Annals of Clinical Case Reports

Case Report
Published: 01 Oct, 2019

Focal Pulmonary Lymphangiectasia Containing an Infantile Hemangioma: An Unprecedented Cause of Refractory Recurrent Unilateral Pneumothoraces

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Abstract

Pneumothoraces are a significant cause of neonatal respiratory distress. We report for the first time an infant with refractory recurrent unilateral left-sided pneumothoraces resulting from a pulmonary lymphangiectasia containing an infantile hemangioma. Known causes of recurrent pneumothoraces include both congenital and acquired lymphangiectasia. Infantile hemangiomas occur in viscera, especially liver, but presence in the lung is very rare. We postulate that lymphangiectasia in this infant was secondary to local lymphatic obstruction by the hemangioma. We recommend consideration of lymphangiectasia from an isolated mass such as congenital infantile hemangiomas in the differential as a newly identified cause of recurrent unilateral pneumothoraces.

Established facts and novel insights:

Established facts: Pneumothoraces are often caused by underlying neonatal lung pathology. Refractory recurrent unilateral pneumothoraxes are rare in the neonate.

Novel insights: Infantile hemangioma can cause neonatal lung pathology. Congenital lymphangiectasia containing an infantile hemangioma for first time is reported to cause of refractory recurrent unilateral pneumothorax in the neonate.

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Received Date: *10 Sep 2019*

Accepted Date: *03 Sep 2019*

Published Date: *01 Oct 2019*

Citation:

Kenny AP, Meinzen-Derr J, Manish Patel N, Bove K, Henry Akinbi T. Focal Pulmonary Lymphangiectasia Containing an Infantile Hemangioma: An Unprecedented Cause of Refractory Recurrent Unilateral Pneumothoraces. Ann Clin Case Rep. 2019; 4: 1765.

ISSN: 2474-1655

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Introduction

Neonatal respiratory distress is a common reason for Neonatal Intensive Care Unit (NICU) admission and is typically caused by difficulty with transition from fetal to neonatal life [1,2]. Clinical severity varies from mild to life-threatening for the neonate. Among the causes of neonatal respiratory distress, pneumothorax, which occurs when air leaks from the perivascular connective tissue sheath to potential spaces between parietal and visceral lung pleura. Pneumothorax can occur spontaneously in healthy infants because of the high transpulmonary pressure present at birth. However, the incidence is much higher when underlying lung disease is present or if the neonate requires mechanical ventilation [3]. Air leaks are more common in the neonatal period than at any other time of life [4]. Recurrent neonatal pneumothoraces are quite rare. We report a unique case of a late preterm neonate with recurrent unilateral pneumothoraces caused by local lymphangiectasia secondary to a peripheral peribronchial capillary hemangioma of infantile type. The recurrent pneumothoraces resolved promptly with resection of this mass. This unique cause should be included in the differential diagnosis when recurrent unilateral pneumothorax requires a surgical remedy.

Case Presentation

A 2.83 kg 36 week male became dusky, at age 4 h and was transferred to a level 2 special care nursery requiring 30% inspired oxygen. On day 3, he experienced sudden increased work of breathing and gasping after prolonged crying. He was subsequently transported to a level 3 Neonatal Intensive Care Unit (NICU) on 90% inspired oxygen. He was endotracheally intubated and needle

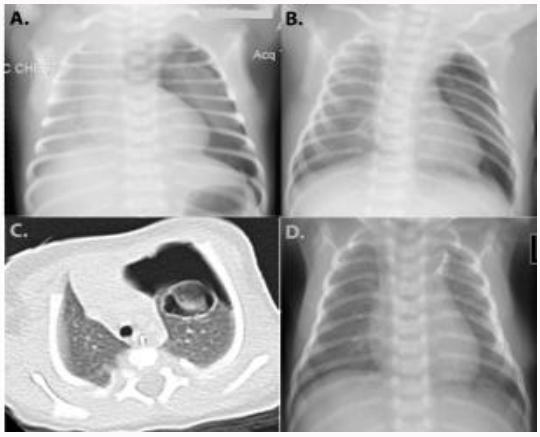

Figure 1: Chest radiography (CXR) from patient over time. A) On DOL 3, left pneumothorax prompted transfer to a level III NICU for thoracostomy tube and surfactant treatment. B) On DOL 8, the pneumothorax recurred for the third time. C) DOL 9: CT revealed left upper lobe gas-filled lesion with a likely calcified rim with soft tissue in anteroinferior portion. D) DOL 25: Cystic lesion resolved post wedge resection.

thoracentesis was performed with evacuation of 60 mL air. At the level 3 NICU, chest radiograph revealed left pneumothorax (Figure 1A); a chest tube was placed. He was extubated 8 h later and remained stable in a head hood until the next day when he was reintubated for increased work of breathing and had a second left needle thoracentesis and a second left chest tube placed for recurrent left pneumothorax with resolution on follow-up radiography.

Chest radiography on the fifth day confirmed recurrent left tension pneumothorax. A left thoracic pigtail catheter was placed and the patient was replaced on the mechanical ventilator. On day 6, the pneumothorax was again resolved. Both chest tubes were removed the next day and the patient was extubated. Chest radiography revealed small pneumothorax reaccumulation and patient received a nitrogen washout. On day 8, the pneumothorax was slightly larger than before (Figure 1B). The patient was transferred to regional level IV NICU for surgical consultation on recurrent pneumothorax and persistent left upper lung lobe lucency, both of which were confirmed in the admission radiography.

Chest Computed Tomography (CT) on day 9 revealed a moderate pneumothorax and non-specific gas-filled lesion in the peripheral anterior left upper lobe measuring 1.5 cm^2 × 1.7 cm^2 with a posterior rimmed nodule, likely calcified, containing soft tissue density (Figure 1C) positioned non-dependently along the anteroinferior aspect. It was deemed atypical for congenital pulmonary airway malformation, pneumatocele, bronchogenic cyst, congenital lobar emphysema, and pulmonary interstitial emphysema. On day 10 the patient underwent left thoracotomy and left upper lobe wedge resection of a cystic bleb, putatively lymphatic in nature in the left upper lobe (Figure 2A). The pneumothorax resolved after placement of thoracostomy tube during surgery, and the patient was extubated postoperatively. The chest tube was removed on day 12, and feedings were advanced with discharge home on day 16. Microscopy revealed a large subpleural markedly dilated lymphatic vessel focally lined by attenuated lymphatic endothelial cells (CD31 positive and weakly D2-40 positive; Figures 2F and 2F') with macrophage reaction. Adjacent to this dilated lymphatic channel was a circumscribed vascular lesion with lobular proliferation of capillary vessels. Capillary vessel lumens were slightly variable in size and most of them were patent and contained red

Table 1: Causes of recurrent and/or persistent pneumothoraces.

Congenital Pulmonary Airway Malformation (CPAM)
Pulmonary sequestration
Bronchogenic cysts
Congenital Lobar Emphysema (CLE)
Respiratory distress syndrome
Ligation of patent ductus arteriosus in very low birth weight infants
Circumcision in a patient with prior history of pneumothorax
Bronchopleural fistula
Pulmonary hypoplasia
Lung agenesis

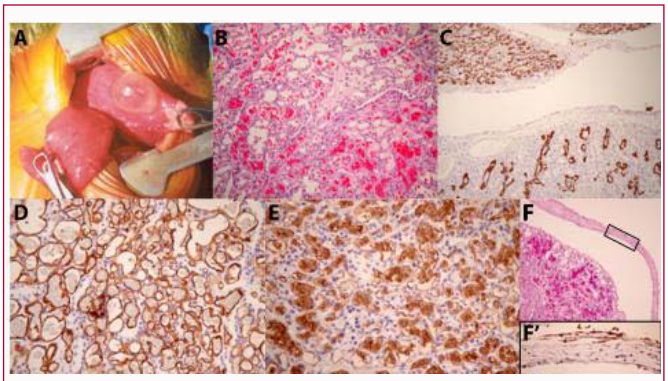

Figure 2: Gross pathologic and histopathologic specimens. A) Intraoperative picture reveals air-filled bleb in left upper lobe. B) Hematoxylin and eosin staining of vascular tumor consistent with hemangioma found in excised lobe. C) Cytokeratin staining confirms tumor was a hemangioma. D and E) CD31 (D) and glucose transporter 1 (E) immunohistochemical staining confirms the tumor is an infantile hemangioma. F) Significant dilatation around the hemangioma by an endothelium that histochemically stains with lymphatic marker D2-40, F') consistent with lymphangiectasia around the hemangioma.

blood cells (Figure 2B). These proliferating capillary vessels were lined by Glut-1 and CD31 positive, flat and plump endothelial cells (Figure 2D and 2E). In between capillary vessels were perithelial cells (SMA positive). This capillary lesion was compressing normal lung tissue except for collapsed alveoli with focal fresh hemorrhage; residual bronchioles were patent. Alveolar spaces were lined by normal pneumocytes (surfactant positive and cytokeratin positive; Figure 2C). CD68 stain highlighted the macrophage reaction in the large lymphatic channel and showed few alveolar macrophages in collapsed lung. Pathological interpretation was local lymphangiectasia produced by an expansile infantile hemangioma resulting in recurrent pneumothoraces. On day 25, the patient was reported to have no skin hemangiomas and was noted to have grunting only after feeds. His left lung lucency had resolved on follow-up chest radiograph (Figure 1D). On day 54, normal head and abdominal ultrasounds ruled out diffuse hemangiomas. On day 104, the patient was discharged from home nursing care with normal feeding and breathing.

Discussion

Pneumothorax occurs in 1% to 2% of live births but is only symptomatic in 0.05% to 0.07% [4-6]. Among 26,007 VLBW (Very Low Birth Weight) infants in 1999, 6.3% had pneumothorax [7]. In the Vermont-Oxford Network, pneumothoraces approached 15% in infants with birth weight 501 g to 750 g [7]. It occurs in 19% of infants with renal anomalies [6] and in 20% to 50% of infants with meconium aspiration syndrome [8]. The incidence has been decreasing

with antenatal steroids, advances in ventilator management, and administration of pulmonary surfactant (RR 0.47 [0.39, 0.58]) [9]. Of 2762 Cincinnati Children's Hospital NICU admissions from 1998 to 2005, 6.7% of patients had pneumothorax (0.8% in BW 1251 g to 1500 g, 1.1% in BW 1001 g to 1250 g, 3.6% in 751 g to 1000 g, 11.3% in 401 g to 750 g) with 40% mortality (compared to 11% mortality in controls). Other risk factors associated with pneumothorax include congenital urinary tract anomalies [10], meconium aspiration syndrome (10% to 25% of patients in the case series [11,12], pulmonary hypoplasia [13], pneumonia (30% of these [14], TTN [15], and RDS [15]. Increasing mean airway pressure [16] can lead to increased incidence of pneumothoraces as can inspire gases with temperatures <36.5°C (43% *vs.* 13% [17]).

Infants with pneumothoraces can be asymptomatic (when the pneumothorax is small) or have respiratory distress. Transillumination using a high intensity fiber optic probe in a darkened room will light up the affected hemithorax and provide rapid diagnosis. Low volume ventilator strategies with permissive hypercapnia and oscillatory ventilation are some respiratory management approaches employed when a pneumothorax requires mechanical ventilation [18].

Causes of recurrent and/or persistent pneumothoraces are listed in Table 1 [19-21]. Very few congenital lung malformations remain asymptomatic throughout life and complications occur in virtually all patients: pneumonia, malignancy (carcinoma, pleuropulmonary blastoma), pneumothorax, hemoptysis, and hemothorax. Surgery is recommended by 3 to 6 months so that compensatory lung growth/alveolarization can occur with one possible exception being asymptomatic congenital lobar emphysema [4,22]. Elective circumcision has been reported to result in recurrent pneumothorax [23], as has patent ductus arteriosus ligation in very low birth weight neonates [24].

In the present case, we report that an infantile hemangioma caused local lymphangiectasia and, as a consequence, recurrent unilateral pneumothorax obligating surgical resection. Infantile hemangiomas are most common in the skin, appearing initially shortly after birth, undergoing rapid growth during infancy followed by gradual involution and potentially causing scarring, ulceration or permanent disfigurement. This type of hemangioma is much less common in viscera except for the liver and GI tract. Pulmonary infantile capillary hemangiomas, and more importantly, symptomatic pulmonary infantile hemangiomas have not been reported to date. Infantile hemangiomas are exceptionally rare in lung, and have never previously been reported to be associated with focal pulmonary lymphangiectasia or with recurrent unilateral pneumothorax [25].

Infantile Hemangiomas (IH) are considered to be benign neoplasms because of monoclonality, rapid early growth and later involution; IH typically appear in the skin or liver shortly after birth and are derived from angioblasts/endothelial cells from the placenta that embolize to receptive fetal tissues during gestation or at birth. The endothelial cells of IH always express glucose transporter 1 (unlike congenital hemangiomas) and placenta-associated vascular antigens including Fc-gamma-receptor II, Merosin, and Lewis Y antigen. IH undergo a proliferative phase characterized by proliferating angioblastic endothelial cells with few capillary lumina and overexpression of markers of angiogenesis including bFGF, FGF2, VEGF, proliferating cell nuclear antigen, and type IV collagenases. This is followed by a spontaneous involution phase which begins in the latter part of the first year and lasts an average of 2 to 10 years [26]. In summary, we have identified a novel cause for our patient's refractory recurrent unilateral pneumothorax: an obstructing IH. Although relatively rare in lung, vascular lesions such as IH should be included in the differential diagnoses of recurrent spontaneous pneumothoraces in neonates, even when the typical skin lesions are absent.

Statement of Ethics

This case report was approved by the institutional IRB committee on human research.

Author Contributions

Drs. Kenny, Akinbi, Bove, and Patel were involved with the clinical care of the patient. Dr. Meinzen-Derr provided local data on neonatal pneumothoraces. Dr. Kenny drafted the manuscript. Drs. Bove, Akinbi, Meinzen-Derr, and Patel provided comments and revision of the manuscript.

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