RESEARCH PAPER

Congenital Lung Malformations: Experience From a Tertiary Care Center in India

KRISHNA MOHAN GULLA[1], MAN SINGH PARIHAR[1], KANA RAM JAT[1], SANDEEP AGARWALA[2], RAKESH LODHA[1] AND SK KABRA[1]

From Department of [1]Pediatrics and [2]Pediatric Surgery, All India Institute of Medical Sciences, New Delhi, India.

Correspondence to: Dr Rakesh Lodha, Professor, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi 110 029, India. rakesh_lodha@hotmail.com
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Background: There are limited data on congenital lung malformations (CLM) and their clinical course from developing countries. **Methods:** A 10-year retrospective chart review of records of children with CLM attending pediatric chest clinic at an Indian tertiary care center was conducted. **Results:** Among the 48 children (24 boys) included in the review, the malformations included congenital lung hypoplasia/agenesis in 24 (50%), cystic pulmonary airway malformation in 9 (19%), bronchogenic/foregut cyst in 8 (18%), and congenital lobar emphysema in 4 (9%). Median (IQR) age at symptom onset and diagnosis were 1.5 (0.4,9.5) and 24 (3,62) months, respectively. Median (IQR) weight for age for age *z*-score at presentation was -2.4 (-1.4,-3.4). More than a third (37.5%) children underwent surgical removal of resectable lesions at median (IQR) age of 14 (6,42) months. 14 (27%) children had associated congenital heart disease. Median duration of follow-up was 13 months. In children with lung hypoplasia, median (IQR) number of hospitalizations in follow-up were significantly less than that prior to diagnosis 0 (0,0) vs 1(0,2) (*P*=0.001). Median (IQR) numbers of hospitalizations in follow up were significantly less than that of prior to surgical resection 0 (0,0) vs 1(1,1) (*P*=0.016) in children with CPAM. **Conclusion:** Lung hypoplasia was the most common congenital lung malformation in our setup. Detection of malformation during antenatal period was poor. Age of diagnosis and surgical intervention is often delayed. Regular follow up and definitive and/or supportive management decreased the morbidity.

Keywords: *Bronchogenic cyst, Congenital lobar emphysema, Lung hypoplasia, Lung agenesis*.

Congenital lung malformation (CLM) is a broad term which includes lung developmental disorders such as cystic pulmonary airway malformation (CPAM) , bronchogenic cysts, pulmonary sequestration (PS), congenital large hyperlucent lobe and bronchial atresia [1]. They are rare diseases of childhood with cumulative incidence of 30–42 cases per 100,000 individuals [2]. The true prevalence of congenital lung malformations in developing countries is underestimated with data being limited to case reports and case series [3-5]. The clinical course of congenital lung malformations is largely unknown from the Indian subcontinent because of lack of antenatal diagnosis, lack of awareness among clinicians and misdiagnosis as pulmonary infections. Hence, authors share their experience with CLMs over a decade, from pediatric pulmonology service in a tertiary care center from India.

METHODS

In this retrospective chart review, records of children with CLM, attending the pediatric chest clinic of a tertiary care center in India, from 2009 to 2019, were evaluated. Congenital lung malformations had been diagnosed based on clinical features, chest *X*-ray (CXR), Contrast enhanced computed tomography (CECT) of chest, and histopathology, if resection was done. Information on demographic profile, anthropometry, respiratory system symptoms, chest imaging, spirometry, hospitalizations, treatment, timing of surgical intervention, associated reactive airway disease and follow-up including final outcome was retrieved. Data regarding echocardiography, barium swallow, nuclear scan or bronchoscopy, wherever available, were also noted. Those who did not attend our clinic after first visit were considered as lost to follow-up. These children were contacted telephonically and any missing data were obtained. This study included the CLMs, namely, congenital small lung (agenesis, aplasia and hypoplasia) and congenital thoracic malformations (CPAM), sequestration, bronchogenic cyst, foregut cyst) [7]. We excluded congenital airway malformations and congenital diaphragmatic hernia. Congenital small lung was diagnosed based on clinical signs of volume loss on particular side, CECT chest showing low lung volume with ipsilateral small pulmonary

artery and bronchial hypoplasia/aplasia if bronchoscopy was performed. Differential diagnoses considered were lung collapse secondary to impacted mucous plug/foreign body or external airway compression. Bronchogenic cyst was diagnosed based on clinical signs, smooth bordered spherical mass, associated vertebral abnormalities on CECT chest and histopathology after surgical resection. Differential diagnoses for cystic lesions considered were lung abscess, hydatid cyst, fungal disease, tuberculosis, infected bullae, vascular malformations and neoplasm based on the clinical symptoms and investigations. Congenital lobar emphysema (CLE) was diagnosed based on signs of hyper-inflation of particular lobe after exclusion of intraluminal/extra luminal compression by CECT chest or bronchoscopy. Differential diagnoses for CLE considered were pneumothorax, foreign body bronchus/external compression of bronchus causing ball-valve mechanism leading to air entrapment. CPAM was diagnosed on solid/cystic mass lesion on CECT and later histopathology. Differential diagnoses for CPAM considered were necrotizing pneumonia, sequestration, congenital diaphragmatic hernia, and peripherally located bronchogenic cyst [7]. Institute ethics committee approved the study protocol with waiver of consent.

Statistical analyses: Data were entered in MS Excel and analyzed using STATA ver.12 (Stata Corp). Significance of difference among various groups were compared using Student t-test (uniformly distributed continuous data), Mann-Whitney test (skewed data) or Chi square test or Fisher exact test (for categorical data) as applicable. Statistical significance was set at P value of <0.05.

RESULTS

Sixty-three children with congenital lung malformations were registered during study period and 48 case records could be retrieved. Major malformations were congenital lung hypoplasia 24 (50%), cystic pulmonary airway malformation 9 (19%), bronchogenic/foregut cyst 8 (17%) and congenital lobar emphysema 4 (8%). Baseline characteristics of enrolled children are shown in **Table I**.

The children with congenital small lung included right hypoplasia (n=6), right agenesis (n=5), left hypoplasia (n=9), left aplasia (n=2), and left agenesis (n=2). Of these, 3 children (13%) were treated as tuberculosis at other medical centers, prior to diagnosis, 7 (29%) were receiving cotrimoxazole prophylaxis and 17 (71%) children were advised pneumococcal and annual influenza vaccines. Two children with congenital small lung underwent pneumonectomy for repeated infections and associated lung sequestration, respectively. One child with right lung hypoplasia had systemic blood supply to the lung, which was coil embolized electively. None of the children with congenital small lung were on home oxygen. Thirteen children with congenital small lung underwent echocardiography and findings included dextrocardia-3, ventricular septal defect-2, tetralogy of fallot-1, atrial septal defect-2, patent ductus arteriosus-2, patent foramen ovale-1, pulmonary arterial hypertension-1 and normal echocardiography-2. One child had horse-shoe lung. Median (IQR) number of hospitalizations during follow-up over 19 months were significantly less than that prior to diagnosis 0 (0,0) vs1 (0,2) (P=0.001). Median (IQR) weight z score at diagnosis were than at follow-up [-2.4 (-3.4, -2.4) vs -1.7 (-2.6, -0.18), P=0.13].

Four children had bronchogenic cysts and another four had foregut duplication cysts. The hospitalization rate in follow up had significantly reduced from that prior to cyst removal, 0.5 (0,1) vs 4 (2,6) (P=0.02), respectively. Two children were treated as tuberculosis prior to referral. One of four children with foregut duplication cyst had features suggestive of gastric mucosa on nuclear scintigraphy study.

Table I Baseline Characteristics of Enrolled Patients (N=48)

Characteristics	*Value*
Type of malformation, *n* (%)	
Congenital lung hypoplasia/aplasia/agenesis	24 (50)
Cystic pulmonary airway malformation	9 (19)
Congenital lobar emphysema	4 (8)
Bronchogenic/foregut duplication cyst	8 (17)
Sequestration	1 (2)
Scimitar syndrome	1 (2)
Pulmonary AV malformation	1 (2)
Antenatal diagnosis, *n* (%)	1 (2)
Age of onset of symptoms (mo)[a]	1.5 (0.4,9.5)
Age of diagnosis (mo)	24 (3,62)
Weight at presentation, *z* score (n=47)[a]	-2.4 (-1.4,-3.4)
Male gender, *n* (%)	24 (50)
No. of hospitalizations per child prior to diagnosis for respiratory symptoms (n=47)	2 (0,3)
Operated/surgical resection done, *n* (%)	18 (37.5)
Age at surgical resection (n=18) (mo)	14 (6,42)
Lost to follow up, *n* (%)	9 (18.8)
Duration of follow-up (mo)	13 (1, 30)
Associated cardiac disease, *n* (%)	14 (27)
Treated as tuberculosis, *n* (%)[b]	5 (10)

[a]*Data in median (IQR);* [b]*prior to diagnosis of malformation.*

There were 9 children with CPAM (left lower lobe-3, right lower lobe-2, right upper lobe-2, left upper lobe-2). Median (IQR) number of hospitalizations before and after surgical resection were 1(1,1) *vs* 0(0,0), respectively (P=0.016).

Right lower lobe pulmonary arteriovenous malformation was diagnosed in a child, 60 months old, who underwent coil embolization 2 months later. Another child with Scimitar syndrome, underwent right lung pneumo-nectomy at 4 months of age. **Table II** depicts demography, clinical features and outcomes of major congenital lung malformations. All children presenting with CLM were symptomatic with almost half of them having associated reactive airway disease, receiving inhaled corticosteroids and 10% being treated as tuberculosis.

Barium swallow report was available for 18 children. Gastro esophageal reflux was seen in 1 child with right lung hypoplasia, esophageal compression in 2 children with bronchogenic cyst and scimitar syndrome, respectively, while 15 children had normal study. Of the 14 children who underwent flexible bronchoscopy, 13 with suspected congenital small lung showed hypoplasia/aplasia/absent bronchus. Bronchoscopy had done in a child with CPAM revealed normal anatomy.

DISCUSSION

In our center, lung hypoplasia was found to be the most common CLM, followed by cystic pulmonary airway malformation (19%), bronchogenic/foregut duplication cysts (17%), and congenital lobar emphysema (8%). Around 60% of non-lung hypoplasia CLMs were operated at a median age of 14 months. Lung hypoplasia was the most common CLM to be associated with congenital heart disease. Almost half of children had concurrent reactive airway disease. Hospitalization rate for respiratory problems were significantly decreased

Table II Demography, Clinical Features and Outcomes of Major Congenital Lung Malformations

Characteristics	*Lung hypoplasia (n=24)*	*CPAM (n=9)*	*CLE (n=4)*	*Bronchogenic cyst/foregut cyst (n=8)*
Antenatal diagnosis, *n* (%)	0	1 (11)	0	0
Laterality, n (%)				
Left	14 (58)	5 (55)	3 (75)	0
Right	10 (42)	4 (45)	1 (25)	2 (25)
Midline	—	—	—	6 (75)
Age of symptoms onset (mo)*	2 (1,12)	1.5 (0.5,4)	0.5 (0.05,5)	2.5 (0.15,15)
Age of diagnosis (mo)*	24 (3,84)	30 (2,60)	6 (2,8)	19.5 (2.5,36.5)
Weight at diagnosis (*z* score)*	-2.47 (-3.45,-1.72)	-1.6 (-2.7,-1.0)	-2 (-3.6,-0.52)	-2.69 (-3.33,-1.43)
Weight at last visit (*z* score)*	-1.71 (-2.6,-0.18)	-0.2 (-1.52,-0.11)	-1.24 (-3.7,-0.72)[b]	-2.27 (-4.14,-1.61)[c]
No. of hospitalizations prior to diagnosis[a]	1 (0,2)	1 (1,1)	1.5 (0.5,6)	3 (2,6)
Age at surgical resection[a]	—	6 (5,42)	8.5 (7,10)	23.5 (10,32)
Duration of follow up (mo)[a]	19 (1,39)	9 (0.75,18.5)	1.5 (0,6.5)	17 (2,25)
Associated malformations, n (%)				
Cardiac	9 (37.5)	0	1 (25)	0
Non-cardiac	1 (4)	0	0	0
Predominant symptoms at presentation, n (%)				
Cough	19 (79)	8 (89)	4 (100)	8 (100)
Fast breathing	19 (79)	5 (55)	3 (75)	6 (75)
Recurrent fever	12 (50)	3 (33)	1 (25)	4 (50)
Hemoptysis	2 (8)	0	0	4 (50)
Noisy breathing	0	0	1 (25)	3 (38)
Chest pain	4 (16)	2 (22)	0	2 (25)
Treated as recurrent pneumonia	8 (33)	2 (22)	0	5 (62)
Associated hyper-reactive airway disease	13 (54)	3 (33)	1 (25)	5 (62)

[a]Values are median (IQR); [b]n=3; [c]n=6. CPAM - cystic pulmonary airway malformation, CLE-cogenital lobar emphysema.

WHAT THIS STUDY ADD?

- The most common congenital lung malformation was pulmonary hypoplasia/aplasia.
- Age of diagnosis and surgical intervention is often delayed due to lack of awareness.

after diagnosis and supportive management or surgical resection, whichever was applicable.

The high proportion of lung hypoplasia among all lung malformations may be due to referral bias for surgical intervention to pediatric surgery clinic. Lung hypoplasia is known to be associated with other lung malformations such as cystic adenoid malformations, congenital diaphragmatic hernia, pleural effusions etc. [4,5]. In our cohort, one each had associated horse-shoe lung and intralobar sequestration, respectively. Though hemoptysis is rarely reported in lung hypoplasia/agenesis [6], 2 children in our cohort had hemoptysis, with one of them requiring coil embolization for the same. The significant decline in hospitalization rate post enrolment in our clinic, was attributed to regular follow up, nutritional and immunization counseling, regular cotrimoxazole prophylaxis and vaccination against pneumococcus and influenza in addition to routine vaccination,

Unlike reports from other parts of the world, where CPAM was reported as the most common lung malformation [7-9), this pattern was not seen in our cohort, probably due to referral bias. The median age of diagnosis of CLM and its surgical intervention was relatively higher (24 months) in our cohort, compared to other reports [7,9-12] thus revealing the low awareness level among clini-cians regarding CLMs. Further, in contrast to those cohorts [9,11], not a single child was asymptomatic at the time of presentation to our centre, highlighting the poor antenatal screening programs for lung malformations. Similar to previous reports [8,12], majority of children had associated hyper-reactive airway disease in our cohort. Our data shows that nearly 10% of the children were being treated empirically as pulmonary tuberculosis, prior to referral, underscoring the fact that persistent imaging abnormalities are often misdiagnosed in endemic countries.

The strength of this study is in its data from large numbers of children, along with a reasonable follow-up, unlike previously published data from India. Further the study brings out the limitations in diagnosing, treating and follow up of such children in lower middle income countries. The limitations of the study is it's retrospective design, substantial loss to follow up (18%), non-availability of data on pulmonary function tests and absence of assessment of chest wall deformities.

Lung hypoplasia was the most common congenital lung malformation referred to a tertiary care pediatric pulmonology centre with almost none having been detected in the antenatal period. Age of diagnosis and surgical intervention was often delayed. Reactive airway disease was the most common associated respiratory morbidity. Further studies regarding follow-up of such children are required, from developing countries.

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