\textsuperscript{33} Sepulveda W, Wong AE, Sepulveda S, Corral E. Fetal scalp cyst or small meningocele: differential diagnosis with three-dimensional ultrasound. Fetal Diagn Ther. 2011;30(1):77-80

\textsuperscript{34} Naidich TP, Altman NR, Bratfman BH, McLone DG, Simmerman RA. Cephaloceles and related malformations, AFNR 1992:13,655-690.


\textsuperscript{37} Sang-Gue Kang, M.D., Chul-Han Kim, M.D., Hong-Ki Cho, M.D.,1 Mi-Youn Park, M.D.,2 Yoon-Jin Lee, M.D., and Moon-Kyun Cho, M.D. Two Cases of Giant Epidermal Cyst Occurring in the Neck.Ann Dermatol. 2011; 23


\textsuperscript{39} Nyberg DA, Mack LA. The spine and neural tube defects, In Nyberg DA, Mahoney SB, Pretorius DH, eds. Diagnostic Ultrasound of Fetal Abnormalities; Text and Atlax. Chicago: Year Book Medical, 1990:152-60.

\textsuperscript{40} Jong Hoon Won, M.D.,1 Min Jung Lee, M.D.,1 Joon Soo Park, M.D. Multiple Epidermal Cysts in Lowe Syndrome. Ann Dermatol. 2010 November; 22(4): 444–446
1.3.8. Prognosis:
There are four cases of epidermal scalp cyst reported\textsuperscript{30,31}. In two of the three cases, the cyst remained a small anechoic mass throughout the gestation as it did in our experience. One case reports the original cystic lesion had regressed to a dense tissue mass by 26 weeks gestation \textsuperscript{30}. In all cases, no reported associated anomalies were identified. The prognosis is excellent. No intervention is required.

1.3.9. Recurrence risk:
All cases are sporadic; therefore the recurrence risk is low.

1.3.10. Management:
Recognition of extracranial masses is important because of their benign nature. It is crucial to identify if a defect is present in the calvarium. When the bony defect is small the diagnosis is very difficult. A transvaginal scan with a high-frequency transducer or MRI may further delineate the mass and confirm that there is no intracranial extension. There have been at least two reported cases where the pregnancy was terminated for benign lesions. One was an occipital hemangioma and the other was an epidermal scalp cyst \textsuperscript{32,42}. The presence of an extracranial mass must lead to a careful consideration of the differential diagnosis. When prenatal diagnosis of an epidermal scan cyst is made with confidence, no further intervention is warranted.

1.3.11. Case report:
A 21-year-old primigravida was referred at 21 week of her pregnancy to rule out a fetal encephalocele. Fetal biometry was normal and a cystic structure was visible at the back of the fetal neck (Image 1). Cervical spine and calvarium were intact which ruled out the encephalocele. The lesion superficial involving only the skin and that is why our final diagnosis was epidermal scalp cyst. The findings were confirmed postnatally. The baby underwent surgery successfully.

Images 1, 2: The image 1 shows sagittal scan of the fetal nuchal region with a cystic structure at the back of the neck representing epidermal cyst.

Image 3 shows transverse color Doppler scan just above the cystic structure described in the image one. A loop of the umbilical cord running around the neck can be seen.


Images 4, 5: 3D images showing a round structure of the neck which turned out to be the epidermal cyst.

1.4. Cervical meningocele:

1.4.1. Definition:

Cervical meningocele is defined as a protrusion of the spinal meninges through the defect of cervical vertebral column.

Cephaloceles are neural tube defects which manifest herniation of the meninges with or without the cerebral tissue. Depending on the structure’s herniation, there are different terms (Image below), meningocele is a form of closed neural tube defect in which no cerebral tissue or spinal cord and spinal nerves are herniated, only the meninge protrudes out of the calvarium or the spinal column.

Cephaloceles include:

- Meningocele
- Meningomyelocele
1.4.2. **Incidence:** According to CDC, it is estimated that 4,000 pregnancies in the United States each year are affected by neural tube defects. Of that number, approximately 2,500 infants are born.

The meningocele can be revealed on skull and spine defect as well. The spinal meningocele is mostly located posterior to the spinal cord (80% of spinal meningocele case), including thoracic spine (70%), thoracolumbar junction (12%), lumbosacral (13%) and cervical (3%) spine. Men is equally affected to women is. Rarely, they could be seen as anterior and lateral meningocele.

1.4.3. **Pathology:**

The cervical meningocele is a malformation that occurs during the neural tube’s development. There are 3 stages of the spinal cord development: gastrulation (week 2-3), primary neurulation (week 3-4) and secondary neurulation (week 5-6). At week 3-4, nine out of tenth of the spinal cord is formed. The final stage is the time for conus medullaris and filum terminal formation. Some rare cases of anterior sacral meningoceles have been reported in which the failure of fusion of the sacrum results in the sacral meninge herniation into the sacral hollow. Because of their occult location, they typically present later on in life with protean neurologic, urological or gastrointestinal complaints.

1.4.4. **Associated findings:**

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90% of patients have associated occult spinal lesions such as tight filum terminale, split cord malformation, and epidermoids.\(^{50}\)

1.4.5. **Sonographic findings:**
A fluid-filled sac protrudes from the occipital region or posterior neck, no solid mass in side.

1.4.6. **Prognosis:** fairly good if there is no associated anomalies, and if the skin covers fully the herniation sac, if not, there would be a leakage of cerebrospinal fluid.

1.4.7. **Management:** Surgery needs to be performed shortly after birth prevent infection and restructure the exposed area of the herniation.

1.4.8. **Differential diagnosis:**
Cervical meningocele can be differentiated from:
- Epidermal scalp cyst.\(^{53}\)
- Cystic hygroma.\(^{51,52}\)

1.4.9. **Case report:**

1.4.9.1. **Case 1:**
A 28-year-old-woman, G2P1, with unknown obstetric risk factors and no relevant medical history underwent a first ultrasound scans at 13 weeks which revealed no anomalies. The nuchal translucency was 1 mm (CRL: 60 mm). The triple test was done (1/10000).
At 24 weeks, a second ultrasound examination revealed a cervical cutaneous posterior anomaly which suggested a possible cervical filiform meningocele (Image 1,2). Our differential diagnosis was epidermal cyst. The skin’s spine was normal, but there was a midline cervical fluid-filled mass (Image 9).

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Image 1-8: 2D ultrasound from 24 to 30 weeks of gestation suggested a cervical filiform meningocele.


Image 9, 10: Postnatal images:
1.4.9.2. Case 2: a cervical filiform meningocele.

Image 1, 2: The cystic, well-demarcated cyst on posterior neck, no solid tissue inside and normal cervical spine.

Image 3, 4: 3D pictures clearly demonstrate that the mass was attached to the fetus.
A coronal 3D reconstruction of the cervical spine is also provided.

No associated anomalies and normal cerebral anatomy.

Image 5, 6, 7: Postmortem view of the baby

2. Mixed cystic and solid lesions

2.1. Hemangiolympangiomas:

Adapted and updated from Adrian Clavelli, MD.; Raúl Martínez MD.

2.1.1. Definition:

Hemangiolympangioma is a malformation of both the lymphatic and the blood vessels. Although histologically it is a benign disorder, local invasion into the muscle, bone, and underlying tissue can lead to severe deformity. It has a propensity for rapid growth and invasion into the adjacent tissues, and to recur locally. It can occur in a variety of anatomical locations, such as the axilla, abdominal cavity, extremities and urinary bladder. Prenatal diagnosis of this condition is rare.

Prenatal recognition of a hemangiolympangioma is extremely rare. The correct diagnosis is frequently made after birth, although the advent of ultrasound has made possible both the prenatal diagnosis of fetal hemangiolympangioma and observation of its progression in utero.

2.1.2. **Etiology:**

Hemangiolympangiomas are believed to be caused by anomalous embryological development of the lymphatic and vascular system.

2.1.3. **Pathogenesis:**

Abnormal development of vascular and lymphatic system leads to a rapid growth tumor. In large tumors with a high proportion of solid tissue, a high percentage of cardiac output is diverted for the perfusion of the hemangiolympangioma, resulting in high cardiac output failure characterized by cardiomegaly, and AV valve insufficiency.

2.1.4. **Sonographic findings:**

On ultrasound, they present as inhomogeneous, hypoechoic or hyperechoic, with cystic cavities and mild internal vascularity.

In the example below, the cystic and solid components can be recognized, but the appearance is not different from that of the lymphangiomas seen earlier. Only the presence on Doppler of increased vascularity yields the diagnosis.

2.1.5. **Associated associated:**

There are no reports of associations with other anomalies

2.1.6. **Differential diagnosis:**

Differential diagnosis is mostly made of lymphangiomas and cystic hygromas.

The other differential diagnosis includes: cephaloceles, meningomyelocoeles, teratomas, lipomas, hemangiomas, hemartomas, and dermoid cysts. Teratomas tend to be much more irregular in their echotexture.

2.1.7. **Prognosis:**

Although malignancy is unlikely, the fetus and newborn may develop local invasion into the muscle, bone and underlying tissue, leading to severe deformity.

2.1.8. **Management:**

Serial ultrasound can be performed to assess the evolution and the appearance of further complications, and to plan delivery. At delivery the patency of the airway has to be established or restored either by intubation, tracheostomy or an EXIT procedure.

Treatment is with surgery or sclerotherapy.

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2.1.9. Case report:

This fetus was examined at 37 weeks gestation. We suspected a teratoma or tyroglossal cyst. However, the postnatal diagnosis was a hemangiolympangioma. Hemangiolympangioma is a malformation of both lymphatic and blood vessels. Note the cystic appearance, which contrasts with the more solid appearance of the case highlighted in the previous sentence. Look also for differential diagnosis under teratoma of the neck and epignathus.

And the baby before surgery.
3. Mostly solid lesions with included cystic components:

   3.1. Hemangioma:

Adapted and updated from Adrian Clavelli, MD; Frantisek Grochal, MD.

   3.1.1. Definition:

Hemangiomas are benign tumors made up of blood vessels. They are classified as:

- Cavernous
- Capillary (strawberry)
- Mixed

Strawberry hemangiomas are red protuberant masses that may occur on any area of the body but in particular on the face, scalp, back, and anterior chest. 1-3% of infants have some and girls are 3 times more likely then boys to have some. They may be solitary or multiple. Spontaneous regression is common (60% of these lesions involute with the first 5 year, and most of the rest by 10 years). It has been reported that those diagnosed prenatally might actually involute faster than those diagnosed postnatally. MRI has occasionally been performed to differentiate from a cephalocele, but the ultrasound appearance is usually characteristic. These are commonly found in the head, heart, limbs, and liver, abdomen, skin and cord. A rare complication is a thrombocytopenic coagulopathy, the Kasabach-Merritt syndrome.

Cavernous hemangiomas are masses of dilated vessels deep in the skin. They appear as pale, skin-colored, red, or blue masses that are not as sharply defined as the strawberry hemangiomas. They also may undergo spontaneous resolution. Prenatally they may be responsible for hydrops\textsuperscript{77}. Some rare cases of cavernous hemangioma was also found in the nasal cavity and the maxillary sinus.\textsuperscript{78,79,80,81}

3.1.2. Incidence:

Hemangiomas are the most common tumors of infancy. Infantile hemangiomas occur in 4% to 10% of white infants, and they are 3 to 5 times more commonly seen in female infants, most frequently in whites and less commonly in those of African or Asian descent\textsuperscript{82}. Congenital hemangiomas are much more rare.

3.1.3. Recurrence risk:

Most hemangiomas occur sporadically, but some families with autosomal dominant inheritance have been reported\textsuperscript{83}.

3.1.4. Pathogenesis:

Pathogenesis of congenital hemangiomas is not very well understood. Some authors believe that they could originate from either invading angioblasts that differentiate toward a placental phenotype or form embolized placental cells. Erythrocyte type glucose transporter

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isoform 1 (GLUT1), a glucose transporter enzyme, is uniquely expressed on endothelial cells of hemangiomas but not in surrounding normal vascular endothelium.\textsuperscript{84} Lymphatic endothelial hyaluronan receptor-1 (LYVE-1), a specific marker for normal and tumor-associated lymphatic vessels, was strongly expressed in tumor cells of infantile hemangiomas but was absent during involution. That is why some authors believe that endothelial cells in proliferating infantile hemangioma are arrested in an early developmental stage of vascular differentiation.\textsuperscript{85} Some overlapping clinical and pathologic features can be found among rapid involuting congenital hemangiomas, non-involuting congenital hemangiomas and infantile hemangiomas. These observations support the hypothesis that these vascular tumors may be variations of a single entity “ab initio”, but it is unknown whether the progenitor cell for these uncommon congenital vascular tumors is the same as for common infantile hemangioma.\textsuperscript{86}

3.1.5. Diagnosis:
The diagnosis clues of probably suggested are: of huge vascular beds, and color Doppler flow imaging could depict marked blood flow in the solid part of the mass.

3.1.6. Sonographic findings:
Usually hypoechoic lesions mostly confined to the subcutaneous fat with diffuse vasculature. Some of the vessels show a venous flow signal, while others demonstrated low resistant arterial flow.\textsuperscript{87} Large and irregular feeding arteries are in disorganized patterns, arterial aneurysms, direct arteriovenous shunts, and intravascular thrombi are present.\textsuperscript{88} Sonographically detectable hemangiomas are usually of the cavernous type, which involve not only cutaneous vessels but also larger venous sinusoids in the deep dermis and subcutaneous tissues. The most common appearance is that of a solid mass with an echotexture similar to placenta, but cystic hemangiomas have also been reported.\textsuperscript{89} Hemangiomas do not change bony anatomy in the region.

3.1.7. Differential diagnosis:
- Lymphangioma (include cystic hygroma)
- Hemangiolympangiomas
- Nuchal teratoma
- Neuroblastoma

\textsuperscript{85} Dadras SS, North PE, Bertocini J, Mihm MC, Detmar M. Infantile hemangiomas are arrested in an early developmental vascular differentiation state. Mod Pathol. 2004; 17:1068-1079.
3.1.8. **Prognosis:**
Good, rare complication. Rapidly involuting congenital hemangioma promptly resolve postnatally over the early months of life, with complete resolution, sometimes with residual atrophy, occurring at less than 1 year of age in most of the patients. 

3.1.9. **Management:**
Management is different to each location of hemangiomas, the size of the mass and the vascularization. Embolization and complete removal the mass could be necessary. Hemangiomas typically recur following incomplete surgical excision.

3.1.10. **Case report:**
Images 1, 2. Transverse sections through the skull showing tumor (hemangioma) in nuchal region with rich vascularization.

Images 3, 4. Color Doppler and 3D image showing prominent vascular mass (hemangioma) in nuchal region.
3.2. Cervical teratoma

Adapted and updated from Beverly A. Mikes, MD; Luc De Catte, MD

3.2.1. Definition:
Teratomas are complex neoplasms consisting of multiple various tissue types and occurring at sites foreign to their natural anatomic origin. Typically, teratomas contain derivatives from all three germinal layers.

A teratoma which arises from the neck, cervical teratoma, like all teratomas, are composed of all 3 germ cell layers.

3.2.2. Synonyms: Cervical teratoma, thyroid teratoma.

3.2.3. Incidence
0.25-0.5:10,000 live birth incidence for any fetal teratoma, with sacrococcygeal accounting for over 50%, cranial 40%, and cervical 5.5%.

3.2.4. Etiology
The midline location of most congenital teratomas has served to support the hypothesis that primordial germ cells migrate along the dorsal midline from the hindgut-yolk sac region into the embryonic genital ridge. Some cells continue their cephalad migration to eventually settle in the mediastinum, neck, nasopharynx, and brain (pineal and hypothalamic regions).

3.2.5. Pathology
The texture of all teratomas is very heterogeneous, from cystic to solid, with calcifications. This is simply a reflection of the variety of tissues involved. Teratomas contain ectodermal components (especially neural tissues, and, in particular, choroid plexus tissue responsible for the production of fluid collections); Mesodermal tissues such as fat, muscle, cartilage and bone (these being responsible for the calcifications seen) and endodermal components such as respiratory or gastrointestinal tissue.
3.2.6. Associated anomalies
Associated anomalies are rare; the following have been reported once each: imperforate anus, chondrodystrophia fetalis, hypoplastic left ventricle with pulmonary hypoplasia, cystic fibrosis, metastasis.

3.2.7. Complications:
Polyhydramnios, trachea, mandible, cervical vessels and hypoglossal nerve compression.

3.2.8. Sonographic findings:
Heteroechogetic mass, from cystic to solid with calcifications. Furthermore, they appear pedunculated as they bulge out of the neck; they are symmetric, unilateral and well delineated. Many will be associated with polyhydramnios resulting from esophageal obstruction.

3.2.9. Prognosis: Depends on the size of the tumor and the tracheal compression.
Malignant degeneration and recurrence are exceptional. Affected fetuses may have growth restriction. Hyperextension of the neck and dystocia are seen at delivery due to malpresentation.

After birth, the immediate danger is respiratory compromise from airway obstruction, but the neck musculature also is abnormally developed and newborns have poor tone. Furthermore, they may have severe reflux and feeding difficulties.

These tumors tend to be large, requiring extensive neck dissection. Even in infants treated surgically, the mortality rate ranges from 9%-17%. Although teratomas are usually nonmalignant, they result in a high mortality of 80%-100%, with 15% of fetuses stillborn.

3.2.10. Differential diagnosis includes:
- Hamartomas
- Hemangioma: homogeneously echogenic or mixed cystic and solid appearance + color flow and pulsed Doppler flow
- Cystic hygromas: asymmetric, thin walled, multiseptated cystic masses of the posterolateral aspect of the neck, sporadically echogenic solid components, midline septation, sometimes associated with hydrops.
- Goiter: bilobed anterior neck mass adjacent to the midline, solid-mixed-cystic-like appearance, fetal tachycardia, polyhydramnion.
- Teratoid cysts
- Epignathus
- Cervical neural tube defects
- Branchial cleft cysts.

3.2.11. Management:
Adequate ventilatory support and surgical excision as soon as possible.
3.2.12. Case report:

3.2.12.1. Case 1:

Ultrasound evaluation demonstrated a right sided solid cervical mass emanating from just below the fetal ear and continuing down the side of the fetal neck measuring 2.5 cm. Color flow Doppler demonstrated blood supply from the mass orientating directly off the right carotid. There were no other structural anomalies and no evidence of fetal hydrops. The tumor grew rapidly, about a centimeter a week initially, and evolved over the course of her pregnancy from a solid mass to a large, semi-cystic structure with vascularity only around the periphery.

A diagnosis of immature teratoma Grade III, with no elements of yolk sac present was determined on pathological examination. The infant did exceptionally well post-operatively, and was discharged home on postoperative day fifteen.

Images 1-4: 23 weeks, solid, encapsulated cervical mass (3-4 cm in diameter), with upper margin just below the ear and located along the side of the neck.
Images 5-6: 25 weeks, Doppler imaging of the tumor mass showing blood supply straight from the carotid artery.

Images 7,8: 34 weeks, note the size of the tumor and semi-cystic structure.

Images 9,10: 37 weeks, delivery via cesarean section, note the large mass on the right side of the fetal neck.
3.2.12.2. Case 2:
The newborn was delivered via cesarean section after premature rupture of amniotic membranes at 33 weeks and 4 days of gestation (boy, 2120 g). The neonate required immediate intubation and seven days later underwent surgical removal of the tumor. The diagnosis was **cervical teratoma**. Postoperative course was uneventful and the child is doing well.

**Images 1-5:** 26 weeks of pregnancy: sagittal and transverse scans of the fetal neck showing mixed (cystic and solid) tumoral mass occupying anterior part of the neck.
Images 6-15: 31 weeks of pregnancy:

3.2.12.3. Case 3:
A large complex mass with contained calcifications was noted adjacent to the neck region and appeared to be anchored to the left anterior aspect of the fetal neck. This complex mass measured 106 x 99 mm (Image 1-4)
On postmortem examination, the huge cervical mass, measuring 200 x 130 x 80 mm, was attached to and involved the left lateral soft tissue of the face and neck (Image 4). The external surface of the mass was glistening and dark red and included structures resembling limbs (Image 4). An attached sac-like structure was seen, also with a limb on the surface.

On microscopic examination of the cervicofacial tumor, an organoid growth pattern was observed. Both mature and immature teratomatous tissues were identified. The immature teratoma was represented predominately by immature neuroepithelium. The amount of neuroepithelium present was characteristic of a histologically grade 3 (Norris classification) immature teratoma. There was no evidence of metastatic disease.

Representative sections of the visceral organs showed development that was appropriate for the estimated gestational age. The visceral organs were uninvolved by the tumor, and no other anomalies were noted. Examination of the placenta revealed a late second trimester placenta with focal hydropic degeneration of the chorionic villi.

### 3.3. Neuroblastoma:

Adapted and updated from Judy A. Estroff, MD.

#### 3.3.1. Definition:

Neuroblastoma is a malignant neoplasm of poorly differentiated nerve cells of embryonic type.
3.3.2. **Synonyms:**
Ganglioneuroblastoma, neuroblastoma in situ.

3.3.3. **Prevalence:**
The prevalence is 0.3-1:10,000.

Neuroblastoma is the most common malignant tumor in infancy and early childhood, originating anywhere along the sympathetic nervous system, and in the adrenal gland. More than half of neuroblastomas are in the abdomen, and two-thirds of these originate in an adrenal gland. Fifteen percent of neuroblastomas are thoracic, arising posteriorly along the sympathetic chain. Other sites include the cervical region, sympathetic chain in the abdomen, nasopharynx and brain.

3.3.4. **Pathology:**
Neuroblastoma is a neuroendocrine tumor which originates from embryonal sympathetic ganglion cells. The most common primary origin site are adrenal glands but it can develop in other locations with sympathetic nerve cells such as neck, chest, abdomen, pelvis.

Defect in neuroblast maturation with embryonal sympathetic ganglion cells undergo malignant transformation. Associated with n-myc oncogene and tumor cell ploidy: if n-myc gene is positive and cells are diploid, then the prognosis is worse.

Metastatic sites: Frequent: Bone, lymph nodes, bone marrow, liver, skin; occasional: extradural extension into spinal canal, rare: lung.

3.3.5. **Sonographic findings:**
The prenatal diagnosis of neuroblastoma has occasionally been reported. The reported cases of prenatally diagnosed neuroblastomas do not display a specific sonographic pattern. Both prenatal and postnatally diagnosed neuroblastomas have been described as cystic, mixed cystic and solid, and solid with areas of calcification.

3.3.6. **Associated anomalies:**
Hydrops, neurofibromatosis, Hirschprung’s disease, some chromosomal abnormalities. May be part of the fetal hydantoin and fetal alcohol syndromes.

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3.3.7. **Differential diagnosis:**

Adrenal site: renal duplex anomaly or tumor, adrenal cyst or hemorrhage are less likely. Extra-adrenal site: solid mass of lung, pelvis, head or neck.

3.3.8. **Prognosis:**

Better with younger age and lower stage at diagnosis. Better with primary thoracic site of tumor. Some may mature into ganglieneuroma.

More than half of patients are less than two years of age at diagnosis. Seventy-five percent of tumors are discovered prior to four years of age. The prognosis ranges from over 90% survival if discovered in patients under one year of age, to less than 10% survival when discovered in older children\(^90\text{--}93\). Accurate early diagnosis is crucial, as the best prognosis is in the youngest patients.

3.3.9. **Recurrence risk:** unknown.

3.3.10. **Management:**

Evans staging system: Stage I: Tumor confined to the organ or structure of origin. Stage II: Tumor extending in continuity beyond the organ or structure of origin but not crossing the midline. Regional lymph nodes on homolateral side may be involved. Stage III: Tumor extending in continuity beyond the midline with or without positive regional nodes. Stage IV: Distant metastases. Stage IV-S: Stage I-II primaries with metastases to liver, skin and/or bone marrow (not bone). Almost all stage IV-S are infants.

Stage I: Surgical resection; no other treatment. Stage II: Surgical resection in infants. Older children: chemotherapy with or without added radiation. Stage III & IV. Surgical debulking, then chemotherapy and radiation. Bone marrow transplant in high risk patients (older patients and those with n-myc amplification).

3.3.11. **Case report:**

Images 1, 2: 21 weeks; Image 1 shows a transverse scan of the fetal head, see echogenic mass located in the frontal lobe; Image 2 shows a multilocular cystic mass arising from the fetal mouth.
Image 3: Image of the female fetus after pregnancy termination at 21 weeks, note the tumor mass coming out of the fetal mouth. Diagnosis was **neuroblastoma**.
<table>
<thead>
<tr>
<th>Name of anomaly</th>
<th>vascularization</th>
<th>Single/multi cystic</th>
<th>Solid</th>
<th>Calcification</th>
<th>Special features</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Hemangioma</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+/-</td>
<td>Solid mass with echotexture similar to placenta, huge vascular beds</td>
<td>Head, limbs, skin, abdomen</td>
</tr>
<tr>
<td>2 Cystic hygroma</td>
<td>-</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>Often septated and multilocular</td>
<td>Posterior neck commonly, others: anterior neck, cheek, axilla, mediastinum, chest wall, mesentery…</td>
</tr>
<tr>
<td>3 Hemangiolemanghiomas</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>A rapid growth tumor confirmed after birth</td>
<td>Axilla, abdomen cavity, limb, bladder</td>
</tr>
<tr>
<td>4 Meningocele</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>Related to neural tube defect</td>
<td>Spine and skull</td>
</tr>
<tr>
<td>5 Neuroblastoma</td>
<td>+/-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Position related to sympathetic nerve</td>
<td>70% adrenal site, Others: abdomen, anterior neck, chest, pelvis,…</td>
</tr>
<tr>
<td>6 Cervical teratoma</td>
<td>+/-</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>Typically, Shadowing with calcification</td>
<td>Anterolateral face, neck or jaw</td>
</tr>
<tr>
<td>7 Epidermal scalp cyst</td>
<td>-</td>
<td>Unilocular</td>
<td>-</td>
<td>-</td>
<td>Extracranial cyst mass with no intracranial extension and no calvarial defect</td>
<td>Face surface and scalp</td>
</tr>
</tbody>
</table>