Case report

Imaging features and enhancement technique to diagnose and classify intrathoracic Lymphatic-venous malformations: A case report and literature review[☆],[☆☆],[★]

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A B S T R A C T

The diagnosis and treatment of pediatric intrathoracic lymphatic-venous malformations (LVM) can be complex due to their rarity, variable presentation and confusing nomenclature in the literature. The International Society for the Study of Vascular Anomalies (ISSVA) has recently (2018) updated their classification to help guide the correct diagnosis, nomenclature and management of such cases. We present the case of a 12-month-old Caucasian female with a lymph-venous malformation (LVM) classified in the updated ISSVA classification as a combined vascular malformation (CLVM) defined as two or more vascular malformations found in one lesion, associated with an underlying "malformation of an individual named vessel". The patient presented with tachypnea, tachycardia and fever. While all the previous cases underwent surgical treatment, our patient was successfully treated with rapamycin and sclerotherapy. Appropriate imaging can aid in the diagnosis of vascular anomalies and in the proper ISSVA classification, saving the patient the need for a biopsy and allow for proper referral to Multidisciplinary Vascular Anomalies centers. The accurate classification can identify cases that can be treated through Interventional Radiology with sclerosing agents and medical therapy as opposed to surgery.

Fig. 1 – Chest x-ray demonstrating a mass occupying the left upper and mid hemithorax with silhouetting of mediastinal and hilar margins. There is tracheal effacement and shift to the right.

Introduction

Pediatric intrathoracic lymphatic-venous malformations (LVM) are rare and require multidisciplinary teams to appropriately diagnose and treat. Recent revisions to the International Society for the Study of Vascular Anomalies (ISSVA) classification has helped further guide diagnosis and management of these lesions [1,2]. We present a case of a combined lymphatic-venous malformation (CLVM) presenting in a 12 month old. The CLVM demonstrates an underlying anomalous 'named vessel' in this case the brachiocephalic vein which has an ectatic peripheral end with entering draining vessels. A systematic review of the literature of pediatric intrathoracic CLVMs reveale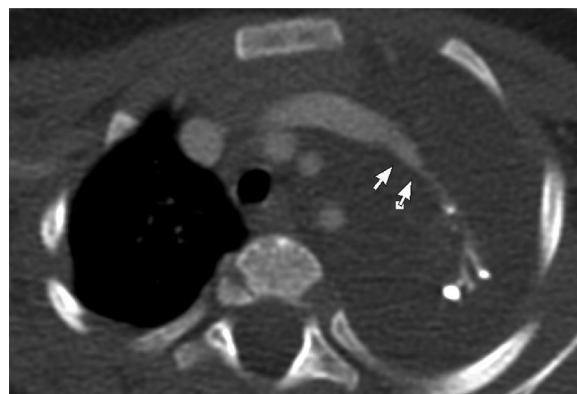d common imaging features with previous isolated case reports supporting the nature of the lesion and allowing comparison of treatment regimens. All previous cases where termed "lymphangiohemangioma or hemangiolymphangioma". By recognizing the imaging features common to this particular entity and utilizing the recent ISSVA classification, a diagnosis can be made, appropriate treatment initiated and valuable information on prognosis gathered.

Case report

A 12-month-old Caucasian female presented to the ER with a history of progressing difficulties in breathing over a 12-hour period. She was tachycardic and febrile upon presentation. A chest radiograph revealed a large soft tissue density mass occupying the left upper and mid hemithorax with silhouetting of the adjacent mediastinal margins and mass effect on mediastinum (Fig. 1). An enhanced CT with contrast injected at the left antecubital fossa demonstrated a multicys-

Fig. 2 – Oblique coronal CT MIP image demonstrating ectatic peripheral end of brachiocephalic vein (short arrow). Left subclavian vein enters just proximal to ectatic end(arrowhead). Areas of high attenuation related to contrast pooling (long arrow). Brachiocephalic vein course labelled B. Structures are encased by a mostly low attenuating mass correlating with the radiograph.

Fig. 3 – Axial CT image demonstrates anomalous vessels joining and draining into ectatic peripheral end of left brachiocephalic vein (arrows) which is encased by the low attenuating mass. Areas of high attenuation reflect contrast pooling.

tic mass with varying attenuation of cystic appearing components along with high attenuating ill-marginated serpiginous structures which coalesced into a vessel joining an ectatic peripheral brachiocephalic vein (arrows) which then normally drained into SVC (Figs. 2 and 3). More focal areas of high attenuation related to contrast medium reflux and pooling into the serpiginous vessels which reflect dysplastic veins mimicked calcification (Fig. 3). Superomedially, the mass infiltrated and encased vasculature without luminal narrowing. Abutting the inferior margin of the mass were lung parenchymal ground glass and consolidative opacities (not shown). Laboratory results revealed elevated White Blood Cell, platelet and LDH values. The patient was placed on antibiotics with subsequent
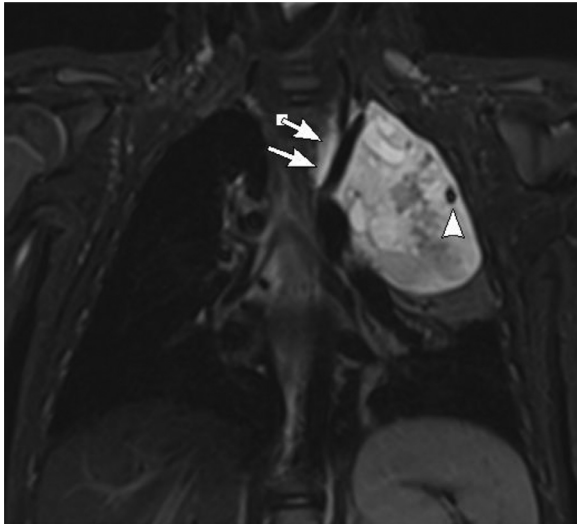
Fig. 4 – Coronal STIR MR better demonstrates the complex multicystic nature of the mass and the encasement of vessels (arrows - left subclavian artery). Focal low signal (arrowhead) was seen withing the mass.
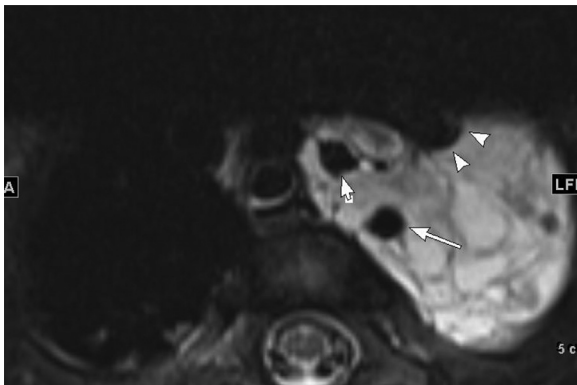
Fig. 5 – Axial T2 MR from a spine protocol series demonstrates ectatic/bulbous nature to peripheral end of brachiocephalic vein(arrowheads). Multicystic complex mass encases left subclavian artery (long arrow) and left carotid artery (short arrow).

resolution of all symptoms. Subsequent MR better demonstrated the multicystic nature of the mass with signal intensities supporting blood or proteinaceous products in a few of the cystic components (Figs. 4 and 5). The patient was started on Rapamycin with partial response. Six months later, the patient underwent 3 consecutive day sessions of sclerotherapy with Sodium Tetradecyl (STS) 3% and Doxycycline (total dose 310 mg in 3 macrocysts) (Fig. 6). A dark yellow fluid was removed from the cysts which was not sent for analysis. This was followed by a single day session of sclerotherapy with STS 3% and Doxycyclin (total dose 60 mg in 4 macrocysts) performed 2 months later. There was resulting complete resolution of the macrocystic components of the lesion. During the entire treatment to present, the patient continues to take Rapamycin. The patient has tolerated the medical treatment and
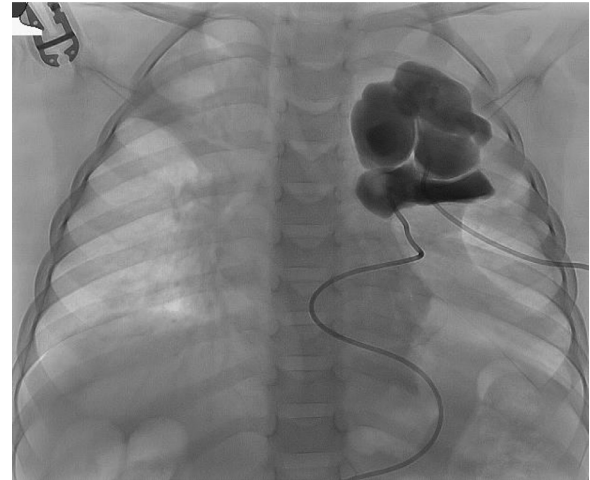
Fig. 6 – Fluoro image depicting contrast within the cystic components of the mass during treatment.
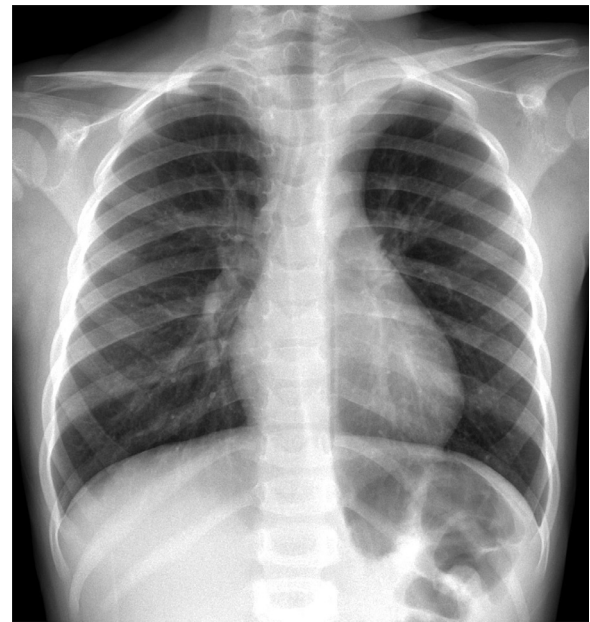
Fig. 7 – Follow-up chest x-ray post treatment demonstrates mild residual widening of mediastinum.

the procedures well with the most recent chest radiographs demonstrating marked decrease in size and extent (Fig. 7) of the lesion.

Systematic literature review

A systematic search of the literature in the past 30 years was performed to identify articles that described pediatric intrathoracic lymphatic-venous malformations. The Pubmed, Embase, Ovid, Scopus and Cochrane databases were searched using a combination of the following terms: intrathoracic lymph venous malformation, mediastinal lymph venous

Table 1 – Systematic literature review of cases involving LVM with management and outcome.

Author	Age at diagnosis	Clinical Presentation	Imaging Report	Treatment	Outcome
Bae, 2011	7 year-old male	Cough for 1 week, normal breath sounds and regular heart beat with no murmur	CT chest: "contrast entered vascular components of the mass vis an abnormal vein originating from left innominate"	Treatment: Two-stage surgical operation	No complications and recurrence 30 months after operation
Xu, 2005	17 year-old male	Asymptomatic	CT chest: "coronal plane reveals a large branch downward from the left innominate vein entering the mass"	Treatment: Surgical excision	Patient fully recovered and discharged after 1 week
Wittram et al, 1998	17-year-old male	History of dyspnea and hemoptysis	CT chest: large soft tissue mass involving the mediastinum. MRI chest: no extension of mediastinal tumor into the neck. Heterogeneous intermediate signal mediastinal mass with integral low signal regions.	Treatment: Sternotomy, radical debridement of the mediastinal mass, ligation of the thoracic duct	Uneventful recovery
Riquet, 1997	15-year-old male	History of asthma	Chest radiograph: right superoanterior mediastinal mass CT chest: large mass surrounding vena cava without calcification	Resected by sternotomy	Uneventful recovery
Riquet, 1997	18 year-old male	Referred for enlarging intrathoracic mass with a history of lymphangioma resection at 16 months of age	CT chest: "a vein originating from the left innominate vein extended into mass"	Treatment: Surgical excision	Uneventful recovery

malformation, lymphangiohemangioma, lymphatic venous malformation, venolymphatic malformation, hemangiolymphangioma and congenital vascular malformation. The population included patients 18 years and younger. The systemic search identified 12 articles. Articles dealing with solely mediastinal lesions with neck involvement were excluded. After review of the abstracts, two authors identified 5 articles with a pathologic diagnosis of lymphangiohemangioma or hemangiolymphangioma (3-6). All studies were case reports. The case described by Wittram et al. was further excluded as the description of the mediastinal mass with pulmonary lymphatic infiltration and pleural effusion was thought more compatible with a diagnosis of lymphangioendotheliosis. The extracted data from each publication consisted of author names, patient related characteristics including age and gender, presenting signs and symptoms, description of imaging performed, diagnosis, treatment and follow-up. The data is summarized in Table 1.

Results

After review, four cases remained with the final pathologic diagnosis of lymphangiohemangioma or hemangiolymphangioma Our case, more correctly termed a CLVM, represents an additional case and is included in the analysis giving a total of 5 cases in the literature. The age of the patients ranged from 12 months (our case) to 18 years. The majority of the patients were male (80%). The presentation was variable comprising fever [1], coughing [1], incidental from routine chest x-ray for military [1] and asthma [1]. One case report did not state presentation symptoms. All 5 cases had chest radiographs and CT imaging performed. Two cases, including ours, underwent MR imaging. Four of the 5 cases had surgical treatment. Our case was the only one describing medical treatment and sclerotherapy. Four of the 5 cases (including ours) described nearly identical CT imaging features consisting of a left sided in-

trathoracic mass with a description of an abnormal vein entering the brachiocephalic vein [3-5]. One case described numerous veins from the mediastinal mass entering the SVC [5]. Three cases had no complications post treatment up to 30 months of follow-up. One patient developed a chylothorax and underwent subsequent thoracic duct ligation and fully recovered [4].

Discussion

Intrathoracic congenital vascular anomalies of the combined lymphatic-venous malformation type are rare in children with only 5 reported cases found in the literature over the last 30 years [3-5]. These lesions have often been thought to be nonspecific on imaging resulting in the need for biopsy to confirm the diagnosis and exclude malignancy. Variable clinical presentations, lesion location and a potential for recurrence of these lesions, along with inadequate or erratic treatment response has resulted in continued confusion in diagnosis and management of these patients [7, 8] Our case was the only one describing medical treatment and sclerotherapy. In general sclerotherapy consist of the drainage of fluid from cysts and injection of a sclerosant substance that irritates and damage the cells covering cysts leading to inflammation and scarring preventing fluid re-accumulation. Our technique is done under General anesthesia and image guidance (Ultrasound, fluoroscopy or Cone Beam CT). A needle is inserted into the cyst, fluid is drained, contrast is injected to confirm that there was no communication with the pleural cavity or the venous system. Then the cyst is instilled with Sodium tetradecyl 3% for 10 minutes (1/2 volume of the cyst to a maximum dose of 0.5 mls/ Kg), drained again and then injected with doxycycline (100 mg diluted in 5 mls of sterile water and 5 mls of contrast). The rationale is to try to collapse as many macrocystic components as possible to reduce the chance of them refilling with fluid. Due to the potential risk of spontaneous bleeding or infection that could lead to expansion and potentially compression on adjacent vital structures treatment was deemed appropriate in our case. The presence of vascular components had no impact on the sclerosing treatment of the lymphatic components as there was no communication and no thought of the treatment agents escape into the venous system. A combination of STS with doxycycline is thought to enhance the sclerotizing effect [17].

Recent revisions in the international society for the study of vascular malformation (ISSVA) classification (May 2018) has helped guide the clinical diagnosis and allowed for optimized management of these patients, often without the need for biopsy. Re-assessment of earlier literature has helped identify common features, which allow for refinement in diagnosis and help elucidate best diagnostic and treatment options.

The ISSVA classification separates vascular anomalies into two main groups – vascular tumors distinguished by the presence of proliferating endothelial cells and endothelial hyperplasia (classified as benign, locally aggressive and malignant) and vascular malformations which are classed into 4 groups comprised of I) simple, II) combined, III) vascular malformations of major named vessels and IV) vascular

malformations associated with other anomalies [1]. Unlike vascular tumors the vascular malformations do not contain hyperplastic endothelial cells but rather are a result of vascular dysmorphogenesis which can be reflected as progressive enlargement of aberrant and ectatic lymph, venous, venules, capillaries or arterial channels or a combination [2,9,10,11]. The vessel anomaly as per the ISSVA classification can be of origin, course, number, length, diameter, valves, communication or persistence of an embryonal vessel [1]. The ectatic peripheral end of the left brachiocephalic vein with draining of vessels into this site, as in our case, we believe meets this criterion. Previous studies have focused on the embryology of the lymphatic system and the possible pathogenesis of the more common lymphatic malformations noted in the head and neck [18]. Theories propose that the lymphatic system arises from seven double and two single primordial which likely have a venous origin and that the anatomic location may be important in determining the histologic characteristics. Earlier descriptions describe a more rare central vascular component in some of these lesions previously described as "lymphangiohemangiomas" suggesting the malformation is the result of an abnormal 'bud' that retained its original venous communication. Updated nomenclature limits comparison with the earlier studies [19].

The review of the literature revealed four cases of intrathoracic lymphatic-venous malformation termed lymphangiohemangioma/hemangiolymphangioma. Assessment of the available imaging and imaging reports allowed for recognition of common descriptors with 4 of the cases including ours [3-5]. All cases had a left sided intrathoracic mass involving the mediastinum. All 4 cases underwent CT scanning with enhancement through the left antecubital fossa. There was description of a multicystic mass with an apparent anomalous vein filling retrograde from the brachiocephalic vein. Reconstruction images of our case demonstrated a coalescence of vessels forming an anomalous vein that drained into an ectatic/ bulbous peripheral end of the brachiocephalic vein. By having the injection of contrast on the side of the intrathoracic abnormality, the reflux of contrast into dysplastic feeding vessels joining the brachiocephalic vein was visualized, helping confirm diagnosis and aiding the classification. This reflux and pooling of contrast medium may mimic calcifications within the mass.

The development of the section of "anomalies of named vessels" in the ISSVA classification acknowledges that within each class, the formation of larger vessels (previously referred to as truncular) may behave differently than those not associated with larger vessel development [2,10]. Vascular malformations in general grow proportional to body growth regardless of vessel type, however, it is thought that if the aberration in embryogenesis happened at an earlier stage the anomalous vessels will be small and the malformation may maintain angioblastic and mesenchymal cell characteristics. Thus these lesions may have the potential to grow or recur in situations such as pregnancy and menarche [10]. The larger anomalous vessel size defining the section of "anomalies of named vessels", as in our case with the ectatic left brachiocephalic vein, suggests the insult occurred later in vasculogenesis with the angioblastic and mesenchymal characteristics likely less dominant and suggest growth and recurrence of this lesion

is less likely. The full embryologic description is beyond the scope of this review which is focused on the CT imaging of CLVM and the new ISSVA classification and readers are guided to the cited references.

The ability of imaging and in particular CT scanning with proper enhancement to identify these anomalous vessels aids in the diagnosis as well as proper treatment management and potentially allows for prognostic information for the parents. The larger size of the anomalous vessels, when the insult happens later in vasculogenesis, could potentially lead to more stagnant blood flow resulting in an increased risk of emboli [3,4,12,13]. Interestingly, D-dimer is elevated and used as a biomarker of venous malformations [7]. The differential for these lesions may include teratoma, neuroblastoma and imaging observations such as identification of an anomalous vessel as described in the updated ISSVA classification can save the patient the added work-up needed to exclude these entities.

Limitations of the study include the lack of available full imaging from the previous documented cases resulting in the reliance on descriptive terms within the articles. Additional, the misunderstanding of previously used inconsistent nomenclature may have limited assessment of the true nature of past lesions described in the literature and emphasizes the value of utilizing the recent ISSVA classification.

Conclusion

Appropriate imaging technique can aid in the diagnosis of vascular anomalies with proper ISSVA classification. On identification of an intrathoracic mass with possible mediastinal involvement the authors support other researchers [4,14] in believing CT enhanced imaging should be performed through the side of involvement. This may save the patient the need for a biopsy and allow for proper referral to centers with the adequate expertise of multidiscipline vascular teams. MR can further allow for improved characterization of the mass and assessment of infiltrative extent. The accurate classification can guide management with the knowledge the lesion is of low flow and susceptible to sclerosing agents with recurrence less likely than with the vascular malformations without noted large 'named' vessel involvement, potentially saving the patient the surgical intervention so common in the past literature [3, 9,15,16].

Ethics approval

This study was reviewed and approved by the Queen's University Health Sciences & Affiliated Teaching Hospitals Research Ethics Board

Consent to participate

Not applicable

Consent for publication

All authors have reviewed and approved this manuscript for publication

Availability of data and material

Available upon request

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