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A case of diffuse persistent pulmonary emphysema: When is difficult the diagnosis?

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ABSTRACT

Persistent pulmonary interstitial emphysema (PPIE) is a rare condition that occurs in both preterm and term infants. It is thought to arise from a disruption of the basement membrane of the alveolar wall allowing air entry into the interstitial space. The characteristic CT scan appearance of PPIE can be used to differentiate it from other congenital cystic lesions that may present similarly. The management of infants suffering from diffuse persistent interstitial pulmonary emphysema varies according to severity and stability of the patient, being either conservative treatment or aggressive surgical treatment by pneumonectomy. We report a case of an unstable patient with diffuse persistent interstitial pulmonary emphysema successfully treated by lobectomy as a form of conservative surgical approach.

The term congenital thoracic malformation (CTM) encloses a large group of lesions present at birth derived from lung and its adnexal tissue. Included in this group we found various types of congenital cystic adenomatoid malformation (CCAM), extra- and intra-lobar and segmental emphysemas together with less common entities such as foregut duplication and bronchogenic cysts [1].

Persistent Interstitial Pulmonary Emphysema (PPIE) is a rare condition that occurs in preterm infants with respiratory distress syndrome as a complication of assisted mechanical ventilation but occasionally, it arises spontaneously with no respiratory symptom [2,3]. This condition is strongly associated with prematurity, respiratory distress syndrome and mechanical ventilation. PPIE may be localized to one lobe or diffusely involve the lungs. The management of infants suffering from PPIE varies according to severity and stability of the patient, being either conservative treatment or aggressive surgical treatment by pneumonectomy [4].

We present a clinical case of pulmonary interstitial emphysema in which the diagnosis was not so easy.

1. Case report

A baby born at 32 + 1 weeks by In Vitro Fertilization and Embryo Transfer (FIVET) with egg donation and with a pregnancy characterized by preeclampsia and diabetes since 17 weeks, he was born by cesarean cut. At birth, the child is presented with Apgar score at 1′ 8 and 5′ 9, weight 1570 g. For the presence of respiratory distress is placed in Mechanical ventilation with positive airway pressure (CPAP) and umbilical venous catheter (CVO). After 30 h of birth presents a major episode of desaturation with bradycardia and respiratory arrest for which he is intubated. At the radiological control he has pneumothorax (PNX) bilateral and two chest drains are placed. It is activated neonatal transport for the transfer at our tertiary center. At the time of his admission, his heart rate, blood pressure, temperature and capillary refill time were found to be normal for his age. An antenatal ultrasonography (USG) and echocardiography were done and were normal.

Upon arrival, the child is placed in high frequmandatory Ventilationency oscillatory ventilation (HFOV) for 4 days and then placed in Synchronized Intermittent (SIMV). The radiological picture to 6 days of life show the presence of reduced diaphany basilar bilateral. Clinical conditions showed an improvement and radiological controls showed reduction of PNX (Fig. 1), for which at 5 days of life the right chest drain has removed and after another 6 days the left drainage has removed. At a distance of 20 days general conditions worsen for which the patient is again placed in HFOV, undertaken therapy with NO and increased oxygen demand. Performs X-ray (Fig. 2) and CT scans of the chest that highlights the presence of “almost complete replacement of the lung parenchyma of the left upper lobe by coarse – emphysematous cystic spaces in accordance with a framework compatible with cystic adenomatous dysplasia.” After that with the help of new software V-Render the rebuilding was performed in order to approach in the best view the mass.

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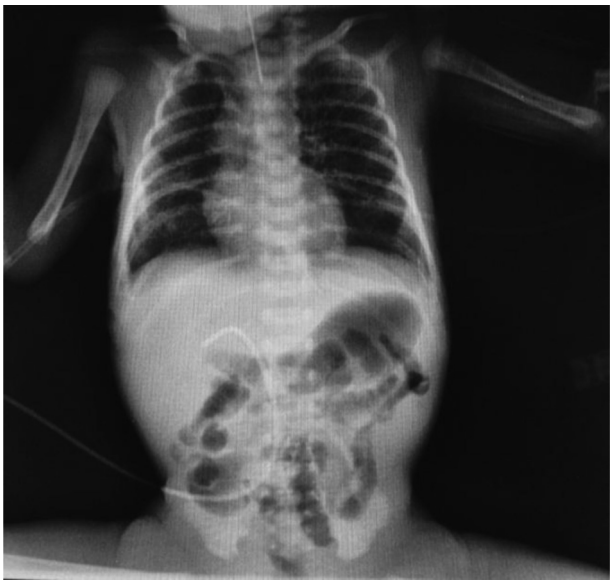

Fig. 1. Radiological controls showed reduction of PNX.

The worsening of the clinical condition, the presence of a saturation of 80% with 100% O_2 make we decided to surgery, and for the critical conditions he was operated in the Neonatal Intensive Care. A surgical excision was performed according to the technical of a "muscle-sparing incision" with a posterolateral mini-thoracotomy with the patient in the right lateral decubitus position. The fifth interspace is used to expose the thoracic cavity, from the anterior axillary line in the middle of a line passing through the scapular angle and the column. The excision of the upper left lobe was performed with ligasure and then the patient recovered completely and discharged in 29th postoperative day. A postoperative chest X-ray (CXR) revealed expansion of the previously atelectatic lobe.

Hystological examination showed macroscopic multiple cystic structure ruptured to the visceral pleura surface, with several variable spaces within the pulmonary interstitial septa with a fibrotic wall. The cystic spaces were lined by mononuclear or multinucleated giant cells, and communicate with the pleural space. The nature of this cell was confirmed by immunostaining for histiocytes and epithelial cells. The cells lining the cystic spaces expressed CD34 and were negative for TTF1, p63. The lung parenchyma adjacent to the cystic spaces was noted to be focally compressed. Parenchymal hemorrhage and congestion was also noted.

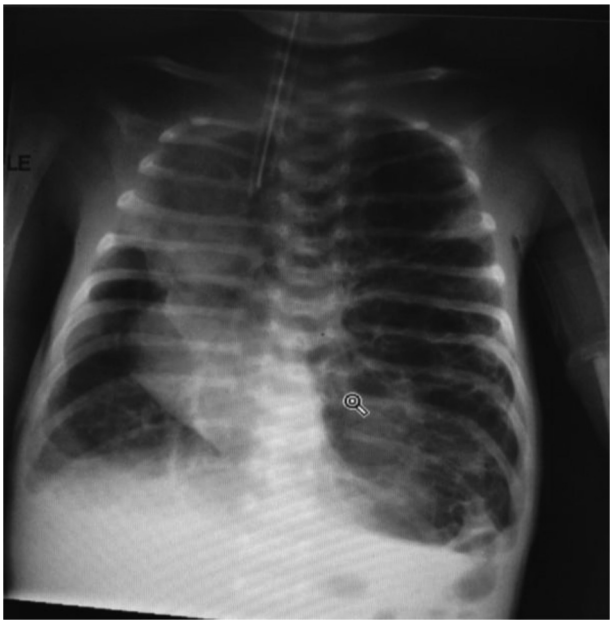

Fig. 2. Framework of the prevailing severe broncodisplasia left with gross bullous formations and dislocation of the mediastinum to the right.

The pathological diagnosis of PPIE was made based on the aforementioned features.

2. Discussion

Persistent interstitial pulmonary emphysema is a rare condition that is mostly associated with mechanical ventilation of preterm infants, however, it has also been reported in both non-ventilated infants and full term infants, and in premature infants with distress respiratory syndrome. PPIE is characterized by abnormal accumulation of air in the pulmonary interstitium, due to disruption of the basement membrane. This accumulation results in cystic air spaces that are typically associated with mediastinal shift and progressive respiratory distress. The air which is not reabsorbed acts as foreign body and triggers a giant cell reaction in the interstitium. Reports in the literature of infants developing persistent PIE with no history of respiratory distress syndrome or mechanical ventilation are scarce, though there are some cases of infants presenting with minimal or no respiratory symptoms, including non specific symptoms of cough and poor feeding, neonatal jaundice and emesis [5]. Some authors described the association even with areas of malacia or stenosis of the bronchial cartilage [4–6]. It is difficult to differentiate between PPIE for the others lung malformations such as congenital lobar emphysema and hyperinflation resulting from extrinsic bronchial obstruction (lymph nodes, vessels, masses, or cysts) that compresses the bronchus and produces valve obstruction, so in cases where there is uncertainty, CT imaging can be useful in making the correct diagnosis even if the diagnosis is often made by the pathologist.

It has two distinct forms: localized and diffused which can be distinguished with pathologic, clinical and radiological features.

The pathophysiology was first described by Macklin and Macklin in 1944 [7]. They demonstrated in the animal experiment that an increase in the alveolar pressure over physiological limits can produce a rupture of the alveolar base at its junction with the less expandable fluid-rich perivascular connective tissue, after that, air leaks into the perivascular sheath and dissect it, giving rise to interstitial emphysema, pneumomediastinum, and pneumothorax, as in our case. It may be localized to one lobe or diffusely present throughout the lung parenchyma. Cystic lesions can become quite large, likely due to the relationship between intraluminal pressure and wall tension. Plane chest radiography can be useful in the management of cases PPIE but the definitive diagnosis of PPIE typically requires a chest CT where the broncovascular bundles appear as soft tissue attenuation nodule or dot in the center of the air-filled cyst [8].

Histology has been proven useful in some cases of PPIE in which the diagnosis of a long-standing lesion is unknown. The presence of multinucleated foreign body-type giant cells in the interstitium is diagnostic since their appearance occurs as a reaction to prolonged air trapping, and the presence of these giant cells implies the diagnosis of PPIE.

The differential diagnosis of PPIE includes congenital cystic lesions, such as cystic adenomatoid malformation, lobar emphysema, diaphragmatic hernia or bronchogenic cyst [9].

Congenital cystic adenomatoid malformation (CCAM), or congenital pulmonary airway malformation (CPAM), refers to a hamartomatous mass of disorganized lung tissue with different degrees of cystic change [10,11]. The lesion, categorized into five types, can often be identified by CT scan visualization of cystic changes associated with abnormal soft tissue.

Congenital lobar emphysema (CLE) is the overexpansion of a pulmonary lobe with alveolar distension without interstitial emphysema. The broncovascular bundles are found at a periphery of the air spaces rather than the center as seen in PPIE.

Diaphragmatic hernia (CDH) can present as an intrathoracic cystic mass in which there is a decrease of both bowel in the abdomen and clarity of the associated hemidiaphragm [11]. The vascular pedicle of the bowel is easily traced back to its subdiaphragmatic origin on contrast CT and thus differentiating from PPIE.

Bronchogenic cysts are a part of a spectrum of bronchopulmonary foregut malformations. CT imaging shows a well marginated cystic mass of soft tissue or liquid.

The development of new software for 3D reconstruction adds other anatomical details. Preoperatively use of 3D reconstruction provide unique insights into the anatomical architecture of the lung malformation and allows to define the relationship with adjacent structures and its vascularization, helping the surgeon in the following surgical treatment (Fig. 3), Other diagnostic instruments that we can use before in the prenatal period are ultrasonogrphy and RMN, not so much to make diagnosis of PPIE but to exclude other pathologies of type pulmonary above.

In the last two decades the improved resolution of ultrasound has allowed early detection of most congenital anomalies, although is not very easy and is necessary a team of expert because in the prenatal imaging normal fetal lung on ultrasound is of similar echogenicity to the fetal liver and spleen but of slightly different echotexture. Congenital lung lesions can either show increased or decreased echogenicity, and a common appearance is that can be due to CCAM, CLE, lung sequestration or airway atresia and also can be confused with non-pulmonary lesions (i.e. Congenital diaphramatic hernia) for this reason ultrasound cannot predict the diagnosis of a fetal abnormality with absolute certainty [12], in other cases as in CLE, the lesion may disappear because it has been suggested that in CLE the build up of bronchoalveolar fluid over time leads to increased pressure within the bronchus, thus allowing fluid to escape, with the consequent disappearance of the echogenicity between 28 and 36 weeks gestation.

So another prenatal exam is MRI that has the advantage of not delivering ionizing radiation that could be harmful to the developing fetus. It is not used in the first trimester for the effect of a strong magnetic field during active organogenesis, and the recent development of ultra-fast MR sequences has allowed artifacts from fetal movements [13,14]. This exam can help us to size the lung lesion, to evaluate the remain normal lung and also to demonstrate the relationship with the other chest structures.

For the fetus with a lung mass or suspected pulmonary lesion or the child who presents with respiratory distress at birth, an important thing should be to born, in the first case, or be transferred urgently, in second case, to a tertiary center with pediatric surgery and intensive care.

The management of PPIE depends largely on the severity of respiratory symptoms. Localized lesions are more frequently resected. Indications for surgery included: persistent respiratory distress, recurrent infection, pneumothorax, inability to wean from mechanical ventilation, and definitive diagnosis when there was a concern for a more pathologic lesion such as CPAM.

Several other approaches to the management of PPIE have been proposed including: selective intubation, selective bronchial occlusion, steroids, surfactant and lateral decubitus positioning. Lateral decubitus positioning was initially described in a case report by Cohen et al. where seven of nine patients with localized PPIE were successfully managed using selective intubation of the right mainstem bronchus due to progressive hyperexpansion of the left upper lobe. Finally, lung puncture with the creation of an artificial pneumothorax has been reported as a successful method, but with this methodic there were few cases in literature, probably for complications as life-threatening lung rupture and hemothorax [15].

In our case, for the progressive worsening of the clinical condition, the difficulty in keeping the patient stable and bradycardia repeated we decided for surgical intervention with emergency thoracotomy.

A PubMed search using the term “persistent pulmonary interstitial emphysema,” with limits set for human studies, English language and infants, shows us a review of 2008, in which is represented a table in which is described the “management approach of localized/diffuse persistent pulmonary interstitial emphysema in preterm and in term infants” [16] (Table 1). In which most cases of localized PPIE were treated surgically. Surgery was typically undertaken in those infants that could not be weaned from mechanical ventilation. Of the localized PPIE cases managed

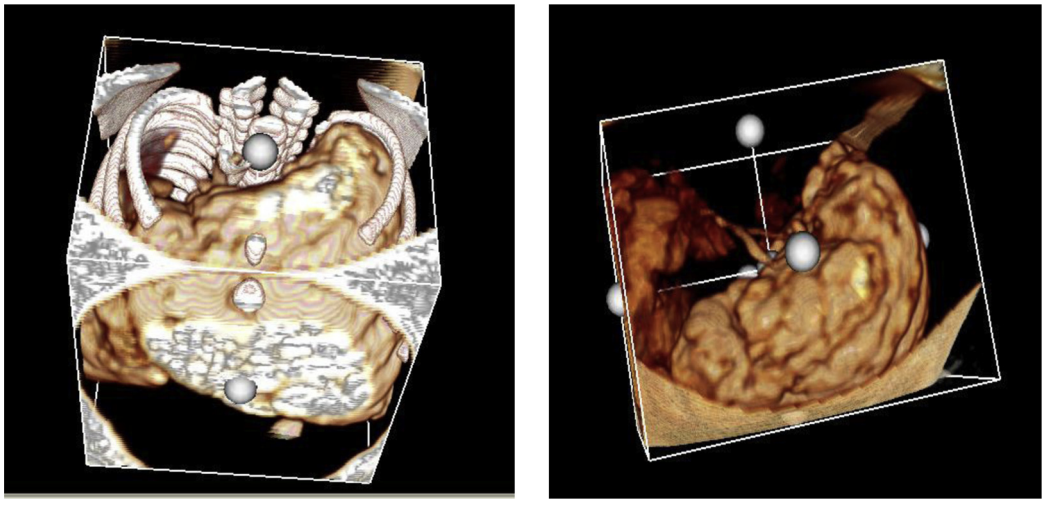

Fig. 3. Chest CT scan with VR reconstruction.

Table 1
Review of published literature in the management approach of localized/diffuse persistent pulmonary interstitial emphysema in preterm and term infants.

References	Study type	Number in study	Term (T) vs Preterm (P) infant	Diagnosis localized PPIE(L), diffuse PPIE (D)	Management S (surgically), N (non surgically)
Freysdottier et al	Case-report	1	T	L	S
Pursnani et al	Case-report	1	T	L	S
Rao et al	Case-report	1	P	L	S
Berk and Varitch	Case-report	1	P	L	N
Donnely et al	Retrospective review	17	P	L=11 D=6	S=9
Sonnappa et al	Case-report	1	T	L	S
Gurakan et al	Case-report	1	P	L	S
Oh et al	Case-report	1	T	L	S
Dani et al	Case-report	1	T	D	N
Drut and Drut	Case-report	1	T	L	S
Cabana et al	Case-report	1	P	L	S
Yaho et al	Case-report	1	P	L	S
Cohen et al	Case-report	3 (1 child)	T	L	S
Jabra et al	Case-report	2	P	L	S
Schneider et al	Case-report	7	P	L	S
Smith et al	Case-report	2	P	L	S
Cohen et al	Prospective study	9	P	L=8 D=1	N
Reyes et al	Case-report	3	T	L	S
Leonidas et al	Case-report	2	P	L	S
Stocker and Madewell	Retrospective study	22	P	L=10 D=12	S=10 N=12
Maglner et al	Case-report	3	P	L	S
Jassal et al	Case-report	1	T	D	N
Bas et al	Case-report	1	P	L	N
Matta et al	Case-report	1	T	L	S
Fujishiro et al	Case-report	2	T	L	S
Srinivasan et al	Case-report	1	T	L	S
Messinen et al	Case-report	1	T	L	N
Messina et al	Case-report	1	P	L	S

non-surgically, none were complicated by an extensive pneumomediastinum as seen in our patient.

The prognosis of this child is good even when more than one lobe is resected and probably reflects the potential for compensatory alveolar growth in children.

For asymptomatic patients there is no consensus on the timing or necessity of resection.

According to our experience, the symptoms are very important for management algorithm.

In conclusion, PPIE is an uncommon disease, and it is still difficult to diagnose it in neonatal Intensive Care Unit and infant care settings. Therefore, PPIE should be suspected in neonates with respiratory distress. Although the diagnosis can be made histologically, particularly differential diagnosis should be made carefully between PPIE, other cystic lesions and pneumothorax, before inserting an intercostal drainage tube (ICD) in a suspected case of pneumothorax, especially in a neonate.

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