Acquired air-filled lung cysts in childhood: pathogenesis of cysts of diverse etiologies; nuances of management

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Background **Air-filled pulmonary parenchymal cysts (pneumatoceles/PCs) – a pathological condition – involving the lung parenchyma may be congenital or acquired. In children, acquired cases are often caused by staphylococcal pneumonias, but other etiologies may also cause PCs and lead to diagnostic confusion.**

Objectives **The aim of this study was to examine the natural history and clinicopathologic features of noncongenital, nonstaphylococcal PCs in children.**

Patients and methods **Four children with nonstaphylococcal PCs were included in this study. A full history, clinical examination, relevant radiological and pathological findings, surgical intervention where relevant, and follow-up were analyzed.**

Results **The cases described represent acquired PCs: one occurred after infarction following cardiac surgery, another was a subpleural pulmonary bleb of inflammatory origin, and the remaining two were post-traumatic pseudocysts. The inflammatory-process bleb and the postinfarction cysts presented with pneumothorax. The postinfarction and post-traumatic PCs responded to observation. The pulmonary bleb was excised.**

Conclusion **Our understanding of the clinicopathologic features and pathogenesis of many types of acquired PCs is incomplete. We propose that PC formation has a basis in destruction of the distal airways of the lung. Damaged tissue may act as a valve, and cause air-trapping, which leads to PC formation. Cysts arising after infarction or after trauma usually resolve on observation. Subpleural blebs may require excision because of nonresolution and recurrence of pneumothorax.** ***Ann Pediatr Surg*** **12:129–132 © 2016 Annals of Pediatric Surgery.**

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Introduction

Pneumatoceles (PCs) are thin-walled, air-filled cysts found subpleurally in the lung parenchyma. In children, cysts of congenital origin are more common. Cystadenomatoid malformations, pulmonary sequestration, bronchogenic cysts, and congenital lobar overinflation are the usual causes of cystic lung lesions in childhood [1]. All these may present early in life, often with cystic air-filled lesions in the periphery of the lung, and usually require surgical treatment.

Cysts occur because of other disparate acquired etiologies as well. Infections in patients with cystic fibrosis and staphylococcal pneumonia as well as intoxications like kerosene poisoning and metal polish also cause cyst formation in lungs [2,3].

We reported individually the processes of ischemia, trauma, and obscure inflammation also leading to cyst formation in the lungs of children [4–6]. Here, these causes are brought together with the intention of the following.

(1) Highlighting the occurrence of cysts with lesser known etiologies.
(2) Outlining their natural history.
(3) Proposing an analytical thinking on their origins and management.

Materials and methods

This was a retrospective study carried out at Aseer Central Hospital, a tertiary care hospital. Children presenting with air-filled cysts on chest radiography with diverse, noncongenital or nonstaphylococcal etiology were the subject of this study. Clinical data at presentation and results of relevant investigations were gathered from their case notes. Radiographs (in all cases) and the pathology report (in one case) were reviewed; the pathological material submitted was subjected to further scrutiny with special stains to clarify etiology in the relevant case (case 2). Progress of the lesions was followed up over a period of 1 year in cases 1, 3, and 4 with serial plain radiographies and computed tomographic (CT) scans.

Case 1

HAA underwent a modified left Blalock-Tausig shunt soon after birth for complex congenital heart disease (double outlet right ventricle, a secundum atrial septal defect, a large inlet ventricular septal defect, transposition of the great vessels, mild hypoplasia of the right ventricle atresia of the pulmonary valve, and hypoplasia of the pulmonary arteries).

At 6 months of age the Blalock-Tausig shunt was taken down and a Glen shunt with augmentation of the left pulmonary artery was implanted. At discharge the parents

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were informed of the appearance of cysts in her left lung. Two months after the second operation she presented to our emergency room (ER) with pneumothorax on the left side. The pneumothorax was drained and a CT scan revealed multiple, large, air-filled cysts in the left lung (Fig. 1). A policy of observation of these cysts was decided upon. At follow-up 1 month later there were no cysts in the left lung on chest radiographies. Six months later complete involution of the cysts was confirmed on CT scan.

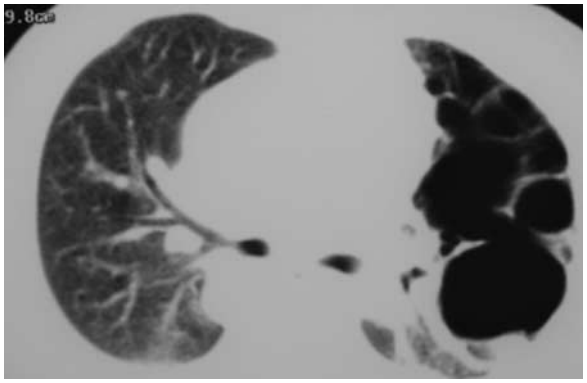
Case 2

A 7-year-old Saudi boy presented to the ER with shortness of breath, normal vital signs and oxygen saturation, and a chest radiography that showed a pneumothorax. Upon drainage of the pneumothorax, a CT scan revealed a 5×3-cm-sized nonloculated cystic lesion (Fig. 2a). At thoracotomy, the cyst, which occupied the apical segment of the basal lobe, was resected with a gastrointestinal anastomosis stapler and submitted for histology.

The cyst lacked an epithelial lining. Its wall was formed of multinucleated giant cells, inflammatory cells, and groups of rounded or oval cells with eosinophilic cytoplasm (Fig. 2b). Immunohistochemical staining of the giant and epithelioid cells revealed the following.

(1) Positive markers for histiocytes (CD68).
(2) Negative reactivity for cytokeratins (epithelial markers).
(3) S100 (marker for Langerhans cells), thus indicating a histiocytic lineage of these cells. The patient remains well at follow-up of more than 4 years.

Fig. 1



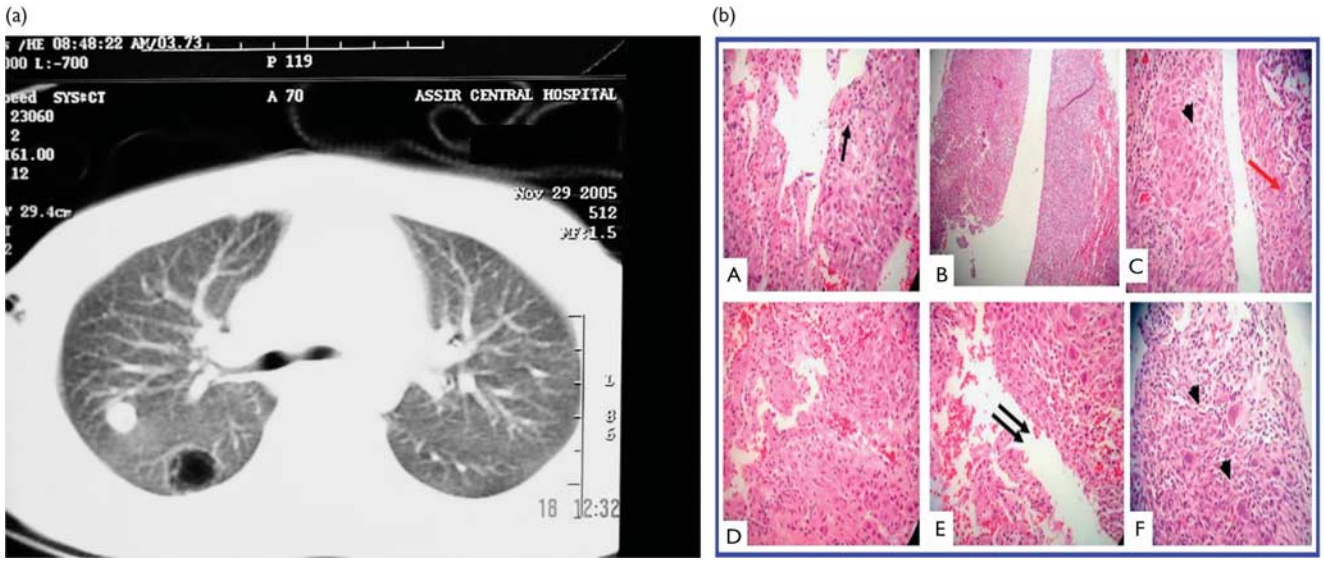
Case 1. Chest computed tomographic scan after the left pulmonary artery augmentation. Multiple cysts have formed in the lung parenchyma of the left lung. Figure reproduced with kind permission from the *Indian Journal of Pediatrics* [5].

Cases 3 and 4

FN, 8 years old, a Saudi boy, was brought to the ER after being thrown out of a car. He was conscious, tacchypnec, and had a rigid abdomen. A chest radiography showed a fractured right first and fifth rib, and a left fourth rib with an area of lucency in the lower zone, surrounded by a zone of contused lung (Fig. 3). CT examination revealed multiple confluent cysts in the right lung and a lacerated liver. Managed conservatively with analgesia and oxygenation, he made a good recovery and was discharged home in a week. A CT done 8 months later revealed complete resolution of the cysts.

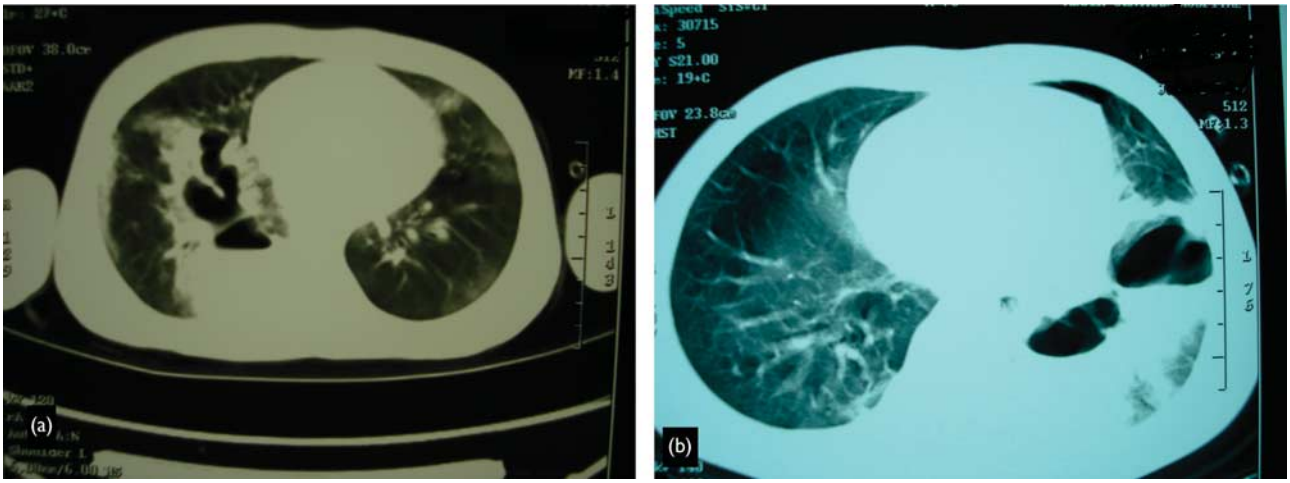
A 7-year-old Saudi boy presented to the ER after being knocked down by a car. He was conscious, dyspnec, with an oxygen saturation of 82%, and had blood-stained sputum. Chest radiography showed a fractured first right rib, and confluent heterogeneous lucencies surrounded by

Fig. 2



(a) Case 2. Chest computed tomographic scan after drainage of the pneumothorax. The subpleural bleb is seen in a section of the apical segment of the lower lobe. (b). The histological features of the resected subpleural bleb. The lesion is composed of cystic spaces without lining epithelium. The cyst wall shows inflammatory cell infiltrate (black arrow: lymphocytes, histiocytes, and plasma cells), multinucleated giant cells (arrowhead), and hemorrhage in the interstitium and inside the cystic spaces (double arrows). Red arrow: cells, positive for CD68 markers, revealing their histiocytic origin. A–D: $\times$ 200 and E: $\times$ 400. Figures reproduced with kind permission from the *Indian Journal of Pediatrics* [6].

Fig. 3



Cases 3 and 4. Trauma-induced pneumatoceles (a) on the right side and (b) on the left. Figures reproduced with kind permission from the *Indian Journal of Pediatrics* [4].

densities in the middle and lower zones of the left lung. Chest CT confirmed the lucencies in the lung fields, and a small left pneumothorax and a fractured occipital bone. A diagnosis of traumatic rupture of the diaphragm was made and a laparotomy was carried out. The diaphragm was found intact. Traumatic lung cysts were then diagnosed and the patient was managed in the ICU with observation of the appearance cysts. With improvement in his condition after a week he was discharged home. A follow-up CT 6 weeks later showed resolution of the cysts.

Discussion

PCs are commonly noted in staphylococcal pneumonias and most theories of their origin and progression emanate from that model. These propose a partial ball valve bronchial obstruction caused by inflammation and tissue disruption. The partial obstruction causes air-trapping and distal distension of the air passages, and eventually a PC [7,8]. Inflammation can also lead to rupture of the bronchial wall and create air corridors that dissect into distal air passages, resulting in PCs [9].

We believe the cysts originate from a sequence of events that start with the destruction of the mucosal lining of the alveoli in a sector of the lung. The causes of this destruction may be diverse: trauma (cases 2 and 3), ischemia (case 1), or an unknown injury of inflammatory nature (case 4). After this initial event diverse mechanisms come into play depending on the etiologic agent and lead to the formation of PCs.

In case 1, the initial event is ostensibly the ischemia caused by the clamping of the pulmonary artery for the purpose of augmentation. This assumption is strengthened by the fact that it was only the left lung that underwent the process of cyst formation; it was the left pulmonary artery that was augmented. Following this initial event, it is safe to assume that the damage to the air passages caused by the ischemia set into motion events that simulate the staphylococcal pneumonia PC model, as mentioned above, and these may then have culminated in the formation of multiple cysts in the left lung. The ischemia and subsequent release of the clamp may also, conceivably, be responsible for a recirculation type of injury, inducing inflammation, edema, and a partial obstruction of the small conducting airways. The swollen air passages acting like check valves allowed air-trapping, overinflation, and finally cyst formation. These cysts have only rarely found mention in the literature; bronchopulmonary arteries in the fetus and neonate have been cited as possible contributors [10,11]. As in most cases of PCs in staphylococcal pneumonia, the cysts were placed under surveillance for the appearance of pneumothorax. Cysts, as in our case, usually involute in a matter of weeks to a few months.

Blunt trauma to the thorax very commonly leads to lung contusions because of the increased capillary permeability and hemorrhage in the traumatized areas. If the blow is considerable in magnitude, compression of the affected part may lead to ruptured parenchyma. The negative pressure in the thorax may further augment this process and cause a laceration, and then a cavity filled with air, blood, and exudate. This may manifest in the immediate aftermath of the traumatic event as was seen in case 2, or may be seen later on, as in case 3. Traumatic PCs present with hemoptysis, pain, dyspnea, cough, and leukocytosis [12,13]. The confusion with traumatic rupture of the diaphragm is a familiar theme as the sensitivity and specificities of a CT scan diagnosing the same have been between 54 and 73% and 86 and 90%, respectively [14]. The accepted treatment for most traumatic PCs is observation. Most resolve spontaneously in the mean time of 25 days, if uncomplicated by hematoma, or less than 2 cm in size. Larger cysts with hemorrhage or those causing respiratory distress may rarely require surgical treatment [12,13].

The fourth PC case is an example of a bleb or a bullous in the lung. After the evacuation of the pneumothorax a CT examination showed it to be an air-filled cystic formation in the apical segment of the right lower lobe. Histo-

pathology showed absence of an epithelial lining and preponderance of inflammatory, giant, and epithelioid cells all pointing toward an inflammatory pathology. Bullae are deemed to be a leading cause of primary spontaneous pneumothorax in adolescents and in asthmatics and smokers [15,16]. Their origins are thought to have a basis in inflammation. Operations on the lungs of these patients frequently reveal adhesions, and an inflammatory cell exudate is seen on histopathology. Smoking has been suggested as the cause of the inflammation in adolescents. In this patient and in other younger patients with primary spontaneous pneumothorax the cause of the inflammation is unknown. Langerhans cell histiocytosis, a cause of cystic lung disease [17], was excluded by the histochemical staining studies, which showed an absence of markers of Langerhans cells. The recommended treatment for these lesions is resection – laparoscopically or by thoracotomy [16].

In summary, apart from the commonly seen parapneumonic PCs, PCs may also occur in other, rarer situations. Ischemia, trauma, and a poorly understood inflammatory process may also lead to PCs. Trauma-induced and ischemia-induced PCs may resolve spontaneously in many instances. Resection, however, is recommended for inflammation-induced bullae, which are the cause of spontaneous pneumothorax in children and adolescents.

A knowledge of the origin and course of these PCs avoids diagnostic confusion and promotes appropriate management.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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