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Case Report

Pre-malignant nature of congenital cystic adenomatoid malformation: a case study and imaging characteristics

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ABSTRACT

Congenital cystic adenomatoid malformation (CPAM) is uncommon developmental anomaly that is often diagnosed in routine prenatal ultrasound. It has various subtypes described by Stocker et al, each with its own characteristics. Patients with symptomatic CPAM are treated surgically while those that are asymptomatic are sometimes management with surveillance only. In this report, a case study of non-malignant type 1 CPAM was managed surgically with histology demonstrating KRAS mutation, linking its potential for malignant transformation as described in literature.

Keywords: Congenital pulmonary airway malformation, Developmental abnormalities, Ultrasound, Mucinous adenocarcinoma

INTRODUCTION

Congenital pulmonary airway malformation (CPAM), formerly known as congenital cystic adenomatoid malformation (CCAM), is a rare developmental anomaly affecting the lower respiratory tract.[1] Its incidence ranges from 1 in 11,000 to 1 in 35,000 live births, with a slight male predominance, and it accounts for approximately 25% of all congenital lung lesions.[2] Typical presentations of CPAM include dyspnoea, cyanosis, pneumothorax, hemothorax, and pneumonia.[3] This usually benign condition manifests as cystic or solid masses, predominantly affecting the lower lobes unilaterally. Bilateral CPAM, although rare, carries a much less favourable prognosis[5].

CPAM has been associated with malignant neoplasms, such as rhabdomyosarcoma, pleuropulmonary blastoma, bronchioloalveolar carcinoma (BAC), and mucinous adenocarcinoma.[3] This case report describes a surgically excised CPAM that demonstrated a KRAS mutation, highlighting its role in malignant transformation.

CASE REPORT

A female infant, born at 41 weeks of gestation, was delivered to a gravida 1, para 1 mother. The prenatal ultrasound at 20 weeks showed normal findings. At birth, the infant had an APGAR score of 9 at both 1 and 5 minutes, with a weight of 3880g. No labored breathing, hypoxia, chest wall deformity, or need for resuscitation was noted on initial examination.

On day 3 of life, the infant developed intermittent tachypnoea while maintaining oxygen saturation at 100%. Chest X-ray revealed a lucent/cystic lesion in the left lung with a right-sided mediastinal shift. The patient was transferred to a specialized centre with a neonatal intensive care unit and paediatric surgery unit. After discussion at a multidisciplinary team meeting, a computed tomography (CT) scan of the chest was performed, revealing a 57 mm multicystic mass in the left upper lobe with thick, irregular internal and peripheral septations and heterogeneous enhancement. The initial concern was for pleuropulmonary blastoma, with CPAM as a differential diagnosis. Given the concerning

radiological findings, surgical management was advised. On day 6 of life, the patient underwent video-assisted thoracotomy and left upper lobe lobectomy.

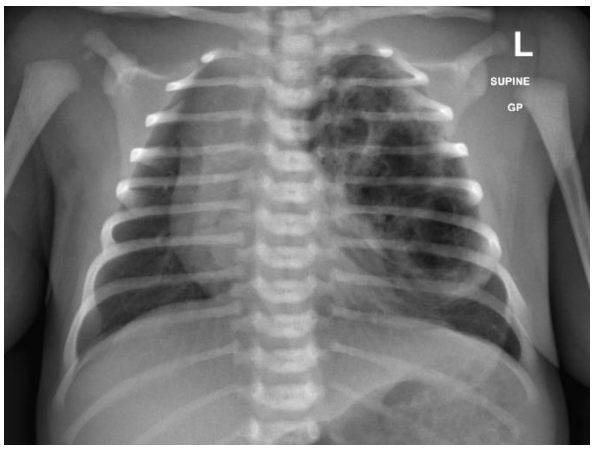

Figure 1: Supine view chest X-ray of patient at initial demonstration of respiratory symptoms. There is large multicystic lesion in the left upper lobe causing tracheal deviation and mediastinal shift.

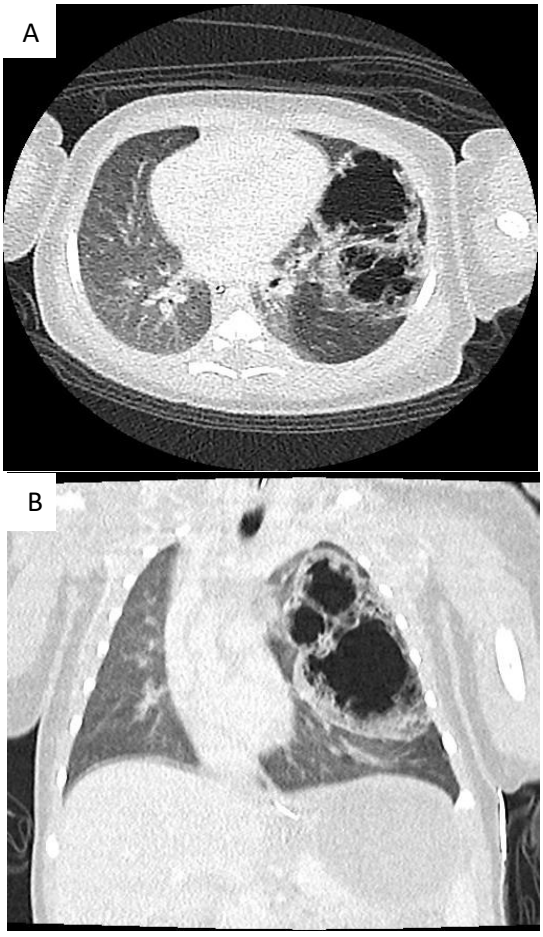

Figure 2 (A and B): Contrast enhanced low dose computed tomography of patient's cystic lung lesions in axial (left) and coronal (right) plane. There is concerning thick and irregular internal and peripheral septations.

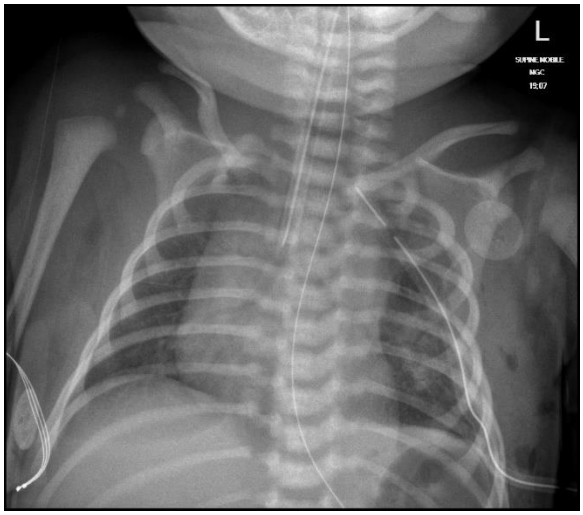

Figure 3: Supine anteroposterior chest X-ray of patient post left upper lobe lobectomy. Patient is intubated with nasogastric tube and left chest drain in situ.

Histologically, the lesion was diagnosed as a type 1 CPAM with a KRAS mutation (35G>A and 34G>T) throughout the lesion, without evidence of invasive mucinous adenocarcinoma. The bronchial margin was involved. The patient had an uneventful recovery and was discharged on day 33 of life. Due to the involved bronchial margin, a follow-up bronchoscopy at 6 months showed unremarkable findings. Further follow-up plans were pending at the time of this report.

DISCUSSION

The exact origin of CPAM remains unclear but is widely believed to represent a hamartomatous malformation or localized developmental arrest.[6] Two primary hypotheses have been proposed in the literature: the environmental hypothesis, which suggests that a persistent genetic defect leads to developmental disruptions in lung morphogenesis, and the obstructive hypothesis, which posits that focal obstruction of the developing lung (due to either impaired peristalsis or mechanical bronchial stenosis) leads to CPAM formation.[7,8] The identification of key genes and molecules involved in CPAM development indicates the complexity of its aetiology.

Stocker et al. initially classified CPAM into three types, later adding two more in the revised version.[9,10] The most common form, accounting for 50%-70% of cases, is type 1 CPAM, which arises from the distal bronchus or proximal bronchiole. Radiologically, it typically appears as one or a few large cysts within the lesion. Type 2 CPAM, originating from terminal bronchioles, constitutes about 15%-30% of cases and features smaller cysts with solid areas. This type is often associated with other foetal anomalies, such as cardiovascular defects, diaphragmatic hernia, bronchopulmonary sequestration, and renal agenesis/dysgenesis.[7] Type 3 CPAM, which arises from

the alveolus, is rare, accounting for 5%-10% of cases, and consists mostly of solid tissue with only microscopic cysts.[11] The revised classification introduces types 0 and 4: type 0 CPAM originates from the trachea or bronchus and is incompatible with life, while type 4 CPAM, like type 3, arises from the alveolus but contains multiple large cysts instead of solid masses. These types are rare, representing 1%-3% and 5%-15% of cases, respectively[12].

Detection of CPAM is often incidental, typically discovered during the second trimester prenatal ultrasound. With increasing use of screening ultrasounds in recent years, more pulmonary lesions are identified, necessitating further monitoring for symptoms, prenatal counselling, intervention, and birth planning. Ultrasound is the preferred imaging modality for CPAM detection, and MRI may be used for volumetric measurements and morphological assessment.[13] On prenatal ultrasound, CPAM typically appears as a hyperechoic cyst, with varying size and number, classified into three types: macrocystic and multicystic masses (type 1), mixed masses with cysts and areas of increased echogenicity (type 2), and microcystic anechogenic masses (type 3).[11]

Sensitivity and specificity of prenatal ultrasound can reach 90% and 77%, respectively.[7] Prenatal MRI has also become increasingly used, with a sensitivity and specificity of at least 95% for detecting lung lesions.[14] However, utilisation of MRI has not shown any additional prognostic benefit over ultrasound.[13] Doppler ultrasound can differentiate CPAM from bronchogenic sequestration by assessing the blood supply, with CPAM receiving blood from the pulmonary circulation and bronchogenic sequestration relying on systemic circulation.[15]

The management of asymptomatic, benign-appearing CPAM remains a topic of debate. Patients with symptoms such as hypoxia, increased work of breathing, mediastinal shift, recurrent infections, pneumothorax, inverted diaphragm, or pleural effusion should be evaluated for surgery.[16] Thoracic malformations, such as thoracic asymmetry, scoliosis, and pectus excavatum, have been described in CPAM.[17]

Some asymptomatic patients without complications may be managed conservatively with serial imaging, balancing the risks of surgery and the possibility of spontaneous resolution. Elective lobectomy in cases with recurrent infections is often more challenging, so early elective resection is preferred to avoid complications.[18,19] The optimal timing for elective resection in asymptomatic patients is generally considered to be within the first 6-12 months of life, to allow compensatory lung growth and prevent restrictive disease.[20]

Malignant transformation within CPAM is rare but has been increasingly documented. In the paediatric population, approximately 4-10% of all lung malignancies are associated with CPAM.[20] Among these malignancies, mucinous adenocarcinoma is commonly found to have a KRAS mutation. The KRAS gene is involved in epithelial growth factor receptor signalling, which regulates cell growth, differentiation, and apoptosis.[21] Although primarily studied in adult malignancies, KRAS mutations in CPAM suggest an increased risk of future pulmonary malignancies in asymptomatic CPAM patients, especially those harbouring the mutation.

CONCLUSION

Congenital pulmonary airway malformation (CPAM) is a common congenital lung lesion with an unclear pathophysiology. It's classification by Stocker et al, which includes five types, is widely accepted. Most patient is diagnosed in the prenatal period with ultrasound with occasional utilization of MRI have very high sensitivity and specificity. Surgical management is recommended for symptomatic patients, those developing complications, or those with concerning imaging findings. Timely surgical intervention maximizes lung development and minimizes the risk of restrictive disease and future neoplastic transformation. In asymptomatic CPAM patients, further research is needed to determine the most appropriate management.

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