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Space occupying lesions in the presence of congenital diaphragmatic hernia☆,☆☆

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ABSTRACT

Introduction: Previous reports describe lung malformations and other chest lesions in association with congenital diaphragmatic hernia (CDH), yet little is known how these lesions affect outcomes. We sought to evaluate the incidence and outcomes of patients diagnosed with chest lesions in association with CDH.
Methods: The charts of all infants treated for CDH in a single tertiary center from January 2004 to January 2015 were reviewed. The outcomes of those with space occupying lesions (SOLs) in association with CDH were compared to those with isolated CDH. Statistical analysis was performed using Student's t-test and Mann–Whitney U test for continuous variables and Fisher's exact for categorical variables.
Results: Of the 214 infants treated, 20 had an associated SOL (4 had >1 lesion). SOLs were confirmed by pathological examination and included: bronchopulmonary sequestration ($n = 10$; 4.7%), ectopic liver ($n = 9$; 4.2%), foregut duplication cyst ($n = 2$; 1%), and other lesions ($n = 3$; 1.4%). No statistical difference was noted in the long-term outcomes of patients with SOL in comparison to those with isolated CDH.
Conclusion: SOLs are not uncommon in neonates with CDH. Despite theoretical concerns, there is no evidence that SOLs are associated with worse outcomes, a finding which is helpful during prenatal counseling of families.

The identification and diagnosis of congenital lesions in the fetus have improved over the years with advances in prenatal imaging [1]. The most common lesions seen in the fetal chest include congenital diaphragmatic hernia (CDH), congenital cystic adenomatoid malformation (CCAM) and bronchopulmonary sequestration (BPS) [2]. Some congenital pulmonary lesions, in isolated cases, will regress spontaneously and have a favorable outcome without the need for surgical interventions. However, others will continue to grow and result in a mass effect in the thorax, which could lead to hemodynamic instability, cardiac failure, fetal hydrops and eventually, at times, even fetal demise [3].

Congenital malformations in the chest are rare findings with an estimated incidence of 2.2%–6.6% [4,5]. Interestingly, very little has been reported in the literature on the outcomes of patients with these lesions in association with CDH. In BPS, for example, 60% of the patients present with coexistent congenital anomalies where CDH is the most common associated anomaly with an incidence of about 15%–30% of the cases [6–9]. Grethel et al. [8] evaluated 16 cases prenatally diagnosed with BPS and CDH. Only 12 of these patients proceeded to delivery where 6 survived and 6 died. Two of these patients were pathologically confirmed after resection to be ectopic liver instead of BPS. Their study observed that BPS in CDH patients had better prognosis than expected even when dismal prenatal predictors such as a low lung-to-head ratio and elevated liver herniation were present. The purpose of our study was to evaluate the incidence of space occupying lesions (i.e. BPS, CCAM, ectopic liver, duplication cysts and other congenital chest lesions) that may be present with CDH, at a single tertiary center. We also set out to determine if their clinical outcomes and prognosis differed from those patients with isolated CDH cases.

1. Patients and methods

The study was approved by Baylor College of Medicine Institutional Review Board (H-26719). A retrospective review of patient's charts was conducted of all neonates treated for congenital diaphragmatic hernia (CDH) at Texas Children's Hospital, Houston, TX from January 2004 to January 2015.

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1.1. Data collection

Each patient's prenatal data were collected from the mother's medical records. These data included gestational age at diagnosis, observed-to-expected total fetal lung volume (O/E-TFLV), percent of liver herniation (%LH), and lung-to-head ratio (LHR) and dimensions of the chest lesion if prenatally identified. For the postnatal data, the neonates' medical records were reviewed for information on gestational age at birth, birth weight, presence of associated anomalies and outcomes at 6 months. Prenatal MRI imaging, operative findings during CDH repair and pathology/autopsy of neonates with CDH were evaluated for presence of space occupying lesions (SOL), i.e., bronchopulmonary sequestration (BPS), ectopic liver, foregut duplication cysts and any other congenital chest mass. Ectopic liver was defined as supradiaphragmatic accessory liver with normal liver tissue seen by histology but clearly distinct from a herniated liver. The prenatal factors and postnatal outcomes of those with a space occupying lesions (SOL) in association with CDH were compared to those with isolated CDH. Isolated CDH was defined as CDH occurring without the presence of any major anomalies. Major anomalies were considered to be chromosomal anomalies, all cardiac anomalies excluding small atrial or ventricular septal defects and patent ductus arteriosus, and any structural anomaly that required medical or surgical interventions.

1.2. Statistical analysis

Student's t-test and Mann–Whitney U test were used for continuous variables, and results were represented as the median value and their range. Fisher's exact test was used for comparison of categorical variables. A statistical analysis was performed using IBM SPSS statistical software version 22 (IBM Corporation, Armonk, NY). A p-value of less than 0.05 was considered to be statistically significant.

2. Results

2.1. Patients

Of the 214 patients diagnosed with CDH during the study period, 96 were determined to be isolated CDH cases, 98 had an associated major cardiac or genetic anomaly, and 20 had CDH and an associated SOL. Four of the 20 SOL cases were found to have more than one SOL present. Only 1 SOL patient had a major anomaly. It was noted that 77% of isolated CDH and 70% of SOL patients were in-born ($p = 0.36$). A female predominance in the SOL patients was observed in comparison to the isolated cases (65% vs. 39%, respectively $p = 0.03$).

2.2. Patients with space occupying lesions

Of the CDH cases with SOL, 10 patients were diagnosed with bronchopulmonary sequestration (4.7%), 9 with ectopic liver (4.2%), 2 with foregut duplication cyst (1%), 1 with an ectopic adrenal gland near the diaphragm (0.5%), 1 with pleural cyst (0.5%) and 1 with epidermoid cyst (0.5%) by pathological examination (Table 1). Of the 20 patients, the hernia defects noted were posterolateral ($n = 14$), diaphragmatic agenesis ($n = 4$) and mediastinal hernia ($n = 2$). The majority were left-sided CDH (75%), and none of the hernias were bilateral. A hernia sac was present in 12 of the patients (60%). Nine of the 20 SOL cases (45%) that were diagnosed prenatally, had BPS in the presence of CDH.

Of those patients in whom pathology showed ectopic liver, 6 of 9 (67%) were incidental at the time of CDH repair. The remaining cases had been suspected to be BPS based on antenatal MRI. In 63% of the cases, the left lateral lobe of the liver was found to be adherent to the diaphragmatic hernia sac, and the sac was the most common location where heterotopic liver tissue was found by histology. Two cases were associated with pericardial defects. Overall survival for the patients with ectopic liver was 88%, with the sole death being a case of right CDH with severe pulmonary hypertension.

2.3. Demographics of patients with space occupying lesions vs. isolated CDH cases

Table 2 shows the prenatal and postnatal characteristics of SOL compared to isolated CDH patients. In comparison to those with isolated CDH, infants with CDH and SOL had no significant difference in the frequency of prenatal diagnosis of CDH (70.2% vs. 68.4%, $p = 1.0$), gestational age at diagnosis of CDH, gestational age at birth or birth weight. In general, neonates in both groups were full term and of adequate weight with an Apgar score >7 at 5 min. The mean O/E TFLV in patients with SOL and CDH was significantly greater in comparison to the isolated CDH group (42%, range: 23%–58% vs. 33%, range: 12%–75%, $p = 0.008$).

Table 1
Prenatal and postnatal characteristics of patients with CDH with an associated space occupying lesions compared to those with isolated CDH.

Patient no.	Diagnosis	Sex	Genetic anomaly	Cardiac anomaly	Structural anomaly	Survivor (yes or no?)
1	• Mesothelial cyst	F	Chromosome 11 anomaly	ASD, PDA	Micrognathia, oculoauricular–vertebral spectrum	N
2	• BPS • Ectopic liver	F	–	–	–	Y
3	• Ectopic liver	F	–	–	–	Y
4	• BPS	M	–	ASD	–	Y
5	• Ectopic liver • Pleural cyst	M	–	–	–	Y
6	• BPS	F	–	–	–	Y
7	• BPS • Foregut duplication cyst	F	–	PDA	–	Y
8	• Ectopic liver	F	–	ASD, PDA	–	N
9	• Ectopic liver	M	–	VSD	–	Y
10	• Ectopic liver	F	–	–	–	Y
11	• Ectopic liver	M	–	ASD	–	Y
12	• BPS	M	–	–	Papillary nephrocalcinosis	Y
13	• BPS	M	–	ASD	–	Y
14	• Ectopic adrenal gland	F	–	–	–	Y
15	• Ectopic liver	F	–	–	–	Y
16	• BPS	F	–	ASD, PDA	–	Y
17	• BPS • Foregut duplication cyst	M	–	PFO, secundum ASD	–	Y
18	• Epidermoid cyst	F	–	–	–	Y
19	• Ectopic liver	F	–	–	–	Y
20	• BPS	F	–	–	–	Y