CASE REPORTS

# LARGE CONGENITAL PULMONARY AIRWAY MALFORMATION WITH MUCINOUS CELL CLUSTERS – A CASE REPORT

Tiago Magalhães[1,2], Rita Costa[2,3], Gustavo Rocha[1],Elson Salgueiro[2,3], Henrique Soares[1,2]

[1] Neonatal Intensive Care Unit, Neonatology Department, Centro Hospitalar Universitário de São João, Porto, Portugal
[2] Faculty of Medicine of the University of Porto, Porto, Portugal
[3] Departmentof Cardiothoracic Surgery, Centro Hospitalar Universitário de São João, Porto, Portugal

* **Corresponding author**: tiagoaugmagalhaes@hotmail.com

## *Abstract*

*We report the clinical case of a 38 weeks gestational age neonate, antenatally diagnosed with a left large macrocystic pulmonary malformation conditioning dextrocardia. At birth, he presented with respiratory distress requiring non-invasive ventilation with high-flow nasal cannula (HFNC). A left inferior lobectomy was performed via thoracotomy on day 21 of life. Histological features of the lesion were compatible with congenital pulmonary airway malformation (CPAM) type I with mucinous cell clusters. No surgical complications were reported and the neonate was discharged six days after surgery. Follow-up two months after surgery was unremarkable.*

**CASE REPORT**

Congenital pulmonary airway malformation (CPAM) is the most common congenital lung malformation with a prevalence of0.69/10,000.[1]CPAM is not hereditary and is a benign lesion that appears prenatally as a thoracic cystic mass. Most CPAM lesions are small enough not to cause consequences. However, some large lesions can originate serious and even fatal complications.[2]

A large macrocystic pulmonary malformation was detected on an obstetrical ultrasound of a healthy 27-year-old woman. At 34-weeks gestation, the lesion occupied most of the left lung causing right mediastinal shift, the larger cyst had 31x29mm.The fetal echocardiogram revealed consequent dextrocardia without other relevant findings.

No other complications were reported. The infant was delivered spontaneously at 38 weeks, weighting 3490grams. The Apgar scores at the 1st, 5th and 10th minutes of life were 9/9/10, respectively.

During the first hours of life, the neonate developed a respiratory distress which motivated his admission to the Neonatal Intensive Care Unit. Due to increasing oxygen needs, the infant required non-invasive ventilation with high-flow nasal cannula (maximum flow rate of 6L/min).

The chest x-ray upon admission (fig.1a) revealed a large cystic mass occupying most of the left hemithorax with mediastinal shifting. The 2D-echocardiography was normal. Evaluation by computed tomography (CT) angiography (fig.1b) revealed a heterogeneous mass with unclear vascularization origin, raising the suspicion of a pulmonary sequestration. Pleuro-pulmonary blastoma (PPB) was another differential diagnosis, although more remote. The cranial ultrasound was

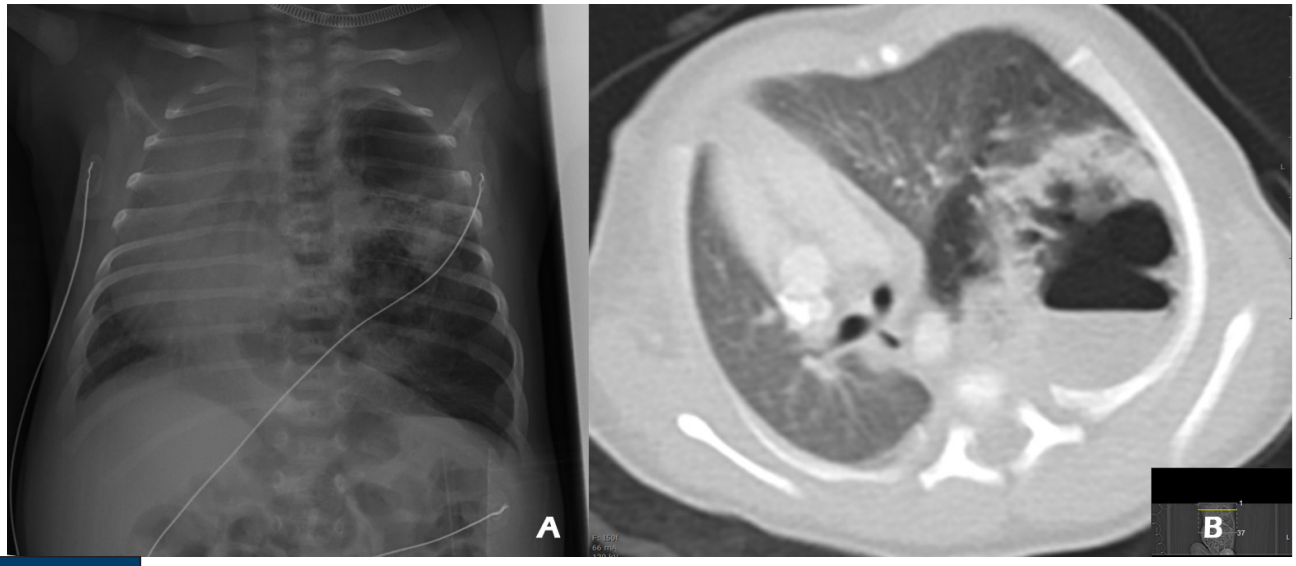


**Figure 1**

*a) X-ray at admission with a large cystic mass occupying the majority of the left hemothorax and shifting of the mediastinum to the right side of the chest; b) Multicystic mass with heterogenous density in the left inferior lobe. The lesion has cystic, solid and air content with the larger cyst having 3,7cm. An important mediastinal shift is observed.*

normal, and urinary catecholamines and bone scintigraphy were negative.

The CT-angiography was repeated on day 14 of life which excluded the possibility of a pulmonary sequestration, turning the diagnosis of CPAM the most likely.

Due to an infectious intercurrence, surgery was postponed until day 21 of life. A left inferior lobectomy was performed via thoracotomy, without complications. During recovery, assisted ventilation was kept for two days, without further need for respiratory support. The post-operative x-ray showed a fully expanded left lung, a centralized mediastinum, and no signs of complications. The chest drain was removed after four days.

The gross examination (fig.2a,b) showed a non-encapsulated mass with multiple cysts (28mm largest diameter). The histologic features (fig.2c-f) showed a type I CPAM with multiple mucinous cell clusters. It consisted of cystic spaces covered by cylindrical ciliated bronchiolar epithelium, with multiple foci of mucinous cell clusters, with cytological atypia, covering the

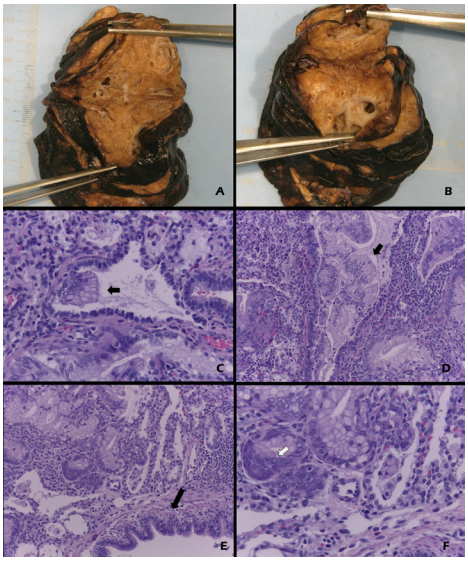


**Figure 2**

*a and b) Gross – remark underlying the pleura, a 47x45x38mm cystic, poorly defined mass; c -f) Histologic features of the lesion – type I congenital airway malformation (CPAM) – (HE- 200x). Microscopically there were fibrous septa, lined by pseudostratified, ciliated columnar or cuboidal cells. Multiple foci of mucinous cell clusters are showed in all figures with more or less complex architecture. In some areas, these foci of mucinous cells, showed cytological atypia with a high nucleo-cytoplasmic ratio, nuclei with loss of polarization, with coarse chromatin and occasionally evident nucleolus. This is more evident in imagese and f.*

cyst and bronchioalveolar structures, assuming aspects of lepidic, acinar and micropapillary pattern.

On the sixth day post-surgery, the newborn was discharged home. During follow-up, he was asymptomatic and a thorax CT-scan, performed four months after surgery, revealed no residual lesions.

The authors report on a case of a large, symptomatic CPAM that initially posed diagnostic difficulties, and needed a lobectomy in the neonatal period.

Type I CPAMs consists of large cysts lined by a pseudostratified columnar epithelium and, occasionally, characteristic islands of mucigenic epithelium.[3] These mucinous cell clusters are considered malignant precursors.[3] In cases where these lesions follow their natural course, cases of mucinous adenocarcinomas, earlier diagnosed as CPAMs, have been described.[4]In the presented case, the mucinous cells clusters are of particular importance since they occasionally grow along the alveolar septa into the adjacent alveoli, and because the observed focal atipia is microscopically indistinguishable from a mucinous adenocarcinoma.[2] Nelson et al showed that the presence of histologic features of adenocarcinoma does not alter clinical behavior if resection is complete.[5]

Approximately 15% of CPAMs diagnosed prenatally regress spontaneously. From the cases diagnosed inutero, around 30% develop respiratory distress. Among these, up to one third may progress to respiratory failure.[6]

Although the management of asymptomatic CPAMs is controversial, in symptomatic CPAMs most will require respiratory support since birth.[7]

Besides most patients becoming symptomatic over time, given the possibility that the lesion is a type I pleuro-pulmonary blastoma - since PPB and CPAM are not distinguishable clinically or radiologically - some authors advocate for resection in infancy.[8] Elective lobectomy by thoracotomy is the most frequent surgical approach with very good outcomes. Limited resection may be considered in some cases but the consensus is that lobectomy is safer.[6]

Following resection, total lung capacity was reported to be preserved. However, concerning the long-term assessment of respiratory function, the literature is conflicting.[9,10]

In conclusion, we presented a clinical case of a large type I CPAM in which it was not possible to initially exclude a PPB. Following respiratory distress, the infant was submitted to a lobectomy, and histological analysis revealed potentially pre-neoplastic features. This strengthens that malignant lesions should be excluded, lesions should be precociously removed and, if considerably large, the infants must keep follow-up for a long period of time.

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## REFERENCES

1. Prevalence charts and tables | EU RD Platform. https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-data/prevalence_en.
2. Chang, W. C. et al. Mucinous adenocarcinoma arising in congenital pulmonary airway malformation: clinicopathological analysis of 37 cases. Histopathology 2020, doi:10.1111/his.14239.
3. MacSweeney, F. et al. An assessment of the expanded classification of congenital cystic adenomatoid malformations and their relationship to malignant transformation. Am. J. Surg. Pathol. 2003, 27, 1139–1146.
4. Ota, H., Langston, C., Honda, T., Katsuyama, T. & Genta, R. M. Histochemical analysis of mucous cells of congenital adenomatoid malformation of the lung: Insights into the carcinogenesis of pulmonary adenocarcinoma expressing gastric mucins. Am. J. Clin. Pathol. 1998, 110, 450–455.
5. Nelson, N. D., Litzky, L. A., Peranteau, W. H. & Pogoriler, J. Mucinous Cell Clusters in Infantile Congenital Pulmonary Airway Malformations Mimic Adult Mucinous Adenocarcinoma but Are Not Associated with Poor Outcomes When Appropriately Resected. Am. J. Surg. Pathol. 2020, 44, 1118–1129.
6. Laje, P. & Liechty, K. W. Postnatal management and outcome of prenatally diagnosed lung lesions. Prenat. Diagn. 2008, 28, 612–618.
7. Durell, J. & Lakhoo, K. Congenital cystic lesions of the lung. Early Hum. Dev. 2014, 90, 935–939.
8. Hall, N. J. & Stanton, M. P. Long-term outcomes of congenital lung malformations. Semin. Pediatr. Surg. 2017, 26, 311–316.
9. Keijzer, R., Chiu, P. P. L., Ratjen, F. & Langer, J. C. Pulmonary function after early vs late lobectomy during childhood: a preliminary study. J. Pediatr. Surg. 2009, 44, 893–895.
10. Rittié, J. L., Morelle, K., Micheau, P., Rancé, F. & Brémont, F. Long-term outcome of bronchopulmonary malformation in children. Arch. Pediatr. 2004, 11, 520–521.