ARTICLE

A ten-year review of Congenital Pulmonary Airway Malformation cases in a Pediatric tertiary hospital

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OBJECTIVE: A retrospective study of the demographic, clinical and diagnostic profile, intervention and outcomes of children with Congenital Pulmonary Airway Malformation (CPAM) in Philippine Children's Medical Center (PCMC) from January 2011 to December 2021 was presented.

METHODOLOGY: Medical charts of identified patients were reviewed. Data obtained included demographic profile, clinical history, diagnostic procedures, intervention, and outcomes. The findings were analyzed and correlated with the synthesized findings from relevant studies about CPAM.

RESULTS: Twenty-three cases (n=23) were included in the study. Most of the patients were diagnosed at 1 to 11 months of age, accounting for 43.48% while there is a minimal disparity in terms of gender distribution. Seventy-five percent of neonates presented with respiratory distress while recurrent pneumonia occurred more frequently beyond the neonatal period. Four patients at 17.39% had incidental findings of CPAM on prenatal ultrasound. All cases were confirmed using a Chest CT scan and only six patients at 26.09% had Chest X-ray results consistent with CPAM. Eight cases were confirmed using biopsy wherein results were mainly Type I seen in 87.5% of cases. Lobectomy is the procedure of choice with 92.86% success rate. Overall, patients who underwent surgical intervention had a low complication rate at 6.25%.

CONCLUSION: CPAM is most common in patients aged 1 to 11 months and has no gender predilection. Neonates often present with respiratory distress while recurrent pneumonia is the most common clinical manifestation beyond neonatal period. CPAM can be detected using ultrasound prenatally and CT scan can confirm CPAM postnatally. Surgical intervention particularly lobectomy is the preferred option over conservative management which showed a favorable outcome. CPAM has an overall good prognosis. Findings of this research may guide clinicians in the diagnosis and management of CPAM in the Philippines.

Keywords: *Congenital Cystic Adenomatoid Malformation, Congenital Pulmonary Airway Malformation, Congenital Cystic Lung*

INTRODUCTION

Congenital Pulmonary Airway Malformation (CPAM), formerly known as Congenital Cystic Adenomatoid Malformation (CCAM), is a rare developmental malformation of the lower respiratory tract characterized by the formation of hamartomatous or dysplastic lung tissue.[1,2] Despite its rarity, CPAM has been recognized internationally with an incidence ranging from 1 in 25,000 to 35,000 births and a prevalence of 1 to 4 in 100,000 births.[3,4,5] In the Philippines, although data on CPAM are limited, the Philippine Pediatric Society (PPS) has reported 84 cases of unspecified congenital lung malformations and 194 cases of congenital cystic lung disease since 2006. Out of these cases, 29 cases were recorded at the Philippine Children's Medical Center (PCMC) as of 2021. Despite the significant number of CPAM cases, limited Philippine literature exists and there has been no reviews made on the cases of CPAM in PCMC. The findings of this study will therefore provide evidence-based data on the local clinico-demographic profile and current local practice in diagnosing and managing CPAM along with its outcomes. It will also highlight the comparison of these findings with the international findings. These data may guide the management of CPAM in hopes of improving patient health care. In addition, it will contribute to the limited number of literatures on CPAM in the Philippines.

Almost all reported CPAM cases are from whites however there is no evidence for racial predilection, neither is it associated with age, sex, weight, gestational age, parity nor intrauterine maternal exposures.[2,3] This can be attributed by the fact that most of the available data were from international journals. The etiology of CPAM remains uncertain, but it is believed to result from embryologic injury before the 35th day of gestation during lung development.[1,3] CPAM can be classified into different types based on embryologic origin and histologic features, which may influence prognosis and malignant potential.[5] Clinical presentation varies from asymptomatic to respiratory distress, and diagnosis can be made prenatally or postnatally using various imaging modalities such as ultrasonography, MRI, X-ray, CT scan.[2,6,7] With the increasing diagnosis of CPAM in utero, conservative management were made including steroid therapy and thoracoamniotic shunts.[5] On the other hand, invasive CPAM resection has already been performed in a 29 week old fetus.[5] In the postnatal period, surgery is indicated for symptomatic patients either by lobectomy, segmentectomy or wedge-resection via thoracotomy or thoracoscopy whereas the timing of surgery for asymptomatic cases is controversial, with advocates for early intervention citing the risk of complications such as recurrent infection, impaired lung growth, growth from mass effect of the lesion, repeated exposure to imaging radiation on

on lesion monitoring and malignant potential.[2,3,6,7] The contrary opinion is that the risk of surgery outweighs the risk of these complications.[6] Furthermore, despite advancements in understanding and managing CPAMs, there remains to be lack of clarity regarding nomenclature, classification, pathogenesis, natural history, diagnosis, and management of CPAM.[6] Continued research efforts are essential to address these gaps and guide clinical practice of CPAM.

The general objective of this study is to provide an evidence-based profile of patients diagnosed with CPAM in PCMC from January 2011 to December 2021. Specifically, it aims to determine the demographic profile, clinical and diagnostic profile, intervention, and outcomes of patients diagnosed with CPAM admitted in PCMC from January 2011 to December 2021.

Methodology

This is a retrospective descriptive study that identified and reviewed all confirmed cases of CPAM in PCMC from January 2011 to December 2021 and correlated it with the synthesized findings from relevant studies about CPAM.

The target population of this study were patients diagnosed with CPAM and admitted at PCMC from January 2011 to December 2021. The basis of the diagnosis is made by confirmed Chest CT scan, Chest MRI, or pathology findings.

Secondary data collection method was used in this study. Medical charts of the confirmed cases of CPAM were retrieved and reviewed. From these medical records, the following data were obtained: demographic data such as patient's age and sex, clinical history, and physical examination, diagnostic procedures, intervention, and outcomes during admission. The collected data was tabulated and presented in graphs. This study utilized descriptive statistics such as measures of frequency, central tendency, and dispersion or variation and position.

Results

Twenty-three patients (n=23) diagnosed with CPAM or CCAM were identified and studied. At the time of diagnosis, the patients' age ranged from 0 to 11 years old, with the majority of the patients presenting at 1 month to 11 months of age, accounting for 43.48% (10 out of 23) of total cases as presented in table 1. All the neonates were born full-term. In terms of gender distribution, there is minimal disparity regardless of age at presentation (Males: 11; Females: 12) (Table 1).

Table 2. Clinical Manifestation Profile of Patients Diagnosed with CPAM Admitted in PCMC from January 2011 to December 2021

Age at presentation	Clinical Manifestation				Total
	Respiratory distress	Recurrent Pneumonia	Feeding difficulties	Asymptomatic	
0- 28 days	3	0	0	1	4
1 month to 11 months	2	6	0	2	10
1 year to 9-year-old	0	6	0	1	7
10 year- 18 years	0	2	0	0	2
Total	5	14	0	4	23

Table 3 shows that during the prenatal period, four patients at 17.39% had incidental findings of CPAM on prenatal ultrasound. The median gestational age at diagnosis was 20 weeks. All four patients were born alive and lesions persisted until birth which were confirmed via Chest CT scan. One was symptomatic while the rest were asymptomatic. Three of them underwent lobectomy which all improved while the remaining one was observed. All of the diagnosed CPAM cases were confirmed using a Chest CT scan, comprising 100% (23 out of 23) of cases. Only six patients at 26.09% had Chest X-ray results consistent with CPAM. Eight cases at 34.78% were confirmed via biopsy with the majority classified as type 1 seen at 87.5% (7 out of 8) of cases. The biopsy of one patient who underwent lobectomy revealed bronchogenic cyst. In PCMC, there were no records of MRI being used to diagnose CPAM cases.

Table 3. Diagnostic Procedure Profile of Patients Diagnosed with CPAM Admitted in PCMC from January 2011 to December 2021

Diagnostic procedure	CCAM/CPAM	Others	Total
Antenatal Ultrasound	4	0	4
Chest X-ray	6	17	23
Chest CT Scan	23	0	23
Biopsy	8	1	9
Chest MRI	0	0	0

In Table 4, only postnatal intervention was employed in PCMC including cyst excision, blebectomy, and lobectomy, wherein most of the patients at 87.5% (14 out of 16) underwent lobectomy. Notably, positive outcomes were observed with most of the patients improved and had no complications postoperatively at 92.86% (13 out of 14); however, there was a mortality rate of 7.14% (1 out of 14) associated with the said procedure. In addition, among the surgical procedures performed, there was one case of cyst excision and one case of blebectomy, both of which also resulted in improved statuses with no complications. Overall, most patients who underwent surgical intervention at 93.75% (15 out of 16) improved with unremarkable postoperative course. Observation and close monitoring methods were chosen for three patients however this study did not include an outpatient follow-up review hence the outcomes were unknown. The four other patients were either lost to follow-up, coordinated to other hospitals, or sent home against medical advice. The average hospitalization day was nine days.

Table 4. Descriptive Comparison of Outcomes According to Management Performed to Patients Diagnosed CPAM Admitted in PCMC from January 2011 to December 2021

Intervention	**Outcome**						
Surgical	**Improved**	**Residual cyst**	**Pneumo-thorax**	**Readmis-sion**	**Mortali-ty**	**Un-known**	**Total**
Cyst Excision	1	0	0	0	0	0	1
Blebectomy	1	0	0	0	0	0	1
Segmental resection	0	0	0	0	0	0	0
Lobectomy	13	0	0	0	1	0	14
Total	15	0	0	0	1	0	16
Medical	**Improved**	**Residual cyst**	**Pneumo-thorax**	**Readmis-sion**	**Mortali-ty**	**Un-known**	**Total**
Observation	0	0	0	0	0	3	3
Others	0	0	0	0	0	4	4
Total	0	0	0	0	0	7	7
						Total	23

DISCUSSION

Congenital Pulmonary Airway Malformation (CPAM), formerly known as Congenital Cystic Adenomatoid Malformation (CCAM), is a developmental malformation of the lower respiratory tract causing formation of hamartomatous or dysplastic lung tissue.[1,2] It belongs to the heterogeneous group of embryologically-related malformations of the lung along with pulmonary agenesis, aplasia, hypoplasia, and sequestration, and bronchogenic cyst.[1,3] It is a rare but well-known congenital lung lesion with an international incidence of 1 in 25,000 to 35, 0000 births and a prevalence of 1 to 4 in 100,000 births.[3,4,5] In the Philippines, 84 cases of unspecified congenital malformation of the lung and 194 cases of congenital

cystic lung were reported by the Philippine Pediatric Society (PPS) since 2006. Out of these recorded cases, 29 were found in Philippine Children's Medical Center as of 2021. According to studies, CPAM has no racial predilection neither is it associated with age, sex, weight, gestational age, parity, nor intrauterine maternal exposures. This coincides with our findings wherein CPAM has no gender predilection. Although some studies state that it is more common in whites and males, and most are diagnosed before two years of age.[2,3,8] This is also congruent with our findings as majority of the CPAM patients were diagnosed at 1 month to 11 months of age.

The exact pathogenesis of CPAM is still uncertain however it is believed to have resulted from an embryologic injury before the 35th day of gestation during the various stages of lung development commonly during the pseudoglandular stage causing maldevelopment of the tracheobronchial tree and formation of cysts.[1,3] Typical histologic findings reveal few normal lung tissues and many glandular elements wherein cysts are very common and the presence of cartilage is rare indicating that the embryological insult occurred later in the 10th to 24th week.[1] CPAM was classified into 3 types by Stocker et. al in 1977 and expanded into 5 types by Stocker in 2002 which differ based on the embryologic level of origin and histologic features subsequently leading to distinct prognosis and malignant potential.[5] The first type is Type 0 which is the least common type (<3%) arising from the trachea and proximal bronchus and consists of microcystic (<5mm) lesions involving all lobes hence has the poorest prognosis and is incompatible with life while Type 1 is the most common type (60%) which arises from the distal bronchus or proximal bronchioles and consists of single or multiple macrocysts (>5mm) lesions lined with ciliated pseudostratified epithelium with one-third of cases characterized with mucus-secreting cells. This lesion involves only a part of one lobe and hence has a good prognosis for survival. Type 2 (20%) arises from terminal bronchioles and consists of multiple microcyst with histology similar to that of the type 1 however carries a poor prognosis since majority of the CPAM cases associated with congenital anomalies including cardiac, renal, gastrointestinal and skeletal anomalies were classified as Type 2 lesions. Another type is Type 3 (<10%) which arises all the way down to alveolus and is characterized with a mixture of microcysts and solid tissue with bronchiole-like structures lined with cuboidal ciliated epithelium separated by areas of nonciliated cuboidal epithelium. This type also carries a poor prognosis. The last type is Type 4 (10%) which arises in the alveoli and is commonly macrocystic and lacks mucus cells. It is the lesion that has been associated with malignancy (pleuropulmonary blastoma).[1,3,8,9] In PCMC, eight cases were confirmed by biopsy wherein the majority were classified as CPAM type 1 seen in 87.5% (7 out of 8) of cases which is consistent with the existing

of cases which is consistent with the existing studies.

The presentation of CPAM ranges from asymptomatic to respiratory distress. Two thirds of affected patients are diagnosed during neonatal period.[2] Approximately 75% of these patients are asymptomatic at birth while the remaining 25% of patients are symptomatic.[2] Affected neonates with expanding cystic lung mass may present with respiratory distress while those with small lesions may remain asymptomatic.[2] Only one-third of CPAMs are diagnosed beyond the neonatal period due to associated cough, decreased breath sounds on physical examination, incidental findings on imaging, and recurrent respiratory infections.[2,3,8] A common presentation in older children is recurrent pneumonia. In contrary to our data, most patients with CPAM were diagnosed beyond the neonatal period and diagnosed neonates often had respiratory distress at 75% (3 out of 4) of cases. Similarly, recurrent pneumonia is the most common presentation after the neonatal period at 60.87% (14 out of 23) of cases.[2]

With the advent of ultrasonographic technology, a more frequent and earlier prenatal diagnosis of CPAM is made with most cases diagnosed at 18-22 weeks age of gestation with a median gestational age of 21 weeks.[1,7] Prenatal diagnosis of CPAM using ultrasound has already been employed in PCMC with most cases diagnosed at 20 weeks age of gestation which was nearly congruent with previous studies. When ultrasound findings are equivocal such as in late pregnancy where there is loss of fluid-tissue interface or inaccessible fetal position, MRI can be used for morphological and volumetric evaluation of this lung lesion.[3,6] However in PCMC, there were no records of MRI being used to diagnose CPAM prenatally. Spontaneous regression of CPAM prenatally on serial fetal ultrasonography which occurs in approximately 50% of cases between 28-37 weeks age of gestation has also been observed.[2,6,7] Among lesions persisted in the postnatal period, spontaneous resolution has also been reported in a small number of cases.[2] Since prenatal ultrasound becomes less sensitive in detecting lung cysts as the pregnancy advances, involution of the lesion can be misleading hence true resolution must be documented using a postnatal Chest CT scan.[6,10] Based on the algorithm of CPAM postulated by Oermann et. Al (2021), all infants with prenatal diagnosis of CPAM should have a Chest X-ray in the neonatal period. However, some studies showed that thin-walled cystic lesions are difficult to see in Chest X-ray hence CT Scan is strongly recommended for definitive diagnosis. In PCMC, CPAM lesions found on fetal ultrasound of four patients persisted until birth which were confirmed using Chest CT scan. On the other hand, Chest X-ray, CT scan, and MRI are used to evaluate for CPAM postnatally.[6,7] According to a study by Shamas and Bohara (2016), CT scan is superior to Chest X-ray in detecting lesions in cases of

CPAM with sensitivity of 100% and 88%, respectively and positive predictive value of 95% and 78%, respectively. This is also true in a case report by Disu et. Al (2019) wherein a 13-day old neonate presented with tachypnea on the third day of life and had a chest X-ray finding consistent with congenital lobar emphysema or congenital pneumonia while CT scan findings was suggestive of CPAM. A similar report was presented by Atalabi et al. (2006) wherein an initial diagnosis of congenital diaphragmatic hernia was suspected based on the Chest X-ray, but chest CT findings revealed CPAM type 2. This was evident in our findings as all the CPAM patients were diagnosed using a Chest CT scan in 100% (23 out of 23) of cases and only six patients at 26.09% had Chest X-ray results consistent with CPAM. MRI could be an alternative to a CT scan but there is no evidence showing which one is the best modality.[6,8] In PCMC, there were no records of MRI being used to diagnose CPAM postnatally. Furthermore, since the signs and symptoms of CPAM are constitutional, the differential diagnosis can be broad, hence imaging studies play a crucial role in distinguishing CPAM from other diseases. Bronchopulmonary sequestration (BPS), congenital lobar emphysema, and bronchogenic cyst are some of the diseases that causes pulmonary cystic changes while congenital diaphragmatic hernia (CDH) can mimic cystic lung changes.[4,8,9] Colour Doppler ultrasound which is a tool that evaluates the arterial and venous blood flows allows differentiation between CPAM and BPS since CPAM is supplied and drained through the pulmonary circulation whereas BPS is supplied through the systemic circulation.[6,9] However, this diagnostic procedure was not yet employed in PCMC hence for one case, the Chest CT scan result was suggestive of CPAM but biopsy result turned out to be BPS.

With the increasing diagnosis of CPAM in utero, conservative managements were made to decrease morbidity and mortality including steroid therapy and thoracoamniotic shunts.[5] On the other hand, a study by Fan et. Al (2017) demonstrated an invasive antenatal procedure performed in case of CPAM wherein the uterine of a 22-year-old at 29 2/7 weeks of gestation was incised and the fetal CPAM lesion was resected through thoracotomy then the fetus was returned back to the uterine cavity. In the postnatal period, surgery is indicated for symptomatic patients either by lobectomy, segmentectomy or wedge-resection via thoracotomy or thoracoscopy.[1,3] Whereas postnatal management of asymptomatic CPAM remains controversial.[6] Only postnatal interventions were employed in PCMC including cyst excision, blebectomy, and lobectomy, wherein majority of the patients at 87.5% (14 out of 16) underwent lobectomy. Although surgery may be delayed for asymptomatic infants because postnatal resolution has been reported, advocates of elective postnatal surgery cite the risk of

recurrent infection, impaired lung growth from mass effect of the lesion, repeated exposure to imaging radiation on lesion monitoring and malignant potential which has been described for some cases, thus surgical resection by one year of age is recommended.[6,7] The contrary opinion is that the risk of surgery outweighs the risk of these complications.[6] Notably in our findings, positive outcomes were observed for patients who underwent lobectomy with majority of them improved and had no complications post operatively at 92.86% (13 out of 14); however, there was a mortality rate of 7.14% (1 out of 14) associated with the said procedure. In addition, among the surgical procedures performed, there was one case of cyst excision and one case of blebectomy, both of which also resulted in improved statuses with no complications. Overall, most patients who underwent surgical intervention at 93.75% (15 out of 16) improved with unremarkable postoperative course.

A consensus was made regarding the management of CPAM presented in the study of Oermann et. Al. (2021). In symptomatic cases, immediate advance thoracic imaging such as CT scan or MRI is required to further define the type and extent of lesion as part of preoperative planning and patient should undergo early surgical resection while in asymptomatic patient, close monitoring and simple chest radiograph should be done due to the possibility of becoming symptomatic and the risk of recurrent infection and malignant transformation. If during monitoring the patient is tagged as high risk which is defined as having large lesion (>20% of hemithorax), bilateral and multifocal cysts, and malignant risk factors then immediate advance thoracic imaging should be done to confirm the diagnosis and surgical intervention is suggested while if patient is low risk with none of the high risk features outlined above, the decision will primarily come from the family after a detailed discussion of the advantages and disadvantages of each approach. If observation is chosen, advance thoracic imaging is done after 6 months and close follow up for development of signs and symptoms with routine annual imaging should be done while if surgical intervention is chosen, elective surgical procedure should be done by one year old.[2] This was apparent in our findings as three patients were observed but since this study did not include out-patient follow up review thus the outcomes were unknown. The prevention of recurrent infection and potential malignancy, the improved restoration of lung volume, and fewer complications favor early elective surgery in asymptomatic patients.

Conclusion

In conclusion, CPAM is most common in patients aged 1 month to 11 months and has no gender predilection. Neonates often present with respiratory distress while recurrent pneumonia is the most common clinical manifestation beyond neonatal period. CPAM can be detected using ultrasound prenatally and CT scan can confirm CPAM postnatally.

Surgical intervention particularly lobectomy was the preferred option over conservative management which showed a favorable outcome. CPAM has an overall good prognosis. The involvement of a multidisciplinary team in the management of these patients is of utmost importance.

As the research aims only to review in-patient cases of CPAM in PCMC over a ten -year period, there is limited population size and short-term evaluation of outcomes. The study as well, was conducted through review of medical charts and some of these records had incomplete documentation therefore were not included in the study.

Due to limited population size, a longer period may be reviewed to account for more CPAM cases. A follow-up review is also recommended to evaluate for the long-term complications. For future study, a review on the profile of pathologic findings and associated anomalies in CPAM cases can also be beneficial.

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