

CASE REPORT

Always expect the unexpected: cystic mediastinal lymphangioma in infants – case report and review of the literature

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ABSTRACT

In the paediatric population, mediastinal tumours occur quite often. They include a variety of entities, with different aetiologies. The most common tumours localised in the anterior mediastinum include thymoma, lymphoma, and teratoma. Herein we present the case of an 8-month-old female infant diagnosed with a huge mediastinal solid-cystic tumour causing superior vena cava syndrome. Ultrasonography-guided needle aspiration was performed. The aspirated fluid contained no epithelial cells but many lymphocytes and neutrophils, based on a cytological analysis. The culture of the material revealed *Staphylococcus aureus* MRSA. In accordance with the antibiogram, the vancomycin therapy was continued. The antibiotic treatment was continued for 6 weeks achieving complete remission of the lymphangioma, which had lasted for one year.

KEY WORDS:

mediastinal tumour, lymphangioma, infant, treatment.

INTRODUCTION

In the paediatric population, mediastinal tumours are quite common. They include a variety of entities, with different aetiologies. The most common tumours localised in the anterior mediastinum include thymoma, lymphoma, and teratoma. Mediastinal lymphangiomas are rare, benign congenital malformations that arise from focal

proliferation of lymphatic vessels [1]. They comprise up to 4.5% all mediastinal tumours.

The most common localisations of lymphangiomas are the head, neck, and axilla, with only 1% being confined to the mediastinum [2]. The former group tends to present in infants, and the latter more commonly occurs later in life. Based on its ultrasonographic (US) characteristics, it is commonly subdivided into cystic or cavernous lymphangioma [3]. Dependent on the size of the lesion, they

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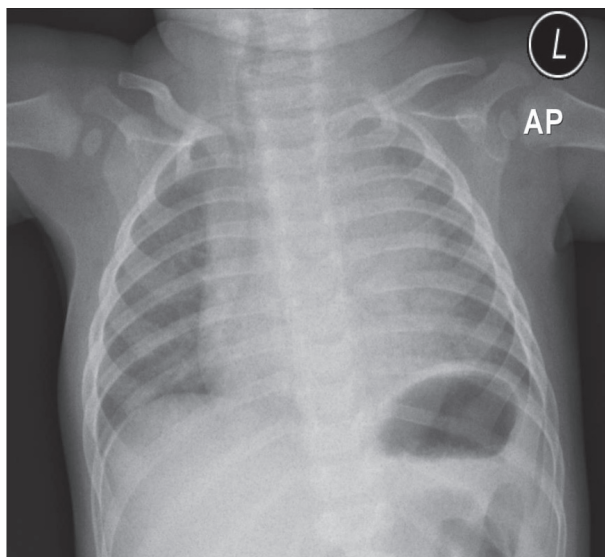


FIGURE 1. Chest X-ray on admission to regional hospital

can be characterised as macrocystic (diameter > 1 cm), microcystic (diameter < 1 cm), or mixed cystic lesions [4]. Clinically lymphangiomas are benign malformations, but complications can occur, including infection, cystic haemorrhage, superior vena cava syndrome (SVCS), airway compromise, chylothorax, and chylopericardium [5].

It is difficult to differentiate mediastinal lymphangiomas on chest radiograms from other benign cystic mediastinal lesions such as bronchogenic, thymic, and pericardial cysts. However, lymphangiomas are easily differentiated on chest radiograms from low-density lesions such as thymoma, lymphoma, and teratoma. For identification and differential diagnosis, US, computed tomography (CT) lymphangiography, and magnetic resonance imaging (MRI) are helpful in determining both the extent of the disease and the cystic and lymphatic nature of the mass [6]. Herein we present a very rare case of huge mediastinal solid-cystic tumour causing SVCS in an 8-month-old female infant.

CASE REPORT

An 8-month-old female infant was admitted to the regional hospital due to fever of unknown aetiology lasting for 5 days and vomiting. The family doctor started antibiotic therapy including amoxicillin and clavulanic acid. The baby was previously healthy, and the pregnancy had been uncomplicated. She did not have a family history of cancer. Physical examination on admission showed a healthy looking child with fever, sore throat, and a hard lump palpable in the left supraclavicular region. The skin over the lesion was erythematous. Blood tests revealed leukocytosis ($24.0 \times 10^9/l$) with 5% of immature neutrophils in differential blood test, high serum C-reactive protein (CRP) level (360.0 mg/l), and very high plasma D-dimer concentration (14707 ng/ml). Chest X-ray disclosed bilateral perihilar interstitial opacities typical for pneu-

monia and a large mass in the mediastinum described by the radiologist as “probably the thymus” (Figure 1). Antibiotic therapy based on cefotaxime was implemented. The lump on the neck disappeared, but the fever persisted and the CRP level decreased very slowly. A control chest X-ray showed the same picture as previously, and vancomycin was added to the treatment. Two days later the girl suddenly presented a lump in suprasternal region, and point-of-care US revealed a solid-cystic mass in the anterior mediastinum. Due to suspicion of a mediastinal tumour, the patient was urgently transferred to the paediatric oncology ward. At presentation, she was found to have elevated WBC count of $11.4 \times 10^9/l$, platelet count of $514 \times 10^9/l$, and CRP level of 210.2 mg/l. The thoracic US revealed a heterogeneous solid-fluid, multi-cystic lesion up to $7.3 \times 3.5 \times 8.5$ cm penetrating also to the cervical area. The thorax CT scan disclosed an extensive, irregularly shaped solid-cystic tumour localised in the anterior mediastinum, mostly on the left side. The tumour penetrated the cervical area through the superior thoracic aperture. The tumour dimensions, including the cervical part, reached up to $6.7 \times 5.8 \times 9.7$ cm. The mediastinal mass caused the constriction of the left brachiocephalic vein. Moreover, the trachea was compressed to almost a slit by the mass. Based on the CT scan results, cystic lymphangioma was diagnosed (Figure 2). Due to an increase of inflammatory markers, the antibiotic treatment comprising cefotaxime and vancomycin was continued. In view of severe breathlessness, an emergency intercostal drain was attempted. On aspiration there was only a small amount of haemorrhagic purulent fluid drained. Flow cytometry of a sample from fine-needle aspiration was not compatible with lymphoma. The cytology showed a majority of neutrophils excluding the possibility of acute myeloid leukaemia, while the fluid culture revealed methicillin-resistant *Staphylococcus aureus*. Based on above results, the antibiotic therapy was continued in accordance with the antibiogram, i.e. vancomycin. Follow-up CT after 8 days of treatment demonstrated significant regression of lymphangioma sizes (Figure 3), not expected in the result of unsuccessful drainage, but rather due to antibiotic therapy, so the treatment was continued. After the next 21 days, the follow-up thoracic MRI showed a further decrease in the size of the tumour with only residual microcystic lesion $2.1 \times 1.6 \times 1.7$ cm in diameter (Figure 4). At that time the patient was free of symptoms and all inflammatory markers were within normal ranges. The treatment was switched to oral clindamycin and continued up to 6 weeks, achieving complete remission of the lymphangioma. The patient is stable with no recurrence at one-year follow-up.

DISCUSSION

Most lymphangiomas are located in the head and neck area [3]. Clinical manifestations of lymphangioma vary

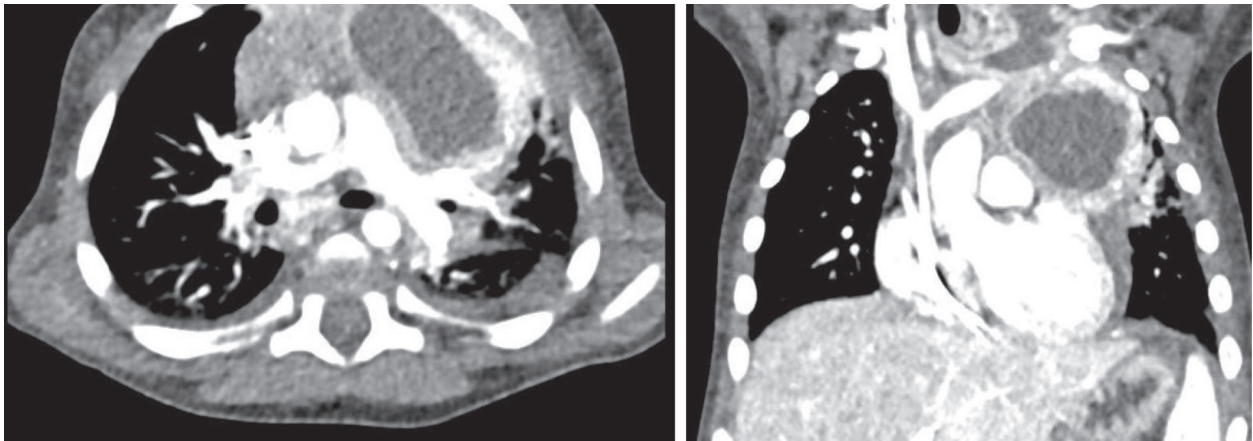


FIGURE 2. Thorax CT scan (with contrast) at diagnosis

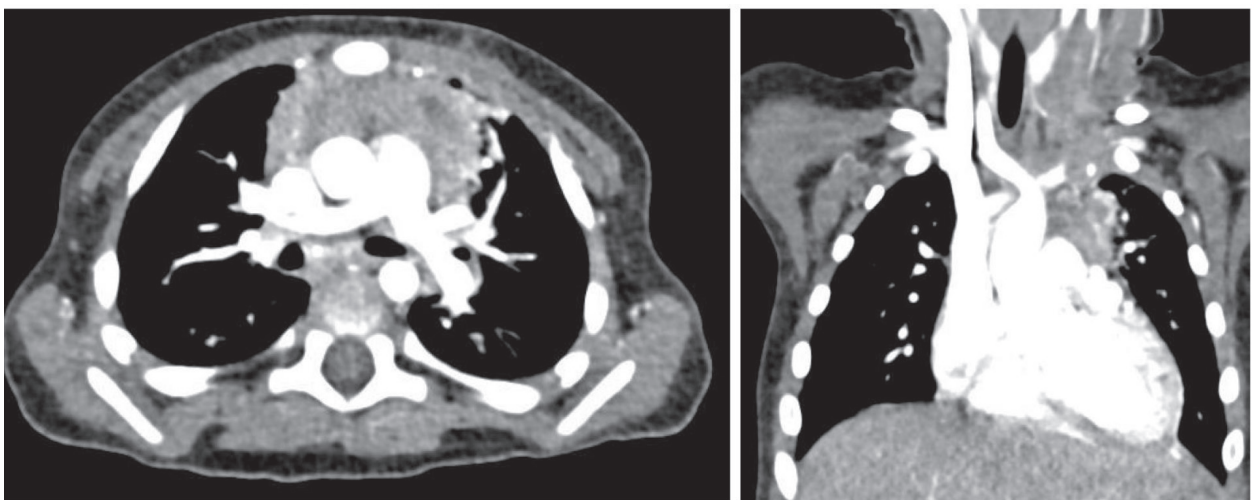


FIGURE 3. Follow-up CT scan of the thorax after 8 days of the antibiotic treatment

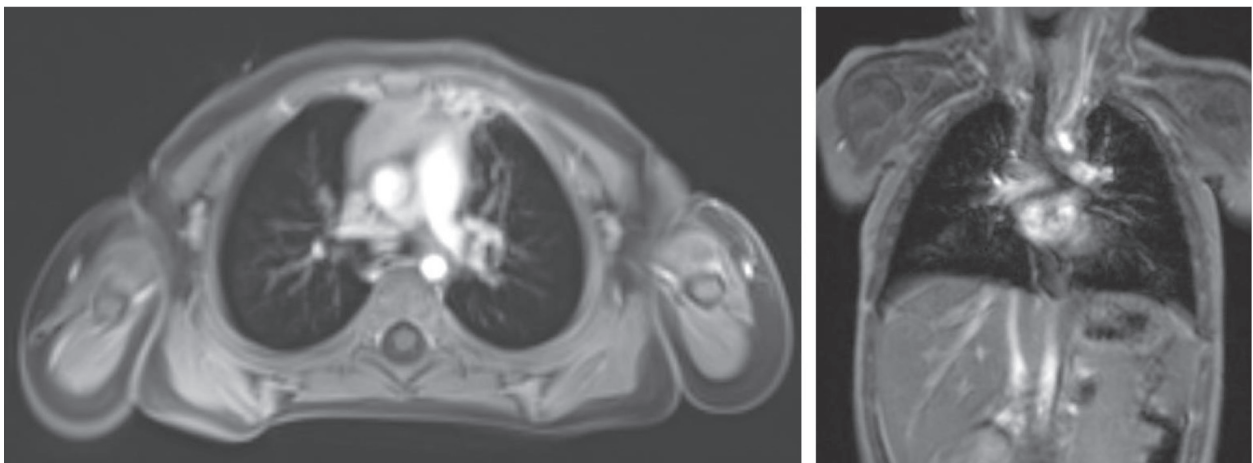


FIGURE 4. Follow-up thoracic T1-weighted MRI 21 days after the previous CT scan

among the patients and depend on tumour location [7]. Histopathologic examination of lymphangioma tissue remains the gold standard for definitive diagnosis and for differentiation from other cystic formations, such as benign mediastinal cyst, bronchogenic cysts, thymic cysts, or others. However, in our case, histologic diagnosis was not possible due to bacterial infection of the cys-

tic formation, which apparently resolved after antibiotic therapy. Thus, diagnosis of lymphangioma was based on imaging modalities, especially CT, which helped differentiate lymphangioma from other cystic mediastinal lesions. On CT scans, lymphangiomas typically appear as well-defined, cystic masses with fluid attenuation, often with internal septations. They may show compression

of adjacent structures and, occasionally, internal debris or calcifications. The appearance can be homogeneous or inhomogeneous, depending on the fluid content, which can vary.

According to the literature, the most common symptoms of mediastinal lymphangioma are dyspnoea, respiratory insufficiency, and SVCS [4, 8]. Lymphangiomas are usually characterised by slow and steady growth [4,9], but under certain conditions, including infection or trauma, they can grow explosively and require immediate treatment [9]. In our patient, the accelerated growth of the tumour was probably caused by the clinically documented infection. Hence, due to the presented symptoms of infection, the patient required urgent antibiotic therapy, which finally covered both the infection and the mediastinal lymphangioma.

As can be seen in the literature, in the treatment of lymphangiomas the first commonly considered possibility is surgery [9]. The priority is resection of the lesion with minimal damage to adjacent structures [10]. Although lymphangiomas are mostly benign, their location is usually linked with the symptoms that exacerbate the patient's state and lead to difficulties in performing the surgical excision. Moreover, the complications reported after the operation are significant, including nerve injury, haemorrhage, seroma, lymphorrhoea, and infections. Furthermore, incomplete resection, high risk of important tissue injury, and high recurrence rate are associated with surgical treatment [9, 10]. The conclusions of a retrospective review, which objected to outlining a rational approach to lymphangioma management, indicated that treatment of this condition requires experience of the physician, awareness of spontaneous resolution, and consideration of the limitations and potential harm of surgery [11]. Other procedures considered in lymphangioma treatment include aspiration, radiofrequency ablation, or laser therapy [12]. In our case, taking into consideration the extensiveness of the tumour and the risk of complications associated with the procedure, surgical excision of the mass was not advisable. Nonetheless, aspiration of the small amount of fluid was performed, which allowed exclusion of the presence of malignant cells through flow cytometry and cytological analysis of the fluid.

Besides surgery, alternative lymphangioma treatment includes sclerosing agents and drugs with specific targets for biological therapy [9]. Sclerosants include OK-432, doxycycline, bleomycin, ethanol, hypertonic saline, acetic acid, and sodium tetradecyl sulphate [7]. The benefits of injection of sclerosing agents into the lesion, in contrast to surgical resection, are lower risk of nerve injury and a simpler procedure [7], which may reduce the role of surgical excision in lymphangiomas treatment in the future [12]. Compared to other medications, because of both their efficiency and safety, sclerotherapy with OK-432 (Picibanil®) is advantageous [4]. It is a freeze-dried biological product that is prepared from the Su

strain of *Streptococcus pyogenes* (group A) by treatment with benzyl-penicillin and heat. Heating in the presence of penicillin at 37°C for 20 min and 45°C for 30 min increases the antitumor activity of the Su strain and eliminates its toxin-producing capacity. The result of its action is the obliteration of lymphatic channels with minimal local fibrosis [4]. Although its usage in children remains controversial, there are significant, positive results reported in the literature [4]. According to the studies, a good response to OK-432 therapy is observed in the majority of patients [4, 8]. Moreover, a positive outcome of OK-432 treatment was observed in the study enrolling paediatric patients with lymphangioma who received this medication as first-line therapy and as well as patients who underwent surgery, which points out the effectiveness of OK-432 in both primitive and recurrent lymphangioma management [13]. Taking into consideration its safe application and, unlike surgery, absence of serious side effects [4, 8], picibanil sclerotherapy could be considered the first-line treatment for macrocystic and mixed-type lymphangiomas [4]. As suggested by the authors of the current meta-analysis aimed at verifying the efficacy of picibanil concerning lymphangioma classification, OK-432 should be used to treat lesions with diameter greater than 1 cm [14]. Concerning all the described data and information given about our patient presented above, the potential use of OK-432 could have resulted in the successful management of the lesion, but its administration was not necessary because of the presence of *Staphylococcus aureus*, which presumably mimicked the effects of picibanil. Thus, the implementation of proper antibiotic therapy was a priority, and it resulted in both infection treatment and reduction of the tumour mass.

Additionally, there are recently observed attempts to treat lymphangioma with oral medical drugs, including sildenafil, propranolol, or sirolimus. Mostly, their exact mechanisms of action, indications, and efficiency in lymphangioma treatment require further research and verification, but the results are promising. Similarly, the combined treatment needs evaluation and investigation, which may eventually lead to lymphangioma treatment improvement [7].

As previously distinguished, the rational and individual approach is essential for lymphangioma treatment. Despite surgery being traditionally considered the first choice of lymphangioma management, the coexisting risks and complications indicate the necessity of searching for different and improved ways of treatment. As described in our patient, the importance of targeted antibiotic therapy cannot be diminished, and the decision about surgical intervention demands balanced scrutiny.

DISCLOSURES

1. Institutional review board statement: Not applicable.
2. Assistance with the article: None.

3. Financial support and sponsorship: None.

4. Conflicts of interest: None.

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