CHAPTER 110
LYMPHANGIOMAS

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Introduction

Lymphangiomas are developmental defects of the lymphatic channels that belong to a large spectrum of vascular malformations. They are most commonly located in the head and neck region, and to a lesser extent on the axilla and trunk, but can occur anywhere there are lymphatic vessels. Even though they are congenital defects, they may not become apparent until several years after birth. Although benign, lymphangiomas frequently present surgical difficulties and challenges due to their propensity to infiltrate and extend around neighbouring structures.

Lymphatic malformations encompass entities other than lymphangiomas. The goal of this chapter is to address the lesions known as lymphangiomas or hygromas. This chapter does not discuss pulmonary and intestinal lymphangiectasia and peripheral lymphoedema, which may be congenital or acquired, or lymphangiomatosis, an ill-defined disease usually implying the coexistence of lymphangiectasia and multiple lymphangiomas in several sites.

Demographics

The incidence of lymphangiomas is difficult to ascertain. Some authors have quoted an incidence of 1.5 to 2.8 per 1,000,[1] but this applies to foetal nuchal translucency, which is a different pathology (see subsection on "Prenatal Presentation"). Others have reported an occurrence of 1 in 12,000 births for cystic lymphangiomas.[2] There are no reported racial or ethnic predispositions; the male-to-female ratio is equal in most large reviews,[3–6] but some authors have described a male predominance.[7,8] In most of Africa, incidence data are not available, but hospital-based reports suggest that at least 1–3 children with lymphangiomas are seen every year in most teaching centres.[4,5,7,9–11]

These lesions are apparent in 50–70% children at birth or prenatally, and 80–90% present within 5 years. However, presentation may occur as late as adolescence or adulthood.[2,3,12,13]

Embryology

The lymphatic system starts to develop by the end of the 5th week of gestation, 2 weeks after the primordia of the cardiovascular system are recognisable and 1 week after coordinated contractions of the primitive heart initiate unidirectional blood flow.[14,15] The lymphatic vessels are thought to be derived from the venous system as endothelial outgrowths.[14–16] By the 8th week of gestation, six lymphatic sacs are formed: two jugular, two iliac, the retroperitoneal sac at the root of the mesentery, and the cysterna chyli, which is dorsal to the latter. From these form new sprouts that grow to the periphery of the embryo, passing along veins. Bilateral thoracic ducts connect the cysterna chyli to the jugular sacs in the 9th week; a large anastomosis forms between the two thoracic ducts, and the final thoracic duct comes from the right duct in the lower chest and the left duct in the upper chest and neck, where it connects with the venous system at the junction between the left internal jugular and subclavian veins.

The majority of lymphangiomas arise from parts of lymph sacs that are pinched off during development or that fail to establish connections with the main lymphatic or venous channels. A small proportion appears to arise from localised lymphatic malformations or obstruction.

Pathology

Lymphangiomas are cysts or pockets of lymphatic fluid collection, which may consist of multiple cysts connected to each other by small lymphatic channels. They usually contain clear, straw-coloured fluid unless infection or bleeding has occurred.

Microcystic lymphangiomas have the propensity to infiltrate and extend into and around neighbouring structures, making complete excision difficult.

Microscopically, the cysts are lined by endothelium, supported by stroma of varying thickness and containing smooth muscle elements and lymphoid tissue. The endothelial lining is quite vulnerable to infection and chemical irritants. This observation forms the basis for sclerotherapy.

Nomenclature

Many misconceptions exist about lymphatic anomalies, and classifications are confusing. The suffix *–oma* is generally associated with tumours and a notion of cellular division and invasion, which does not apply to lymphangiomas. Used in the broad sense of a "space-occupying lesion", such as a haematoma or seroma, the term lymphangioma continues to be used, but it should not be considered a tumour in the neoplastic sense.

Cystic hygroma is a term coined in 1843 by Wernher, which was perpetuated since the classification proposed by Landing and Farber in 1956.[17] Because hygroma means a fluid-filled mass, the term "cystic hygroma" is redundant and should be abandoned. Hygromas are often used to describe cystic lymphangiomas occurring in the cervical area. In the abdomen, mesenteric cysts are generally synonymous with lymphangioma of the mesentery in the paediatric literature, even though some authors distinguish the two entities. The former is thought to occur mainly in adults, whereas mesenteric lymphangiomas usually present at birth or in infancy.

Furthermore, the classification of lymphangiomas into capillary, cavernous, and cystic has no clinical usefulness, as the various types may coexist in the same lesion. This nomenclature has been largely replaced by the unifying classification of Mulliken,[18] which

Table 110.1: Classification of lymphatic malformations.

Lymphatic malformation classification	Types
Primary lymphoedema	
Lymphangioma	Macrocystic (formerly cystic hygroma) Microcystic (formerly cavernous lymphangioma) Mixed
Diffuse lymphatic anomalies	Pulmonary or pleural or intestinal lymphangiomatosis Gorham-Stout disease (the so-called "vanishing bone disease")
Combined/complex malformations	Klippel-Trenaunay syndrome (capillary-lymphatico-venous malformation) Proteus syndrome Maffucci syndrome

was adopted by the International Society for the Study of Vascular Anomalies in 1996.[19] However the term "lymphatic malformation" used by Mulliken in this classification is very broad (Table 110.1).

The term "lymphangioma" continues to be used by most clinicians and will be used in this chapter. Lymphangiomas can be divided into macrocystic, microcystic, and mixed forms on the basis of imaging studies (see Table 110.1). This classification has important therapeutic and prognostic implications, as will be seen in this chapter.

Natural History

Lymphangiomas tend to grow slowly with the child, but sudden enlargement may be seen during a viral infection or when bacterial infection or spontaneous bleeding occurs in some cysts. Spontaneous resolution is uncommon but has been reported in up to 15% of cases.[8,12,16,20] Resolution may occasionally follow infection.

Clinical Presentation

History

Generally, lymphangiomas are asymptomatic at diagnosis; however, presentation may be delayed in Africa, particularly if the lymphangioma is outside the head and neck region.

The most common site of involvement is the neck, with other common sites being the head (especially the tongue), the axilla and chest wall, the abdominal wall and flank, and the extremities (Figure 110.1, Table 110.2). Internal organs are involved in 10% of patients, the most common being the bowel mesentery.

Presentation depends on the site. Reasons for presentation include disfigurement; mass lesion; pain (and fever); pressure effect (e.g., respiratory obstruction or dysphagia); and acute abdomen or intestinal obstruction.

Physical Examination

Patients presenting with uncomplicated lymphangiomas usually look healthy otherwise. Local warmth and tenderness with pyrexia generally signify infection of the lesion. In such circumstances, the skin may be erythematous (in light-skinned patients), or simply appear shiny. Tachypnea and cyanosis may be present in those with airway obstruction.

In the neck, 85% of lymphangiomas are unilateral. There may be extension into the ipsilateral face or floor of the mouth in some patients. Fifteen percent are midline or extend to both sides of the neck.[6] The lesion may be quite large; some may attain massive proportions.

Diagnosis is based on the finding of a soft, multiloculated mass, which transilluminates brilliantly. However, lymphangiomas with infection or intracystic haemorrhage may not transilluminate. Microcystic lymphangiomas, due to the significant amount of stroma, may have solid areas that could create diagnostic difficulty.

Prenatal Presentation

Lymphangiomas are increasingly being diagnosed by prenatal ultrasonography (US), particularly when located in the neck. Posterior nuchal translucency, confusingly called nuchal cystic hygroma, is not the same as lymphangioma.[21] Foetal nuchal translucency is an important marker for aneuploidy in the first trimester and early part of the second; it may be associated with pleural effusion and hydrops. It is usually bilateral and posterior, whereas lymphangiomas are lateral or anterior and are diagnosed in the second and third trimesters. In the absence of chromosomal anomalies, 80% of foetuses with first-trimester nuchal translucency have a normal outcome unless there is spontaneous abortion; in favorable cases, the translucency usually resolves spontaneously by the end of the second trimester. Turner and Noonan syndromes are often accompanied by nuchal translucency; the prenatal diagnosis of the latter is difficult to make because the karyotype would be normal.[22]

The differential diagnosis of cervical cystic lesions includes cystic teratomas, thymic and branchial cysts, and congenital fibrosarcomas. In the abdomen, ovarian cysts are most common, followed by enteric duplications; cystic renal masses are also common but are usually readily distinguishable. Rare abdominal cystic lesions in the foetus include cystic teratomas, mesenchymal hamartomas of the liver, choledochal cysts, urachal cysts, and congenital fibrosarcoma.[21]

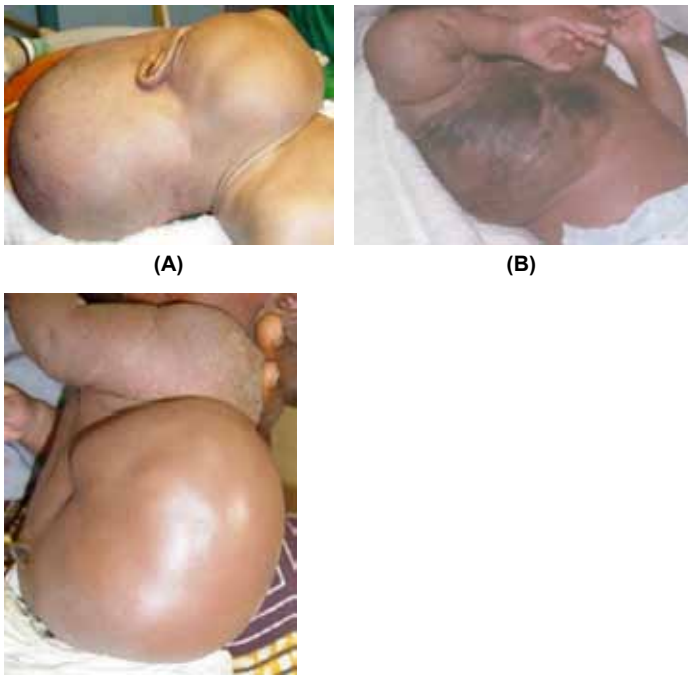


Figure 110.1: Lymphangiomas at various sites: (A) cervical, (B) axillary, (C) left flank.

Table 110.2: Anatomic distribution of lymphangiomas in two large paediatric series.

Site	Number	Percentage
Cervical	116	31
Craniofacial	72	19
Trunk (including axilla and genitalia)	89	23
Extremities	59	16
Intraabdominal and mediastinal	43	11
Totals	379	100

Sources: Hancock BJ, St-Vil D, Luks FI, Di Lorenzo M, Blanchard H. Complications of lymphangiomas in children. J Pediatr Surg 1992; 27: 220–224. Alqahtani A, Nguyen LT, Flageole H, Shaw K, Laberge JM. 25 years' experience with lymphangiomas in children. J Pediatr Surg 1999; 34:1164–1168.

Prenatal diagnosis is especially important for large lymphatic malformations because they may cause dystocia. Prenatal aspiration of selected macrocystic lesions may allow for vaginal delivery or facilitate caesarean section in some cases. Prenatal diagnosis is even more important for large cervical lesions, which may cause respiratory distress at birth. When tracheal obstruction is predicted on prenatal imaging, an EXIT procedure is the safest way to deliver the baby.[23] EXIT, which stands for EX-utero Intrapartum Treatment, is essentially a large caesarean section done under deep maternal general anesthesia; the foetal head is delivered and an airway is secured while placental circulation maintains foetal oxygenation. Sometimes a tracheostomy will be required, but often the baby can be intubated successfully with the help and confirmation of flexible bronchoscopy. Prenatal imaging is usually accurate in predicting airway compression and the need for caesarian section (Figure 110.2).

Prenatal treatment of foetal lymphatic malformations with sclerosants, such as OK-432 (see subsection "Types of Lesions"), has been advocated by some authors, but its role remains to be determined.[24,25] The problem is that the rate of incorrect prenatal diagnosis of lymphatic malformations may be as high as 38–50%.[21,26]

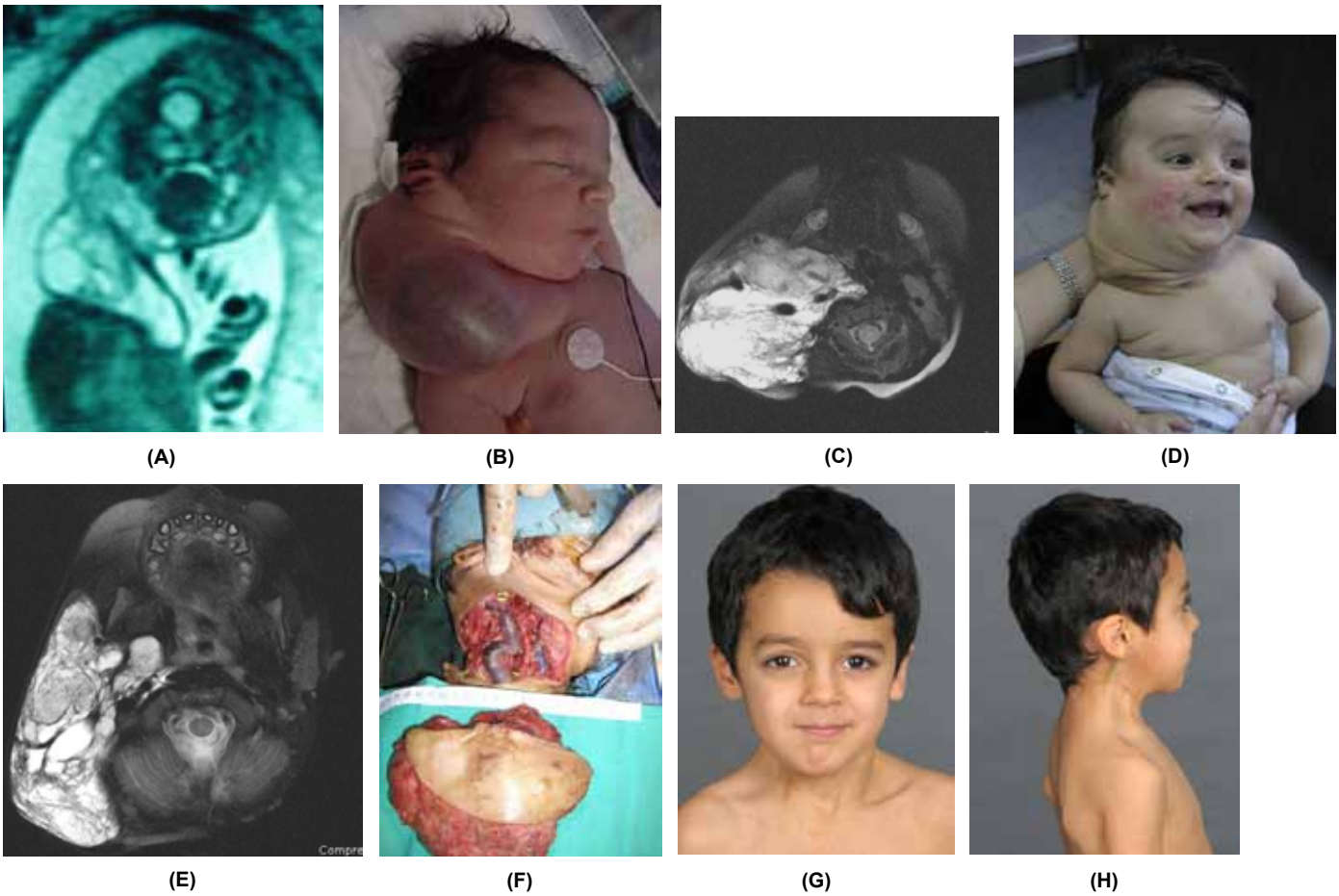


Figure 110.2: Giant cervical lymphangioma (unilateral supra and infra hyoid, mixed macro and microcystic): (A) Prenatal MRI, showing right cervical cysts (white on this T-2-weighted image, right eye seen in top part of picture). (B) Child after delivery by caesarian section, with paediatric surgeon in attendance. (C) MRI at 4.5 months of age. (D) Child at 4.5 months of age; note scarring from Ethibloc extrusion on lower neck. (E) MRI at 18 months of age, prior to surgical resection (after two sclerotherapies with Ethibloc and one streptococcal infection). (F) Cervical dissection with cranial nerves VII, X, XI, XII, and phrenic nerve, hugely dilated dysplastic jugular vein, and resected specimen. (G) Frontal view, 3.5 years postoperatively. (H) Lateral view, 3.5 years postoperatively.

Investigations

Although the diagnosis of most lymphangiomas is clinical, various modalities are required for confirmation of the diagnosis, planning of treatment, and follow-up.

Ultrasonography

US helps in classifying the lesion (macrocystic, microcystic, or mixed), as well as ascertaining the extent of the disease. This should be the minimum imaging modality for evaluation. Neighbouring and susceptible regions of the body should also be assessed adequately by US.

Plain Radiography

Plain radiography is useful when the lymphangioma may extend into or is located in a body cavity, particularly in the absence of computed tomography (CT) scan and magnetic resonance imaging (MRI). For example, normal chest radiographs exclude any significant mediastinal extension of large cervical lymphangioma. Plain radiographs may also be useful in evaluating the trachea in such patients, as this will be helpful during anaesthesia and tracheal intubation.

CT Scan and MRI

CT scan and MRI are being used increasingly for evaluation. MRI is now considered to be the most accurate imaging modality for evaluation. However, these imaging modalities have limited application in resource-limited settings due to cost and availability. The CT scan is superior to US in detecting small areas of calcifications or fat, which would change the diagnosis to teratoma.

Needle Aspiration and Culture

Needle aspiration and cytological examination of the fluid should be done in any patient who will be treated by sclerosants or who will be observed for a period of time. This will avoid delaying resection of a teratoma, with its inherent risk of malignant transformation (Figure 110.3).

Needle aspiration may also be used in situations where intracystic haemorrhage is suspected (rapid increase in size), or infection has occurred and abscess formation is suspected. In the latter instance, culture of the pus will help to direct antibiotic treatment; in the former, aspiration may decompress the lesion until definitive treatment is undertaken.

In patients presenting with airway obstruction, needle aspiration may be performed as a temporising measure. Any aspirated fluid in all situations should be sent for microbiological culture, cell count (the differential will show at least 80–90% lymphocytes in lymphangiomas), and cytology.

Complications

In Africa, many children with lymphangiomas present with complications, which can be life threatening, particularly in the cervical area.[4,7]

Respiratory Obstruction

Respiratory obstruction is a feared complication of head and neck lymphangiomas and can be due to the infiltration of the malformation in the tongue, pharynx, or larynx, or compression of a normal airway by large cysts. Emergency management includes cyst aspiration, positional nursing, endotracheal intubation, and tracheostomy. Aspiration of a macrocystic lesion is a temporary measure and carries a risk of

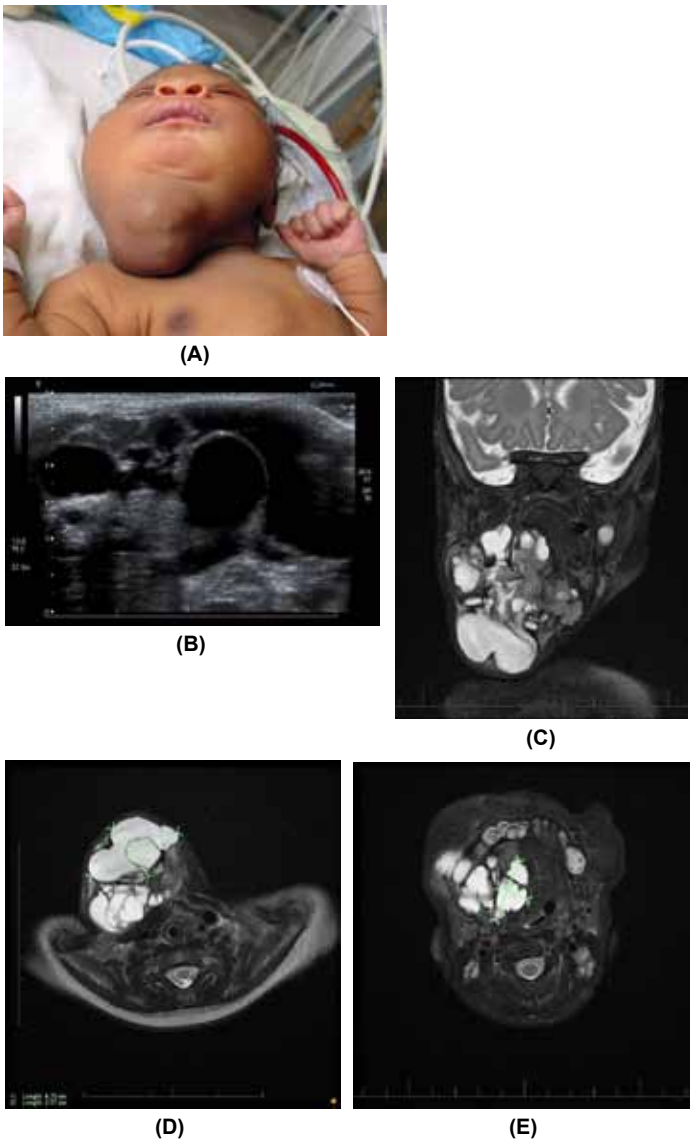


Figure 110.3: Difficulties in diagnosis: (A) A large lobulated neck mass in a newborn. (B) US showing multicystic lesion; patient was initially observed, but was readmitted with feeding difficulty. (C) MRI (coronal view, T-2 weighted) showing extent in the floor of the mouth. (D) Axial view demonstrating an intact trachea. (E) Proximally, the mass displacing the larynx and base of the tongue. The patient failed two attempts at sclerosis with doxycycline and required nasogastric tube feedings and a tracheostomy following an episode of bronchiolitis. Excision carried out at 5 months of age revealed a mature teratoma.

infection. It can be repeated once or twice while preparing for definitive treatment. A sterile technique is mandatory, and US guidance helps to achieve efficient aspiration.

Positional nursing on the ipsilateral side (if unilateral) or on the more affected side (if the cyst extends to both sides of the neck) helps to take the pressure and weight off the trachea and to temporarily relieve airway obstruction. Endotracheal intubation or tracheostomy may be necessary, especially when the larynx is directly involved by the lymphangioma. Endotracheal intubation can be maintained for a few weeks to relieve the obstruction by cyst aspiration, antibiotherapy, sclerotherapy, or early surgical resection. Tracheostomy carries a significant risk for early and late complications in neonates and should be avoided as much as possible, but it is unavoidable in certain circumstances.[27] If a tracheostomy is done, it should be left in place until definitive treatment is achieved. Oxygen supplementation should always be given in patients with airway obstruction.

Rapid Size Increase

A rapid increase in the size of the lymphatic malformation can occur in reaction to a viral or bacterial infection anywhere in the body, but it is more frequent with upper airway infection. This is due to increased lymphatic flow. This usually resolves as the primary infection is controlled. The increase in size may cause airway obstruction, discomfort, transient nerve compression, or pressure necrosis, which in turn increases the risk of infection. A sudden increase in size may also be due to intracystic haemorrhage. In large cysts, bleeding due to the rupture of a blood vessel normally present in intracystic septae can be severe and necessitate transfusions.

Infection

Infection of the lymphatic malformation should be treated promptly. The incidence of infection in cervical lymphatic malformations varies in different series from 17% to 71%.[6,7,28] Since infection often follows an episode of upper respiratory tract infection, initial antibiotic therapy should be directed at the prevalent bacteria in the nasopharynx, particularly group B streptococcus. Parenteral administration of ampicillin (or amoxicillin) and gentamicin is usually effective. A cephalosporin may be used as a single agent. In patients who develop infection following cyst aspiration, coverage for staphylococcus is essential, and metronidazole can be added to cover for anaerobes. When an abscess is suspected, aspiration is indicated to confirm diagnosis and obtain cultures; often a drainage procedure (percutaneous or incisional) will be required. Ultrasonographic guidance may be helpful, particularly in the cervical area, to decrease the risk of damage to adjacent structures.

Ulceration

Ulceration is due to pressure necrosis. The ulcerated area often rapidly becomes infected, and the infection may extend into the cyst (Figure 110.4). This should be managed by dressings and the use of antibiotics if infected. To decrease the risk of postoperative wound infection, it is usually safer to wait until the ulceration has healed before embarking on surgical excision.

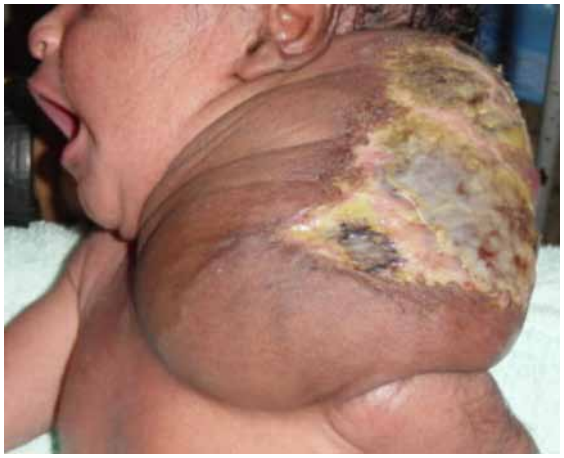


Figure 110.4: Ulcerated left cervical cystic lymphangioma.

Feeding and Speech Difficulties

Feeding and speech difficulties can be present in lesions of the suprahyoid area with tongue involvement or can occur sporadically during episodes of rapid increase of the size of the lesion. Tube feeding or a gastrostomy may be required to maintain adequate nutrition.

Mortality

Reported mortality as a result of one or a combination of these complications, particularly in neonates, ranges from 0% to 2%[7,12] and may be much higher in the African setting.[4] The incidence in other reports may be underestimated, as many of the severely obstructed neonates may never reach the tertiary centres where case series are reviewed.

Other Complications

Skeletal overgrowth and maxillary malocclusion are also well documented.[28,29]

Treatment

Lymphangiomas are benign vascular malformations; therefore, growth is not a concern, although the size of the lesions varies over time, depending on inflammation, infection, bleeding, or fluid accumulation in the cysts. Once the diagnosis has been established, observation during the first years of life is adequate unless the lesion causes severe deformity or a complication occurs. Reports of spontaneous resolution, sometimes following an episode of infection, have been published,[8,12,16,20] but it remains uncommon. The mainstays of treatment are sclerotherapy and surgical excision. Radiation therapy, although occasionally used in the past, carries a risk of growth retardation and malignancy and is not recommended. Before considering surgery, the feasibility of complete excision and the risks of postoperative complications and damage to adjacent structures, as well as the scarring involved, should be carefully weighed against the advantages and risks of sclerotherapy. In recent years, many centres have switched to using sclerotherapy as a primary treatment, followed by surgery if needed, rather than using sclerotherapy as rescue treatment. The prognosis varies with the type of malformation (macrocystic, microcystic, or mixed lesion) and its location.

Types of Lesions

Macrocystic lesions

Macrocystic lesions have the best prognosis for successful treatment with sclerotherapy or surgery.[13,30–32] The large cysts are more easily removed completely, and there is less infiltration of the adjacent structures, which can usually be completely preserved. If sclerotherapy is done, the large cysts provide an easy access for successful treatment. The two treatment modalities can be combined if necessary.

Mixed lesions

In mixed lesions, the large cysts provide an access for sclerotherapy and the inflammatory response reduces the size of the macrocysts but may also have a positive effect on the microcystic components adjacent to the macrocysts. It is therefore essential not to surgically remove the large cysts before addressing the microcystic component infiltrating adjacent structures. Mixed lesions of the suprahyoid region are not completely resectable due to the infiltration of the tongue, floor of the mouth, pharynx, and larynx. Sclerotherapy has significantly improved the prognosis for such patients (Figures 110.2 and 110.5).

Microcystic lesions

Microcystic lesions are infiltrating lesions that are more difficult to treat both surgically and with sclerotherapy. There is little space available for the sclerosing material, and surgical resection is limited by the infiltration of important structures. Residual malformation is the rule in the majority of cases unless the lesion is well delineated and completely excised. When the skin overlying the lesion is involved (angiokeratosis or lymphangiomata circumscriptum), it should be removed whenever feasible.

Treatment Modalities

Percutaneous sclerotherapy

Percutaneous sclerotherapy is performed with a sterile technique, usually under sedation or general anaesthesia, depending on the age of the child, with US guidance. Fluid is aspirated and sent for cell count and cytological examination to confirm the diagnosis. A contrast medium may be injected to identify and quantify the number of cysts and intercystic communications under fluoroscopy. The sclerosing material is then introduced into the cysts. Many sclerosing agents have been used, including absolute ethanol (98%); doxycycline;[33–36] OK-432 (Picibanil, Chugai Pharmaceutical, Tokyo, Japan);[31,32,37–40] bleomycin;[41–46] and Ethibloc (Ethicon, Norderstedt, Germany).[13,47] Doxycycline has been used by radiologists as well as surgeons for cervical lesions as well as for those on the extremities and trunk, including intraabdominal/retroperitoneal lymphangiomas.

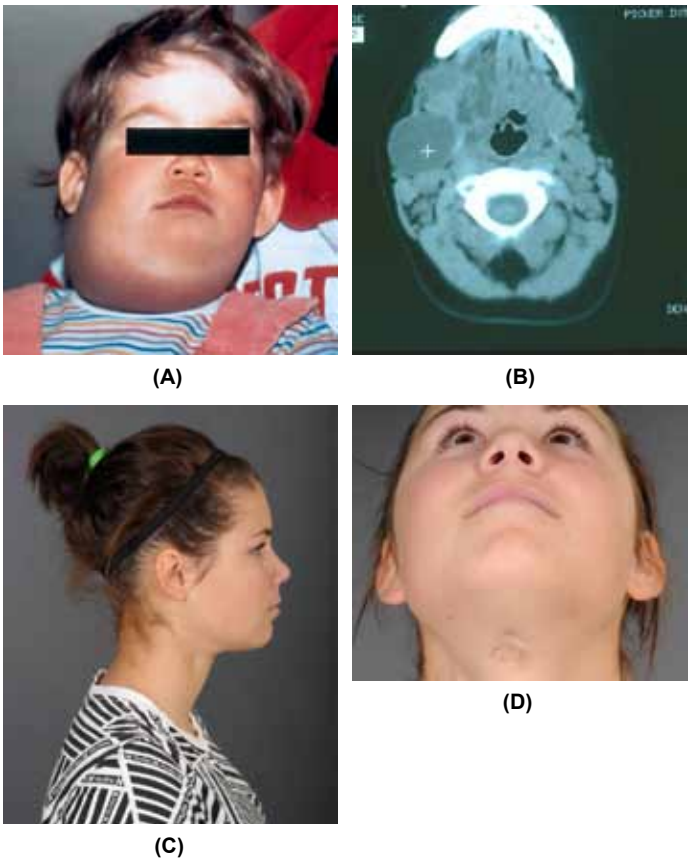


Figure 110.5: Unilateral suprahyoid, mixed macro- and microcystic: (A) At age 2 years, inflammatory response postsclerotherapy with Ethibloc. (B) CT scan at age 2 years; note microcystic infiltrating lesions anterior to large cyst. (C) 13 years follow-up after two sclerotherapies with Ethibloc and one infection at age 2 years. (D) Residual submental scar from Ethibloc extrusion.

The majority of sclerosing agents destroy the endothelial layer of the cysts and produce a marked inflammatory reaction. The use of prophylactic antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDS), or systemic steroids to minimise swelling and the risk of infection are recommended by some authors. OK-432, an inactivated (by incubation with benzathine penicillin) strain of human *Streptococcus pyogenes* has a theoretical advantage over other sclerosants because it produces little or no perilesional fibrosis. However, surgery after other types of sclerosants has been reported without complications.[13] Significant swelling of the lesion is expected following sclerosis; therefore, in lesions of the cervical and oral area, the children should be monitored closely and endotracheal intubation should be performed if the airway is compromised.

Even though OK-432 appears to be a "magic bullet" in many series that advocate its use as a first-line treatment, others have not found it as effective.[39] Furthermore, it has been difficult to obtain at times; contacting a paediatric surgical colleague in Japan may be helpful. As with any sclerosing agent, repeat sclerotherapy is required in most cases, at intervals varying from a few weeks to a few months. In some patients, sclerotherapy has no effect and has to be abandoned.

Surgical resection

Surgical resection should follow the precise documentation of the lesion with MRI or CT scan and should remove the entire lesion whenever feasible.[48] One complete excision is technically easier than repeat surgical excisions of the same area. In cases where the lesion is too extensive for complete resection in one procedure, anatomic areas

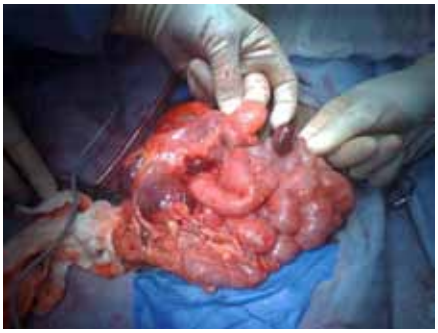
are resected in staged procedures.[49] The skin presenting intradermal involvement with visible angiokeratosis and clear vesicles should be resected when feasible because it increases the risk of infection and recurrence and may lead to persistent lymphatic cutaneous fistulas.

Important structures, such as nerves, major vessels, and muscles, are dissected free from the cysts under loupe magnification and kept intact. The use of a nerve simulator in an unparalysed patient makes nerve identification easier, particularly in the head and neck area. A bipolar cautery is helpful to coagulate afferent lymphatic and blood vessels and limit injury to adjacent structures. A suction drain is left in place, and antibiotics are kept until the drain is removed. In cases of prolonged drainage, sclerotherapy can be used as an adjunct to surgery. Conversely, in cases where regression of the lymphatic malformation following sclerotherapy is incomplete, surgical resection of the residual lesion can be done. The surgery is done once the inflammation has completely subsided after the last sclerotherapy. Contrary to a widely accepted belief, the authors find that the procedure is often easier than for an untreated lesion because the cysts are smaller and their walls are thicker and easier to identify. The child is also generally older (see Figure 110.2).

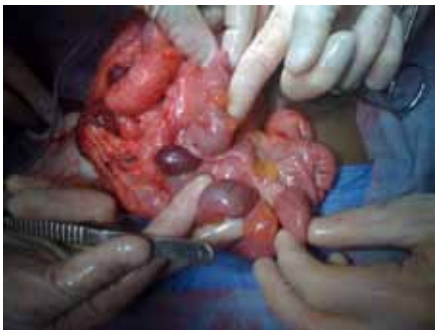
Specific Locations

Lymphangiomas of the tongue usually require partial glossectomy. Those involving the pharyngeal and laryngeal mucosa cannot be resected or sclerosed, but may improve with laser ablation. Mediastinal lesions have been traditionally resected, but the positive results obtained with sclerosants for extensive retroperitoneal lymphangiomas may shift the treatment strategy.

Complete resection of mesenteric lymphangiomas generally requires resection of the adjacent bowel (Figure 110.6), but sometimes this is not possible. In such circumstances, as well as for multiple intestinal lesions, as much as possible of the cyst walls is resected, and the remnant can be cauterised, ideally with an argon beam coagulator. Fibrin glue has also been used.



(A)



(B)

Figure 110.6: This patient had an incomplete excision of a mesenteric lymphangioma of the sigmoid in the neonatal period. She presented at 3 years of age with an acute abdomen and fever. At operation, a large infected lymphangioma (A, top left) required resection of the descending colon and sigmoid, as well as multiple other lesions, both mesenteric and antimesenteric, most containing serous fluid, others haemorrhagic; two were chylous (B).

Complications Following Treatment

As a rule, the same complications already discussed (airway obstruction, bleeding, infection) can occur after sclerotherapy or surgical excision, and the treatment is the same. Complications more specific to either treatment are discussed next.

Postsclerotherapy

Pain, oedema, and localised inflammation as well as mild fever, are expected for 24 to 48 hours postsclerotherapy. In large neck lesions, this may cause airway obstruction, and careful monitoring is essential. Depending on the agent used, skin necrosis, nerve damage and cardiac arrhythmia (ethanol), skin erosion, material extrusion (see Figures 110.2 and 110.5) and infection (Ethibloc), staining of unerupted teeth (doxycyclin), alopecia, skin discolouration, and pulmonary fibrosis (bleomycin) have been reported, although this latter serious complication did not occur in a series of 200 patients with long-term follow-up.[46]

Postoperative

Postoperative complication rates vary significantly among published series,[3,4,6,7,9,12] but the location of the lesion, mucosal involvement,[8,27] and the type of malformation (macrocystic, microcystic, or mixed) significantly affect the prognosis. For cervical lymphangiomas that are suprahyoid, bilateral, mixed, or microcystic, the complication and recurrence rate is close to 100%.[6] Conversely, with unilateral macrocystic infrahyoid lesions or with lymphangiomas located outside the head and neck area, complete excision is often possible, and the complication rate is low (Table 110.3).

Table 110.3: Complications of surgical excision of cystic lymphangiomas in African series.

All sites (n = 47)*	Number (%)	Cervical location (n = 60)**	Number (%)
Wound infection	14 (29.8)	Respiratory obstruction	11 (18.3)
Seroma	11 (23.4)	Wound infection	7 (11.7)
Respiratory obstruction	9 (19.1)	Facial nerve palsy	6 (10.0)
Pneumonia	7 (14.9)	Skin disfigurement	4 (6.7)
Nerve palsies	6 (12.8)	Hypoglossal nerve palsy	2 (3.3)
Skin disfigurement	4 (8.5)	Injury to pharynx	2 (3.3)
Injury to pharyn	1 (2.1)	Recurrent laryngeal nerve palsy	1 (1.7)
		Parotid duct injury	1 (1.7)
		Injury to internal jugular vein	1 (1.7)

*Sources: Uba AF, Chirdan LB. Management of cystic lymphangioma in children: experience in Jos, Nigeria. Pediatr Surg Int 2006; 22:353–356. Sowande OA, Adejuyigbe O, Abubakar AM. Management of cystic lymphangiomas in Ile-Ife, Nigeria. Niger J Surg Res 2003; 5:32–37.

**Sources: Ameh EA, Nmadu PT. Cervical cystic hygroma: pre-, intra-, and postoperative morbidity and mortality in Zaria, Nigeria. Pediatr Surg Int 2001; 17:342–343. Sowande OA, Adejuyigbe O, Abubakar AM. Management of cystic lymphangiomas in Ile-Ife, Nigeria. Niger J Surg Res 2003; 5:32–37.

The presence of a complication at the time of initial presentation and the age at surgery (neonates versus older children) also affect the prognosis. Newborns have a high risk of laryngeal oedema and airway obstruction following extensive neck dissection. The endotracheal tube should be left in place in susceptible infants and ventilation maintained for 48–72 hours to allow oedema to subside. Airway obstruction is the leading cause of postoperative mortality in Africa, particularly in children younger than 1 year of age.[4,5,7]

Prolonged drainage and seroma (9.8%) are more frequent after incomplete excision, although they can occur after a macroscopically

complete excision. They can be treated with repeat aspiration or sclerotherapy.

Infections occur even with the use of perioperative antibiotics (6.6% to 27%). Children presenting with an ulcerated lesion have a higher risk of infection.

Damage to nerves (VII, X, XI, XII, recurrent laryngeal, phrenic, sympathetic chain) during excision of large cervical lymphangiomas is reported to occur in 1% to 25% of cases and represents a significant morbidity. This includes facial asymmetry, speech impairment, and Horner's syndrome.

Recurrence or enlargement of residual lesions occurs frequently. A series of 144 patients reported a 17% recurrence rate in completely excised lesions compared to 40% after incomplete excisions.[12] Some of these "recurrences" are actually due to the enlargement of preexisting microscopic lesions neighbouring the surgical resection margins.[5,8,28,50]

Prognosis and Outcome

In large series, considering all sites and types of lymphangiomas, complete excision of the malformation can be obtained with one surgical procedure in >70% of the children.[3,12] For cervicofacial lymphangiomas, recurrence and complications depend on the initial extent of the lesion.[6,27] Depending on the size, location, and symptomatology of residual or recurrent lesions, more than one surgery may be necessary. It is important to understand that some lesions (e.g., suprahyoid microcystic infiltrating lesions) will never be completely resectable, however, and research for other means of treatment is essential.

The use of sclerotherapy has markedly increased in the recent years. However, not all sclerosing materials are available in every country, and studies comparing the different sclerosing agents are missing. Many centres have published very good results with 50% or more regression of the lesions in >75% of the cases.[8,13,30–32,41] Unfortunately, not all lesions are amenable to sclerotherapy; as for the surgical treatment, the macrocystic lesions have the best prognosis (see Figure 110.5). There is some indication, however, that sclerotherapy of the macrocysts included in the mixed lesions has improved the microcystic component. A multidisciplinary team approach and the combination of sclerotherapy and surgery offer many advantages.

Evidence-Based Research

At the present time, there are no prospective, randomised studies comparing surgical excision and sclerotherapy. Available guidelines have to be based on reports of large retrospective experiences. Table 110.4 presents a study comparing the usage of bleomycin and OK-432 with surgery in two time periods.

Table 110.4: Evidence-based research.

Title	Treatment of lymphangiomas in children: our experience of 128 cases
Authors	Okazaki T, Iwatani A, Yanai T, et al.
Institution	Department of Pediatric General and Urological Surgery, Juntendo University School of Medicine, Tokyo 113-8421, Japan
Reference	J Pediatr Surg 2007; 42:386–389
Problem	Role of surgical excision and sclerotherapy in the management of lymphangiomas.
Intervention	Surgical excision, sclerotherapy.
Comparison/ control (quality of evidence)	Two periods of treatment divided arbitrarily into period I (1979–1988, n = 53) and period II (1989–2005, n = 75). Bleomycin was used as sclerosant in period I, and OK-432 was introduced in period II. Sclerotherapy was used as the primary treatment in 64% of patients in period II.
Outcome/ effect	Effectiveness of sclerotherapy in single cysts, macrocystic, microcystic, and cavernous (mixed) types was 90.9%, 100%, 68%, and 10%, respectively. Seventeen patients who had primary sclerotherapy required surgical excision with good outcome. Primary surgical excision was significantly more successful than sclerotherapy (88.5% versus 64.0%, $p < 0.01$). Complications after sclerotherapy included transient fever and swelling (32%), infection (6%), airway obstruction (4%), and nerve palsy (2%). In comparison, complications after surgical excision were more serious: lymphorrhea (27%), nerve palsy (9%), infection (6%), airway obstruction (1%), and persistent pain (1%).
Historical significance/ comments	This report of a large series of children with various types of lymphangiomas at various sites (head and neck, 53.9%), provides a useful practice guide. Although both surgical excision and sclerotherapy were used for more than two decades, sclerotherapy became increasingly used in later years. Irrespective of site, primary surgical excision was more effective than sclerotherapy, and the latter was more effective for single cysts and macrocystic lesions. It is noted that surgical excision may still be required after primary sclerotherapy, with good outcome. The complication rate following surgical excision and sclerotherapy was similar (44%), but it fell to 12% after sclerotherapy if transient fever and swelling were excluded. The authors of the study recommend sclerotherapy alone (using OK-432) for single cysts and macrocystic lesions and surgical excision after initial sclerotherapy for microcystic and cavernous lesions. The findings of this report have important implications for the African setting: primary surgery is effective, but initial sclerotherapy should be considered in patients at risk of postoperative complications (e.g., neonates and infants with large cervical lymphangiomas). In the African setting, bleomycin and doxycycline may be more readily available for sclerotherapy, and the latter is relatively inexpensive.

Key Summary Points

1. Cystic lymphangiomas are not common.
2. Cervical location is the most common and important site.
3. Airway obstruction and infection are common complications in cervical lymphangioma, both before and after surgery.
4. Ultrasonography is the minimum evaluation modality and is necessary to categorise and ascertain the extent of the lesion.
5. Surgical excision is effective, particularly in macrocystic malformations, and can be combined with sclerotherapy.
6. Sclerotherapy is more effective in single cysts and macrocystic lesions.
7. Cystic teratoma should be excluded by imaging and cytology if nonoperative management is initially chosen.
8. Morbidity can be high after surgery: complete excision should not be performed if injury to important structures is likely. Sclerotherapy should be the first-line treatment if complete surgical excision does not appear likely from imaging studies.
9. Morbidity and mortality are most common in cervical lymphangiomas and in infants younger than 1 year of age.
10. In infants younger than 1 year of age presenting without complications, surgery should be delayed to minimise operative morbidity and mortality.

References

1. Filston HC. Hemangiomas, cystic hygromas, and teratomas of the head and neck. Semin Pediatr Surg 1994; 3:147–159.
2. Fonkalsrud EW. Congenital malformations of the lymphatic system. Semin Pediatr Surg 1994; 3:62–69.
3. Hancock BJ, St-Vil D, Luks FI, Di Lorenzo M, Blanchard H. Complications of lymphangiomas in children. J Pediatr Surg 1992; 27:220–224.
4. Uba AF, Chirdan LB. Management of cystic lymphangioma in children: experience in Jos, Nigeria. Pediatr Surg Int 2006; 22:353–356.
5. Adeyemi SD. Management of cystic hygroma of the head and neck in Lagos, Nigeria; a 10-year experience. Int J Pediatr Otorhinolaryngol 1992; 23:245–251.
6. de Serres LM, Sie KC, Richardson MA. Lymphatic malformations of the head and neck. Arch Otolaryngol Head Neck Surg 1995; 121:577–582.
7. Ameh EA, Nmadu PT. Cervical cystic hygroma: pre-, intra-, and post-operative morbidity and mortality in Zaria, Nigeria. Pediatr Surg Int 2001; 17:342–343.
8. Kennedy TL, Whitaker M, Pellitteri P, Wood WE. Cystic hygroma/lymphangioma: a rational approach to management. Laryngoscope 2001; 111:1929–1937.
9. Miloundja J, Manfoumbi Ngoma AB, Mba ER, Nguema EB, N'Zouba L. Cystic cervicofacial lymphangioma in children in Gabon. Ann Otolaryngol Chir Cervicofac 2007; 124:277–284.
10. Ofodile FA, Oluwasanmi JO. Lymphangiomas in Nigeria. East Afr Med J 1980; 57:279–284.
11. Sowande OA, Adejuyigbe O, Abubakar AM. Management of cystic lymphangiomas in Ile-Ife, Nigeria. Niger Jour Surg Res 2003; 5:32–37.
12. Alqahtani A, Nguyen LT, Flageole H, Shaw K, Laberge JM. 25 years' experience with lymphangiomas in children. J Pediatr Surg 1999; 34:1164–1168.
13. Emran MA, Dubois J, Laberge L, Al-Jazaeri A, Butter A, Yazbeck S. Alcoholic solution of zein (Ethibloc) sclerotherapy for treatment of lymphangiomas in children. J Pediatr Surg 2006; 41:975–979.
14. Moore KL, Persaud TVN. Development of the lymphatic system. In: Moore KL, Persaud TVN, eds. The Developing Human: Clinically Oriented Embryology. Saunders, 1998, Pp 398–401.
15. Breugem CC, van der Horst CM, Hennekam RC. Progress toward understanding vascular malformations. Plast Reconstr Surg 2001; 107:1509–1523.
16. Chappuis JP. Current aspects of cystic lymphangioma in the neck. Arch Pediatr 1994; 1:186–192.
17. Landing BH, Farber S. Tumors of the cardiovascular system. In: Atlas of Tumor Pathology. Armed Forces Institute of Pathology, 1956.
18. Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. Plast Reconstr Surg 1982; 69:412–422.
19. Enjolras O, Mulliken JB. Vascular tumors and vascular malformations (new issues). Adv Dermatol 1997; 13:375–423.
20. Williams HB. Hemangiomas and lymphangiomas. Adv Surg 1981; 15:317–349.
21. Marler JJ, Fishman SJ, Upton J, et al. Prenatal diagnosis of vascular anomalies. J Pediatr Surg 2002; 37:318–326.
22. Longaker MT, Laberge JM, Dansereau J, et al. Primary foetal hydrothorax: natural history and management. J Pediatr Surg 1989; 24:573–576.
23. Bouchard S, Johnson MP, Flake AW, et al. The EXIT procedure: experience and outcome in 31 cases. J Pediatr Surg 2002; 37:418–426.
24. Chen M, Chen CP, Shih JC, et al. Antenatal treatment of chylothorax and cystic hygroma with OK-432 in nonimmune hydrops fetalis. Fetal Diagn Ther 2005; 20:309–315.
25. Sasaki Y, Chiba Y. Successful intrauterine treatment of cystic hygroma colli using OK-432. A case report. Fetal Diagn Ther 2003; 18:391–396.
26. Fisher R, Partington A, Dykes E. Cystic hygroma: comparison between prenatal and postnatal diagnosis. J Pediatr Surg 1996; 31:473–476.
27. Hartl DM, Roger G, Denoyelle F, Nicollas R, Triglia JM, Garabedian EN. Extensive lymphangioma presenting with upper airway obstruction. Arch Otolaryngol Head Neck Surg 2000; 126:1378–1382.
28. Padwa BL, Hayward PG, Ferraro NF, Mulliken JB. Cervicofacial lymphatic malformation: clinical course, surgical intervention, and pathogenesis of skeletal hypertrophy. Plast Reconstr Surg 1995; 95:951–960.
29. Mulliken JB, Fishman SJ, Burrows PE. Vascular anomalies. Curr Probl Surg 2000; 37:517–584.
30. Dubois J, Garel L, Abela A, Laberge L, Yazbeck S. Lymphangiomas in children: percutaneous sclerotherapy with an alcoholic solution of zein. Radiology 1997; 204:651–654.
31. Luzzatto C, Lo PR, Fascetti LF, Zanon GF, Toffolutti T, Tregnaghi A. Further experience with OK-432 for lymphangiomas. Pediatr Surg Int 2005; 21:969–972.
32. Sichel JY, Udassin R, Gozal D, Koplewitz BZ, Dano I, Eliashar R. OK-432 therapy for cervical lymphangioma. Laryngoscope 2004; 114:1805–1809.
33. Burrows PE, Mitri RK, Alomari A, et al. Percutaneous sclerotherapy of lymphatic malformations with doxycycline. Lymphat Res Biol 2008; 6:209–216.
34. Mabrut JY, Grandjean JP, Henry L, et al. Mesenteric and mesocolic cystic lymphangiomas. Diagnostic and therapeutic management. Ann Chir 2002; 127:343–349.
35. Nehra D, Jacobson L, Barnes P, Mallory B, Albanese CT, Sylvester KG. Doxycycline sclerotherapy as primary treatment of head and neck lymphatic malformations in children. J Pediatr Surg 2008; 43:451–460.
36. Shiels WE, Kenney BD, Caniano DA, Besner GE. Definitive percutaneous treatment of lymphatic malformations of the trunk and extremities. J Pediatr Surg 2008; 43:136–139.
37. Banieghbal B, Davies MR. Guidelines for the successful treatment of lymphangioma with OK-432. Eur J Pediatr Surg 2003; 13:103–107.
38. Claesson G, Kuylenstierna R. OK-432 therapy for lymphatic malformation in 32 patients (28 children). Int J Pediatr Otorhinolaryngol 2002; 65:1–6.
39. Hall N, Ade-Ajayi N, Brewis C, et al. Is intralesional injection of OK-432 effective in the treatment of lymphangioma in children? Surgery 2003; 133:238–242.
40. Giguere CM, Bauman NM, Sato Y, et al. Treatment of lymphangiomas with OK-432 (Picibanil) sclerotherapy: a prospective multi-institutional trial. Arch Otolaryngol Head Neck Surg 2002; 128:1137–1144.
41. Baskin D, Tander B, Bankaoglu M. Local bleomycin injection in the treatment of lymphangioma. Eur J Pediatr Surg 2005; 15:383–386.
42. Mathur NN, Rana I, Bothra R, Dhawan R, Kathuria G, Pradhan T. Bleomycin sclerotherapy in congenital lymphatic and vascular malformations of head and neck. Int J Pediatr Otorhinolaryngol 2005; 69:75–80.
43. Okazaki T, Iwatani S, Yanai T, et al. Treatment of lymphangioma in children: our experience of 128 cases. J Pediatr Surg 2007; 42:386–389.

44. Muir T, Kirsten M, Fourie P, Dippenaar N, Ionescu GO. Intralesional bleomycin injection (IBI) treatment for haemangiomas and congenital vascular malformations. Pediatr Surg Int 2004; 19:766–773.
45. Sanlialp I, Karnak I, Tanyel FC, Senocak ME, Buyukpamukcu N. Sclerotherapy for lymphangioma in children. Int J Pediatr Otorhinolaryngol 2003; 67:795–800.
46. Zhong PQ, Zhi FX, Li R, Xue JL, Shu GY. Long-term results of intratumorous bleomycin-A5 injection for head and neck lymphangioma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998; 86:139–144.
47. Baud AV, Breton P, Guibaud L, Freidel M. Treatment of low-pressure vascular malformations by injection of Ethibloc. Study of 19 cases and analysis of complications. Rev Stomatol Chir Maxillofac 2000; 101:181–188.
48. Fung K, Poenaru D, Soboleski DA, Kamal IM. Impact of magnetic resonance imaging on the surgical management of cystic hygromas. J Pediatr Surg 1998; 33:839–841.
49. Marler JJ, Mulliken JB. Current management of hemangiomas and vascular malformations. Clin Plast Surg 2005; 32:99–116, ix.
50. Ricciardelli EJ, Richardson MA. Cervicofacial cystic hygroma. Patterns of recurrence and management of the difficult case. Arch Otolaryngol Head Neck Surg 1991; 117:546–553.