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CASE REPORT PEER REVIEWED | OPEN ACCESS

Early detection and management of congenital pulmonary airway malformation in a newborn with stable clinical course

Yasaman Dasteh Goli, Harsh Datta

ABSTRACT

Introduction: Congenital pulmonary airway malformation (CPAM) is a rare developmental lung anomaly characterized by cystic lung lesions, constituting about 25% of congenital pulmonary anomalies. It typically occurs sporadically and is not significantly associated with race, age, or other maternal factors. The prenatal course of CPAM can vary based on factors such as lesion size, mediastinal shift, and associated anomalies. While the overall prognosis is generally favorable in the absence of severe complications like hydrops fetalis, which can adversely affect outcomes, management strategies include corticosteroids, thoracoamniotic shunt (TAS), and, in severe cases, open fetal surgery or the EXIT procedure. Postnatal surgical excision usually offers a curative outcome with an excellent prognosis. Without surgical intervention, there are risks of recurrent infections and, rarely, malignant transformation. Effective prenatal detection significantly impacts clinical decision-making and neonatal outcomes, and the necessity and timing of surgery for asymptomatic infants remain subjects of ongoing debate, underscoring the need for personalized, multidisciplinary care.

Case Report: A female infant, delivered at 38 weeks via Cesarean section, was diagnosed with CPAM following routine prenatal ultrasound. Presence of extensive cystic regions in the right lung confirmed the diagnosis and a CPAM volume ratio (CVR) of 0.37 indicated a low risk of severe complications. The pregnancy was largely uneventful, with maternal chronic hypertension managed by Nifedipine and mild intermittent asthma. Postnatal chest radiography corroborated the CPAM diagnosis, while an abdominal ultrasound investigated intrahepatic calcifications. Maternal screening for cytomegalovirus and toxoplasmosis yielded negative results, and postnatally, the infant also tested negative for both infections. The neonate, though asymptomatic and stable, required close monitoring in the neonatal intensive care unit to prevent potential respiratory compromise.

Conclusion: Advances in prenatal imaging have greatly improved the early detection and management of CPAM, allowing for targeted neonatal care and strategic planning. This case highlights the importance of a multidisciplinary approach involving obstetricians, maternal-fetal medicine specialists, neonatologists, and pediatric thoracic surgeons in the effective management of CPAM. Early identification and diligent postnatal monitoring are essential for ensuring optimal outcomes and minimizing the risk of complications. The coordinated care and strategic decision-making exemplified in this case underscore the potential for enhanced neonatal health and long-term well-being through comprehensive management of congenital anomalies.

Keywords: Congenital pulmonary airway malformation (CPAM), Fetal intervention, Neonatal management, Prenatal diagnosis

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INTRODUCTION

Congenital lung malformations (CLM) represent a diverse group of developmental anomalies originating during the embryonic period that include congenital pulmonary airway malformation (CPAM), bronchopulmonary sequestrations (BPS), bronchial atresia, lobar agenesis, bronchogenic cysts, and hybrid forms of these lesions [1–5]. Among these, CPAM, previously known as congenital cystic adenomatoid malformation (CCAM), is the most prevalent type, constituting approximately 25% of all congenital pulmonary anomalies and occurring in about 1 in 25,000 to 1 in 35,000 live births with a male predominance. Congenital pulmonary airway malformations are generally unilateral and can arise in any lobe, with no significant predominance between the right and left lungs [6]. Congenital pulmonary airway malformation is generally considered a sporadic developmental anomaly and no association between race, age, maternal exposure to specific factors or genetic factors has been identified [3, 7–10].

The prenatal course of CPAM varies depending on factors such as lesion size, the degree of mediastinal shift, fetal hemodynamics, and associated anomalies. In the absence of hydrops fetalis, the prognosis is generally positive, with live birth rates exceeding 95%. However, fetal lesions can remain stable, enlarge, or lead to complications like polyhydramnios or hydrops fetalis, which significantly worsen the prognosis [6–9, 11–14].

Prenatal management of CPAMs involves a range of interventions aimed at optimizing fetal outcomes based on lesion type and associated risks. Maternal administration of steroids, minimally invasive procedures such as thoracoamniotic shunt (TAS) placement for macrocystic lesions or fetal surgery for microcystic ones, and open fetal surgery are options to alleviate mass effects, prevent complications, and improve prognosis [4, 7, 12, 15]. Corticosteroid therapy with maternal administration of betamethasone has shown efficacy in reducing CPAM size and reversing hydrops, particularly in larger lesions, although response variability exists [1, 7, 9, 12, 16]. Thoracoamniotic shunt placement is indicated for severe cases with high-risk hydrops, facilitating lung development and improving survival rates [1, 7, 9, 11, 12].

Laser treatment or fetal sclerotherapy using agents like ethanolamine or aethoxysklerol under ultrasound guidance are alternative therapies with varying success rates, while open fetal surgery remains a high-risk option primarily used in severe cases where maternal risks, including uterine rupture, are carefully weighed [5, 9, 11, 12]. For cases with persistent mediastinal shift or high CVR despite medical management, the ex utero intrapartum (EXIT) procedure allows controlled resection of large lesions at delivery, ensuring fetal stability and reducing postnatal complications [1, 7, 9, 11, 12]. These interventions are tailored based on lesion characteristics, gestational age, and associated fetal anomalies, requiring multidisciplinary coordination for optimal outcomes.

Chest radiography is the preferred imaging modality for the initial postnatal evaluation of CPAM due to its effectiveness in identifying the size of CPAM lesion and presence of mediastinal shift, accessibility, rapid results, and its role in guiding further imaging and monitoring. Subsequent evaluation using cross-sectional imaging techniques like multidetector-computed tomography (MDCT), MR imaging, or Doppler sonography may be necessary to delineate the vascular supply and provide more detailed information [1, 7, 12, 17, 18].

Postnatal management typically involves surgical excision, which is considered curative and offers an excellent prognosis. Without surgical intervention, the most common complications include recurrent resistant pulmonary infections and, in rare cases, malignant transformation of the lesion into pleuropulmonary blastoma and bronchioalveolar carcinoma which subsequently can progress to metastatic adenocarcinoma [1–3, 7, 11, 12, 14, 16, 18, 19]. The necessity and timing of elective surgical resection in asymptomatic infants with CPAM remains a subject of ongoing debate and discussion.

CASE REPORT

A female infant, appropriate for gestational age (AGA), was delivered at 38 weeks and 3 days of gestation via repeat Cesarean section to a 38-year-old G4 P2012 mother. The pregnancy was largely uneventful, except for maternal chronic hypertension managed with Nifedipine and mild intermittent asthma. An antenatal anatomy scan revealed multiple large cystic anechoic areas within the right lung and increased echogenicity of the thoracic pulmonary parenchyma, suggestive of CPAM. The echogenic mass in the lower lobe of the right lung measured 3.2 × 1.8 2.8 cm, with small cystic structures within the mass and a CVR of 0.37. A normal cardiac axis and the fetal heart were noted in the left chest, but an abnormal heart structure with a possible partial atrioventricular (AV) canal defect was suspected. Additionally, nonspecific intraperitoneal echogenic foci were identified, appearing extraluminal from the fetal bowel. The remainder of the anatomy survey was normal, with fetal growth at the 69th percentile.

These findings raised concerns for chromosomal conditions such as Down syndrome. Non-invasive prenatal screening with a cell-free DNA test returned low risk for trisomy 21, trisomy 18, trisomy 13, and sex chromosomal aneuploidies. Maternal carrier screening was negative for 442 conditions, including cystic

fibrosis, spinal muscular atrophy, fragile X syndrome, and hemoglobinopathies. However, she was a carrier for congenital adrenal hyperplasia, 21-hydroxylase deficiency, Triple A syndrome, and Wilson disease. The father was screened and found negative for these conditions.

Due to concerns about congenital heart disease and a suspected primum defect, a fetal echocardiogram was performed, showing normal fetal cardiovascular anatomy and function for the gestational age. Normal right-to-left flow across the patent ductus arteriosus and patent foramen ovale was observed, and a primum atrial septal defect (ASD) was not visualized.

A follow-up ultrasound at 26 weeks of gestation showed that the CPAM in the lower lobe of the right lung had grown to 3.4 × 2.5 × 2.8 cm, with a CVR of 0.49. Echogenic bowel and calcifications were also seen. At 28 weeks, the CPAM lesion remained stable with a CVR of 0.51. A new calcification in the left fetal lung was also noted. Abdominal calcifications persisted, most prominent in the liver, which appeared enlarged consistent with hepatomegaly. Toxoplasmosis and CMV testing were negative, and serum labs did not indicate a recent CMV infection, though a very early infection could not be ruled out. The mother declined amniocentesis for CMV diagnosis in utero. The mother underwent fetal ultrasounds for CPAM monitoring every two weeks, but the CPAM lesions were obscured after 32 weeks of gestation secondary to loss of fluid–tissue interface. Weekly antepartum testing continued till birth. The maternal-fetal medicine specialist recommended postnatal CMV testing and an abdominal ultrasound to evaluate the calcifications.

At birth, the infant had Apgar scores of 8 and 9 at 1 and 5 minutes, respectively, with a birth weight of 3290 g, length of 50.5 cm, and head circumference of 34 cm. Although the infant was stable, she was assessed to be at high risk for respiratory compromise and sudden deterioration due to CPAM. She was transferred to the neonatal intensive care unit (NICU) for continuous observation and monitoring of apnea, bradycardia, and desaturation (ABD) spells for at least 48 hours.

An X-ray of the chest and abdomen showed hazy density projecting over the medial right lower lung corresponding to CPAM (Figure 1). No pneumothorax or pleural effusion was noted. Heart size was normal. A nonspecific bowel gas pattern in the abdomen was noted. No pneumatosis, free air, abnormal calcification, or mass effect was noted.

Abdominal ultrasound was done to evaluate the intraperitoneal echogenic calcifications. The gallbladder was contracted with no mural thickening. The common bile duct measured 2 mm in diameter. Multifocal non-shadowing echogenic foci were seen throughout the liver. The portal vein was patent on color Doppler imaging with a normal direction of blood flow toward the liver. No abnormalities in the inferior vena cava were seen. A visualized portion of the pancreas was unremarkable. The size and appearance of the spleen were within normal limits. The right kidney length of 4.8 cm and the left kidney length of 5.1 cm were reported. No urinary tract dilation or shadowing calculi were seen bilaterally. No abdominal aorta aneurysm was visualized (Figure 2).

The infant remained asymptomatic, well-appearing, and on room air. Appropriate feedings and adequate voiding and stooling were noted. Postnatal CMV testing was negative. The newborn metabolic screening was unremarkable. The patient was discharged home with plans to follow up with a pediatric thoracic surgeon at one month of age for management of CPAM.

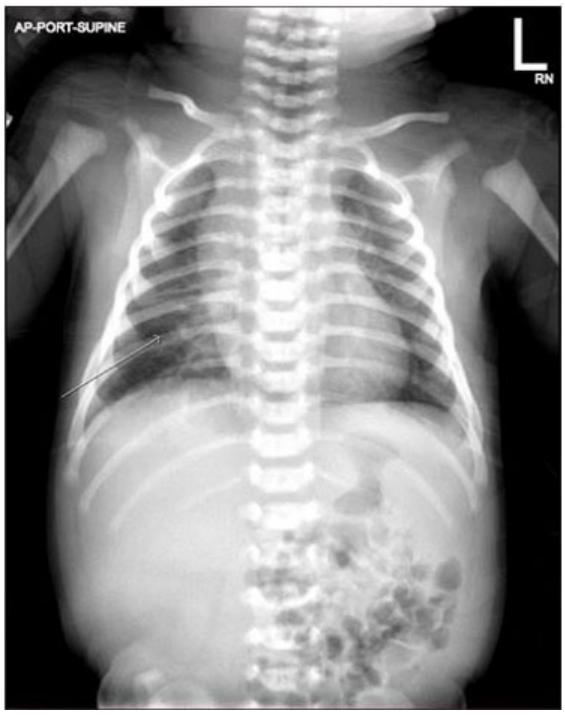

Figure 1: Chest radiograph obtained shortly after birth, indicating hazy opacity projecting over the medial lower lobe of the right lung. Patient is asymptomatic.

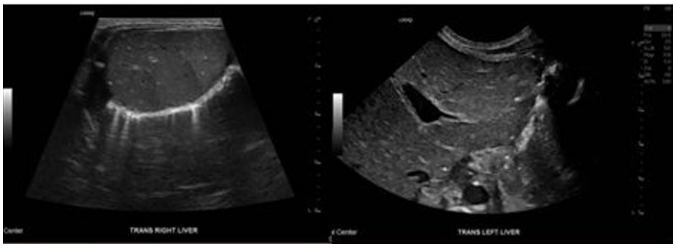

Figure 2: Multifocal non-shadowing echogenic foci throughout the liver corresponding to hepatic calcification.

DISCUSSION

Characterized by abnormal branching of the bronchiolar structures during the pseudoglandular stage of lung development, resulting in the overgrowth of terminal bronchopulmonary tissue, CPAM is often detected during routine prenatal ultrasound screenings

[9, 12, 13]. Advances in prenatal imaging have made it possible to detect CPAM lesions typically around 18–21 weeks of gestation [9].

The congenital pulmonary airway malformation volume ratio (CVR) is an essential sonographic indicator used for prognostic prediction and evaluation of fetuses at risk for hydrops fetalis [20]. The CVR is calculated by dividing the CPAM volume by the head circumference (measured in cm), normalized for gestational age:

$$CVR = (Length \times Height \times Width \times 0.52)/Head\ Circumference$$

A CVR of <1.6 at presentation suggests a low risk of developing hydrops fetalis in the absence of a dominant large cyst. In contrast, a CVR of ≥1.6 or a CPAM with a dominant large cyst increases the risk of developing hydrops [7, 9, 12, 20, 21].

Color Doppler studies also play a vital role in differentiating CPAM from BPS by delineating vascular supply. Congenital pulmonary airway malformations derive their blood supply from the pulmonary circulation and drain via the pulmonary veins, whereas BPS typically has a systemic arterial supply. This distinction is crucial for accurate diagnosis and management [1, 7, 8, 12].

There is no established evidence of a conventional genetic inheritance pattern associated with the disorder, which primarily presents sporadically. The underlying cellular mechanisms behind CPAM are not fully understood. However, studies of large fetal CPAM specimens in comparison to normal fetal lung tissue indicate an increased cell proliferation and significantly decreased apoptosis [7, 12, 22].

Furthermore, gene expression analyses of CPAM tissue have identified that aberrant expression of HOXB5, fibroblast growth factor family members (FGF-7 and FGF10), and platelet-derived growth factor-B (PDGF-B) alter signaling pathways during lung organogenesis which may be implicated in CPAM pathogenesis [7, 12, 21–24]. Congenital pulmonary airway malformation lesions progressing to hydrops and requiring in utero resection, exhibit elevated expression of PDGF-B gene and increased production of PDGF-BB protein, suggesting that targeting PDGF-BB-mediated CPAM proliferation can be a potential therapeutic approach [17, 24].

This neonate was diagnosed with CPAM via routine antenatal anatomy ultrasound, revealing cystic masses in the right lung.

The prenatal management of CPAM in this case involved meticulous monitoring with serial imaging to assess lesion progression and associated risks. The CVR measurement played a pivotal role in guiding clinical decisions, particularly regarding the use of corticosteroids and other interventions. Given that the CVR remained below 1.6 and was relatively stable throughout the pregnancy, the risk of severe complications such as hydrops fetalis and significant respiratory compromise was considered low. A CVR below 1.6 is generally associated with a lower risk for adverse outcomes that would typically necessitate corticosteroid treatment. Consequently, the decision was made to forgo corticosteroids and focus on close monitoring, as the stable CVR indicated that the risk of complications was minimal and did not warrant such intervention.

She was born at term, and remained stable since the lesion's size did not exert sufficient mass effect to adversely impact the infant's respiratory function at birth. However, she was monitored in the NICU due to the potential risk of respiratory compromise. The infant's stable clinical course allowed for thorough postnatal assessment and planning. The CPAM lesion was confirmed via postnatal imaging, leading to discussions on elective surgical resection to prevent future complications such as recurrent infections or potential malignant transformation. The infant was discharged with plans for follow-up with a pediatric cardiothoracic surgeon to determine the appropriate timing for any necessary surgical intervention.

Moreover, given the intrahepatic calcification found on this neonate's imaging, screenings for cytomegalovirus (CMV) and toxoplasmosis were conducted. Intrahepatic calcifications in utero are associated with various causes, including TORCHeS infections (toxoplasmosis, rubella, CMV, herpes, and syphilis) and vascular pathologies such as portal venous emboli [25, 26]. These calcifications can also indicate an increased risk of chromosomal anomalies, especially when other anomalies are present. Therefore, we screened the mother for toxoplasmosis and CMV, and subsequently tested the infant for CMV after delivery, to ensure a thorough evaluation and appropriate management of potential underlying conditions.

In this case presentation, the prenatal identification of CPAM and associated anomalies such as intraperitoneal calcifications and suspected congenital heart disease significantly influences the clinical management strategy and decision-making process. It is evident that prompt diagnosis and appropriate treatment of CPAMs are crucial due to the potentially fatal nature of this condition. Antenatal detection allows for serial monitoring of the lesion, assessment for possible postnatal surgical intervention, and planning delivery in a facility with advanced respiratory and surgical expertise. Symptomatic CPAM should be promptly resected via thoracotomy or thoracoscopy, utilizing lobectomy, segmentectomy, or wedge resection. The postnatal management of asymptomatic CPAM remains controversial, with elective surgery versus conservative management being debated.

When evaluating the risks of recurrent pneumonia, impaired lung growth from the mass effect, and malignant transformation, elective postnatal surgery is often justified. However, some contend that the risks of surgery may outweigh these potential complications. The therapeutic management of CPAM can include pharmacologic treatment of complications, surgical intervention, or simple follow-up, depending on disease severity and evolution. Advocating for elective resection of asymptomatic CPAM is imperative to leverage pulmonary compensation in children and avoid risks of infection and malignant evolution while ensuring optimal

long-term health for the affected neonates.

CONCLUSION

Prenatal detection of CPAM, a rare developmental lung malformation, alongside associated anomalies, is crucial in guiding clinical decisions and management strategies. Early diagnosis allows for tailored monitoring and intervention, emphasizing the importance of weighing elective surgery against conservative approaches. Ultimately, advocating for individualized treatment plans ensures the best health outcomes for affected neonates.

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Author Contributions

Yasaman Dasteh Goli – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Harsh Datta – Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.