Spontaneous pneumothorax or no pneumothorax at all?

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Shareable abstract (@ERSpublications)
Care of a simple pneumothorax in a paediatric patient is often anything but simple, and a refractory and complex pneumothorax requires thoughtful and deliberate care
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Introduction

In this report, we describe a small child with spontaneous pneumothorax who was transferred to a tertiary referral hospital and discovered to represent a classic presentation of a rare entity.

Case

A 13-month-old male initially presented with respiratory distress. He had a fever of 38.9°C (102°F), a non-productive cough, and shortness of breath that had gradually worsened over the preceding week. There was no rash, cyanosis, nausea, vomiting or diarrhoea. There were no known sick contacts. He was born at full term without complications. His primary care physician had recently noted concern over new weight loss with concomitant decreased oral intake, causing him to drop below the 10th percentile for height and 1st percentile for weight. There was no prior chest imaging available for review. He had no other reported medical problems.

On arrival at the emergency department, he had a peripheral oxygenation saturation of 65%, with tachycardia, tachypnoea and bilateral subcostal retractions. Decreased breath sounds were heard on the left but preserved on the right. No wheezing, rhonchi, rales or crackles were heard. Oxygenation did not improve with administration of 100% supplemental oxygen *via* nasal cannula.

Task 1

What is the most appropriate next step?

a) Intubation
b) Urgent echocardiogram
c) Administration of an inhaled therapy
d) Viral testing
e) Emergent chest radiography

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A large left-sided pneumothorax was seen on plain film (figure 1). A percutaneous pigtail catheter was placed, with immediate improvement in condition; however, the patient remained tachypnoeic, with peripheral saturation consistently around 90%. The decision was made to admit the patient to an intensive care unit. A respiratory viral PCR was positive for parainfluenza virus type 2.

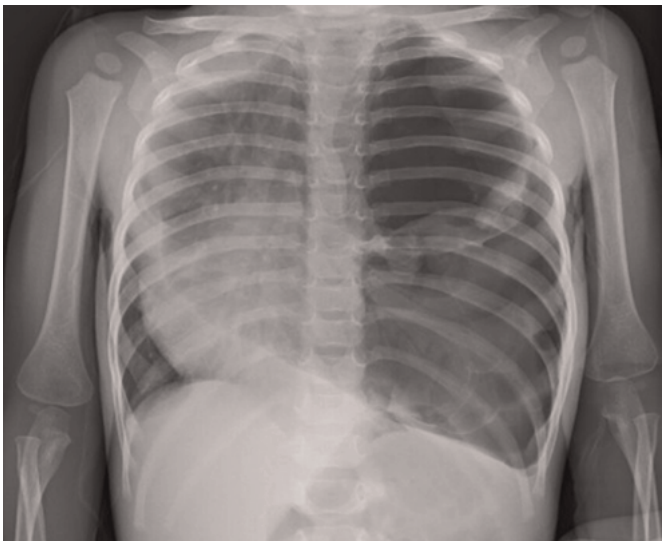

FIGURE 1 Anterior–posterior-oriented plain radiography of the patient with hypolucency of the entire left upper lobe, initially read as spontaneous tension pneumothorax.

Task 2

What study would be most helpful to determine the next steps in evaluation and care?

a) Computed tomography (CT) of the chest, with contrast
b) Echocardiogram
c) Electrocardiogram
d) Ultrasound of the chest

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CT of the chest demonstrated a multilocular cystic lesion believed to be most consistent with congenital pulmonary airway malformation (CPAM) in the left hemithorax, originating from the left upper lobe and extending to the right mediastinum, with residual left-sided pneumothorax status post-thoracostomy (figure 2). The patient was initially treated with broad-spectrum antibiotics and insertion of a second chest tube to evacuate residual pneumothorax, with slow improvement of his condition over the following days. However, after 4 days, he began worsening clinically, with newly recurrent fevers and re-escalation of

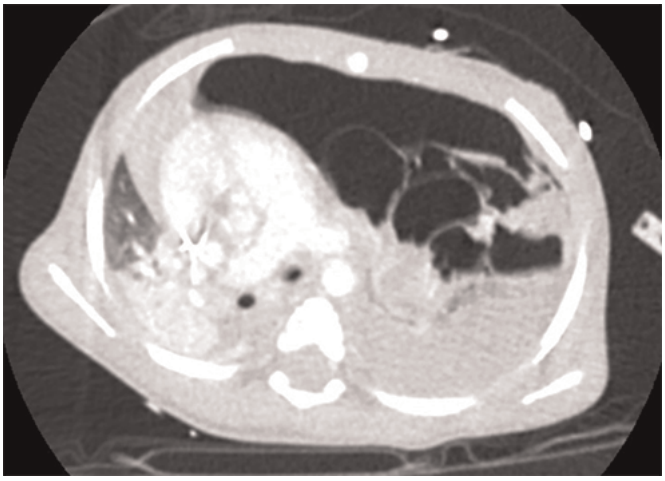

FIGURE 2 Axial view of chest computed tomography with intravenous contrast, showing what appears to be residual pneumothorax in the left upper lobe.

supplemental oxygen requirements. Repeat chest radiography showed enlarging pneumothorax despite multiple thoracostomies. A persistent air leak was observed in the newly placed chest tube.

Task 3

Which of the following is an indication for open thoracoscopy?

a) Recurrent pneumothorax associated with bullous lung disease
b) Concern for malignant transformation of the lesion
c) Mild to moderate asthma
d) Primary pneumothorax with failure to wean oxygen after 3 days

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The patient underwent video-assisted thoracoscopy, where the chest tube was found to terminate in the lesion arising from the left lower lobe. The lesion was completely resected (figure 3), after which the supplemental oxygen requirement rapidly improved. The patient was able to be discharged home the following week. Pathology confirmed a type I cystic pleuropulmonary blastoma (PPB) with negative margins.

Task 4

What genetic testing should be obtained in patients with confirmed PPB?

a) p53 mutation assay
b) DICER1 mutation assay
c) Complete karyotype
d) FLCN mutation assay

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Germline testing for a DICER1 gene mutation revealed a pathogenic mutation. With a complete resection, no adjuvant therapy was indicated for type I PPB. The patient has been followed with serial imaging, without clinical recurrence of disease as of the time of this publication, with weight above the 60th percentile and height above the 40th percentile.

Discussion

Pneumothoraces are unusual in children beyond the neonatal period, ranging from 1 in 100 000 in females to 1 in 400 000 in males [7]. While a spontaneous pneumothorax is most likely to afflict an adolescent male with tall, thin body habitus, our patient's age and clinical course did not fit the typical presentation, although rare occurrences of early spontaneous pneumothorax have been reported in patients with neonatal Marfan syndrome [8, 9]. Our patient's failure to respond to initial intervention resulted in additional radiological evaluation, which revealed a complex cystic lung lesion. While the presence of simple cysts or bullae does not predict recurrence of pneumothoraces in children, the presence of a complex cystic lung

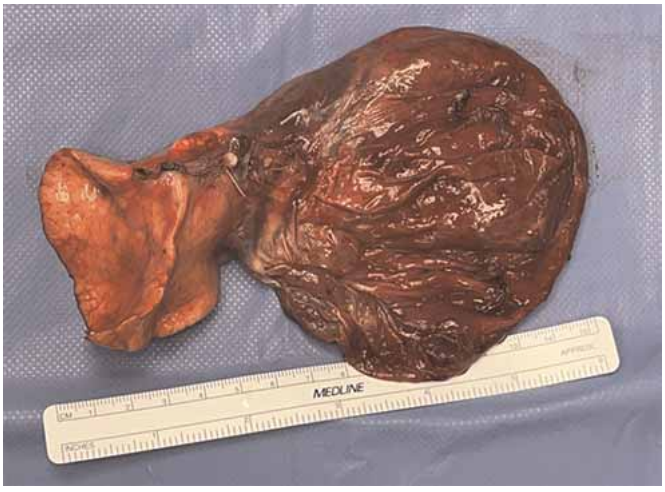

FIGURE 3 The lesion arising from the left upper lobe after resection.

lesion concerning for CPAM, failure to improve after 5 days of conservative treatment and clinical worsening of our patient warranted further intervention [3].

Primary pulmonary malignancies are rarely seen in childhood, with the most common being PPB. PPB most commonly occurs before the age of 4 years and may arise from lung or pleural tissue. Childhood lung cancer represents <1% of all pulmonary malignancies, with PPB being the most common [10]. PPB is subdivided into type I, type I-regressed (Ir), type II and type III lesions. Type I PPB is purely cystic and requires no adjuvant therapy, given the very favourable prognosis in the setting of a complete resection with negative margins. Types II and III PPB have solid components, are associated with a more guarded prognosis, and require adjuvant therapy. Type Ir is a prior PPB that has regressed [11, 12].

PPB with a large cystic component, as in our patient, is often initially misdiagnosed as other conditions such as CPAM [13]. Initial presentation depends on the lesion but may include fever, respiratory distress and pneumothorax, with imaging showing variation from single- to multi-cystic disease or solid lesions without any cystic component. For persistent cystic lesions without clinical improvement, surgical intervention as both a therapeutic and diagnostic intervention is currently recommended.

As further cases are contributed to our current medical knowledge, there are some who recommend serum-based DICER1 mutation assays as a guide for surgical intervention in selected cases, as radiology-based assessments often fail to differentiate between congenital and malignant lesions [14]. DICER1 mutations have been associated not only with type I PPB but also with cystic nephromas, thyroid carcinoma and gynaecological cancers, making testing important for immediate as well as long-term prognosis [5]. Both type II and III PPB have increased risk for distal metastasis, with reports of local nodal extension and spread to brain, spine, bone and liver [15]. CT imaging of the chest, abdomen and pelvis, and magnetic resonance imaging of the brain and spine, are recommended for evaluation of metastasis. Type III PPB has a greater risk for cerebral involvement. Both type II and III have variable treatments, but these typically consist of excision if amenable, as well as combination chemotherapy and radiation [16].

While our patient had a positive outcome, PPB continues to represent a rarely encountered malignancy, both in our selected population and in clinical practice. The adherence to evidence-based and guideline-directed investigation and intervention resulted in the correct diagnosis in our case, allowing for both continued addition to our global understanding of this malignancy as well as better understanding of how adept our current recommendations are at helping us to both identify and optimally treat this disease.

Answer 1

e. Emergent chest radiography. Respiratory distress with unilateral decreased breath sounds and failure to respond to supplemental oxygen should raise significant concern for a pneumothorax, which can be confirmed by point-of-care ultrasound or chest radiography if clinical condition allows. If tension pneumothorax is highly suspected and there is not sufficient time to obtain a chest radiograph, then needle thoracostomy should be considered prior to formal imaging being performed. The patient was awake, failed to respond to supplemental oxygen, and had unilateral decreased breath sounds, making pneumothorax highly likely. If the pneumothorax is the principal driving aetiology of the patient's presentation, then intubation is not likely to have substantial benefit. No abnormal birth history or cyanosis were reported, which made a cardiac defect less likely. There was no wheezing or history of respiratory difficulties in the past, making inhaled therapies less likely to help. Viral testing can be helpful, depending on the clinical course, but has no role in emergent resuscitation.

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Answer 2

a. CT of the chest, with contrast. The evacuation of a clinically significant pneumothorax with continued ill appearance of the patient and incomplete resolution of hypoxia after appropriate intervention calls into question the initial diagnosis. Chest CT not only allows for confirmation of chest tube positioning, but also allows for better delineation of existing pulmonary anatomy and more detailed assessment of the pulmonary parenchyma in its entirety than chest radiography or chest ultrasound, although available literature suggests that CT may be inadequate to accurately differentiate lung malformations and does not obviate the need for pathological diagnosis [1]. An ultrasound of the chest could confirm resolution of the pneumothorax and provide evidence for hidden pleural or pericardial effusion, but is less helpful for defining pulmonary anatomy and the location of radiopaque structures, like a chest tube. Echocardiography could be considered if cyanosis or clinical signs of tamponade (*i.e.* electrical alternans, pulse pressure variation) were present. A screening electrocardiogram is reasonable but is not likely to be immediately helpful, given the clinical features of the case thus far.

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Answer 3

a. Recurrent pneumothorax associated with bullous lung disease. The American College of Chest Physicians provides a consensus statement recommending thoracoscopy for those with secondary pneumothorax believed to be associated with cystic or bullous disease [2]. While this is based on review of evidence in adult patients, prevailing expert opinion applies this to the paediatric population as well. Baird *et al*. [3] provide a review of available reports that are inconclusive regarding resecting an asymptomatic cystic lesion believed to be attributed to CPAM but agree that a cystic lesion causing clinically significant illness warrants removal. Expert opinions are mixed as to whether removal of the relevant lesion reduces the risk of malignant transformation if the lesion is confirmed to be a CPAM, making answer b less correct. Thoracoscopy is contraindicated in those with mild asthma, though may be considered in those with severe asthma that fails to improve. Thoracoscopy with possible pleurodesis can be considered in patients with primary pneumothorax that fail to improve after 5 days or in cases of recurrent pneumothorax.

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Answer 4

b. A germline DICER1 gene mutation is observed in a high percentage of patients with PPB, providing highly significant prognostic and treatment indications for future care [4]. p53 mutations have been associated with Li–Fraumeni syndrome and numerous neoplasms, including sarcomas, brain tumours, adrenocortical carcinoma and breast cancer, but have not been directly associated with PPB [5]. A whole chromosome defect has also not been associated with a syndrome predisposing to PPB, making a karyotype unhelpful. Mutations in the tumour suppressor gene FLCN are seen in Birt–Hogg–Dubé syndrome, which commonly manifests with recurrent spontaneous pneumothorax as well as bilateral pulmonary cysts and renal tumours. FLCN mutations are not known to cause PPB [6].

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Conflict of interest: The authors have nothing to disclose.

References

1 Engwall-Gill AJ, Chan SS, Boyd KP, *et al.* Accuracy of chest computed tomography in distinguishing cystic pleuropulmonary blastoma from benign congenital lung malformations in children. *JAMA Netw Open* 2022; 5: e2219814.
2 Baumann MH, Strange C, Heffner JE, *et al.* Management of spontaneous pneumothorax: an American College of Chest Physicians Delphi consensus statement. *Chest* 2001; 119: 590–602.
3 Baird R, Puligandla PS, Laberge JM. Congenital lung malformations: informing best practice. *Semin Pediatr Surg* 2014; 23: 270–277.
4 Hill DA, Ivanovich J, Priest JR, *et al.* DICER1 mutations in familial pleuropulmonary blastoma. *Science* 2009; 325: 965.
5 Stewart DR, Best AF, Williams GM, *et al.* Neoplasm risk among individuals with pathogenic germline variant in DICER1. *J Clin Oncol* 2019; 37: 668–676.
6 Daccord C, Good JM, Morren MA, *et al*. Birt–Hogg–Dubé syndrome. *Eur Respir Rev* 2020; 29: 200042.
7 Dotson K, Johnson LH. Pediatric spontaneous pneumothorax. *Pediatr Emerg Care* 2012; 28: 715–720.
8 Robinson PD, Cooper P, Ranganathan SC. Evidence-based management of paediatric primary spontaneous pneumothorax. *Paediatr Respir Rev* 2009; 10: 110–117.
9 Le Gloan L, Hauet Q, David A, *et al.* Neonatal Marfan syndrome: report of a case with an inherited splicing mutation outside the neonatal domain. *Mol Syndromol* 2016; 6: 281–286.
10 Mlika M, Anjum F, El Mezni F. Pleuropulmonary blastoma. Treasure Island, StatPearls Publishing LLC, 2023.
11 Knight S, Knight T, Khan A, *et al.* Current management of pleuropulmonary blastoma: a surgical perspective. *Children* 2019; 6: 86.
12 Messinger YH, Stewart DR, Priest JR, *et al.* Pleuropulmonary blastoma: a report on 350 central pathology-confirmed pleuropulmonary blastoma cases by the International Pleuropulmonary Blastoma Registry. *Cancer* 2015; 121: 276–285.
13 Dehner LP, Schultz KA, Hill DA. Pleuropulmonary blastoma: more than a lung neoplasm of childhood. *Mo Med* 2019; 116: 206–210.
14 Murphy AJ. Can computed tomography scans reliably distinguish pleuropulmonary blastoma from congenital lung malformations? *JAMA Netw Open* 2022; 5: 2219826.
15 Hamad SG, Al-Naimi A, Abu-Hasan M. Pleuropulmonary blastoma (PPB) in child with DICER1 mutation: the first case report in the state of Qatar. *Case Rep Pulmonol* 2021; 2021: 1983864.
16 Priest JR, Magnuson J, Williams GM, *et al.* Cerebral metastasis and other central nervous system complications of pleuropulmonary blastoma. *Pediatr Blood Cancer* 2007; 49: 266–273.