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RESEARCH ARTICLE

Congenital Pulmonary Malformations From The Prenatal to The Postnatal Period: Tertiary Center Experience

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Abstract

Introduction: Our purpose was to review our experience with the fetuses diagnosed prenatally with congenital pulmonary malformations (CPM). **Methods:** Retrospective study of fetuses prenatally diagnosed with congenital pulmonary airway malformation (CPAM), bronchopulmonary sequestration (BPS), bronchogenic cyst (BC) by ultrasonography between September 2020 and December 2022 **Results:** Sample analysis was based on 34 pregnancies with CPMs. On the basis of prenatal sonographic appearance, CPAM, BPS and BC were identified antenatally in 79.4% (27/34), 14.7% (5/34) and 5.8% (2/34), respectively. Most (76.5%) were isolated, all cases were unilateral (100%) and majority (64.7%) were regressed late antenatally or postnatally with expectant management. Of the 27 fetuses presented with CPAM, postsurgical resection was necessary for 5 cases (18.5%). There was only one case with hydrops and a CPAM volume ratio >1.6 and was managed with thoraco-amniotic shunt prenatally and right lower lobe resection postnatally. Of the 5 fetuses presented with BPS, thoracoscopic excision was necessary for 2 cases. Of the 2 fetuses presented with BC, cyst excision was performed or planned to cases. **Conclusion:** The results from our center in last two years reflect overall favorable outcomes for all CPMs. The role of ultrasound is cost-effective during perinatal period rather than fetal MRI.

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Introduction

Congenital pulmonary malformations (CPM) are a rare group of developmental pulmonary abnormalities that are often first identified prenatally on routine second-trimester ultrasound, including CPAM formally known as congenital cystic adenomatoid malformation, bronchopulmonary sequestration (BPS), congenital lobar overinflation, bronchogenic cyst (BC) and bronchial atresia. Due to widespread availability of prenatal ultrasound combined with the improved resolution of ultrasound technology that enables the detection of smaller lung lesions, the incidence of these malformations is increasing and estimated to be around 1 in 2500 to 8000 live births.[1,2] CPAM and BPS account for a majority of CPMs, while CPAM represents 75% and BPS consists 0.15–6.4% of all congenital lung malformations. Other lesions, such as BCs, are even less common.

CPAM is a developmental malformation of the lower respiratory tract due to failure of maturation of bronchiolar structures during the pseudoglandular stage of lung development, resulting in overgrowth of the terminal bronchioles without corresponding alveoli. The lesion communicates with the tracheobronchial tree and derives its blood supply from the pulmonary arteries. CPAMs can be further categorized into microcystic, macrocystic, or mixed lesions based on prenatal ultrasound (Figure 1-2). BPS is a nonfunctioning lung tissue with anomalous systemic arterial supply that does not communicate with tracheobronchial tree while localised within the normal lung tissue (intralobar) or the development of separate pleura (extralobar) (Figure 2). Hybrid lesions displaying characteristics of CPAM and BPS have been described sonographically and histopathologically. BC is part of the family of foregut duplication cysts, which also includes enteric and neuroenteric cysts and may be located in the mediastinum or in the medial lung parenchyma (Figure 4).

Clinical presentation of CPM is highly variable, ranging from apparent in-utero resolution to even severe mass effect with resultant hydrops fetalis and even fetal demise. Prenatal imaging characteristics on fetal and neonatal outcomes, such as size, appearance (cystic versus solid), mediastinal shift, feeding vessel presence, CPAM-volume ratio (CVR) and hydrops, determine the prenatal and postnatal management strategies.[3,4]

In this study, we describe and evaluate our current experience and to review current literature on the fetuses diagnosed prenatally with the following pulmonary malformations: CPAM, BPS and BC.

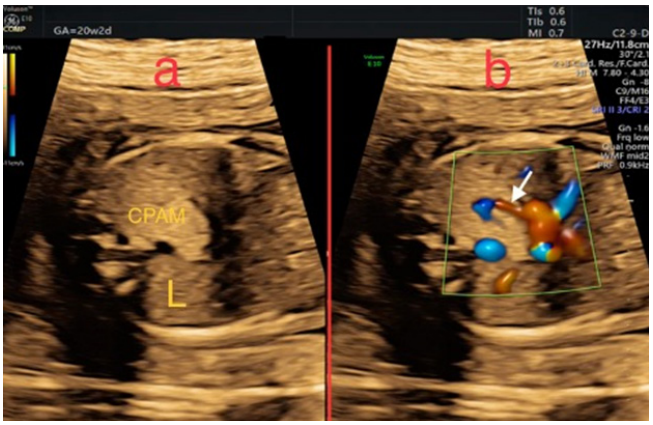

Figure 1. Congenital pulmonary airway malformation (CPAM). a Transverse sonographic image through the fetal chest at 20 weeks of gestation shows a hyperechoic mass (CPAM) and the normal intermediate echogenicity lung parenchyma (L) is visible. b Power Doppler US image of the same image shows a feeding vessel (arrow) from the pulmonary artery supplying the CPAM.

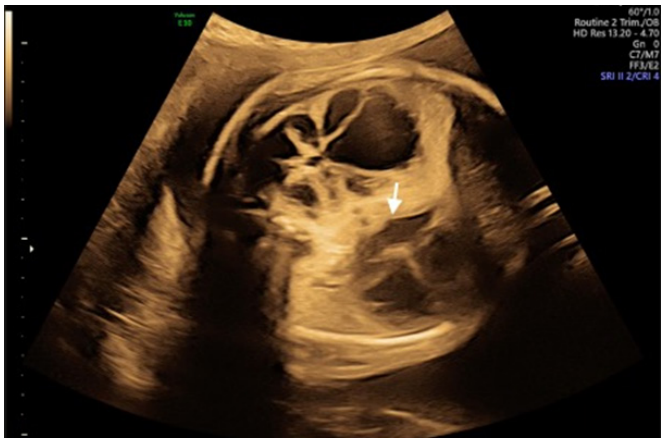

Figure 2. Macrocystic congenital pulmonary airway malformation (CPAM). Transverse sonographic image through the fetal chest demonstrates a multiseptated, primarily anechoic intrathoracic mass (arrow). Cardiomediastinal shift is present, with leftward displacement of the heart.

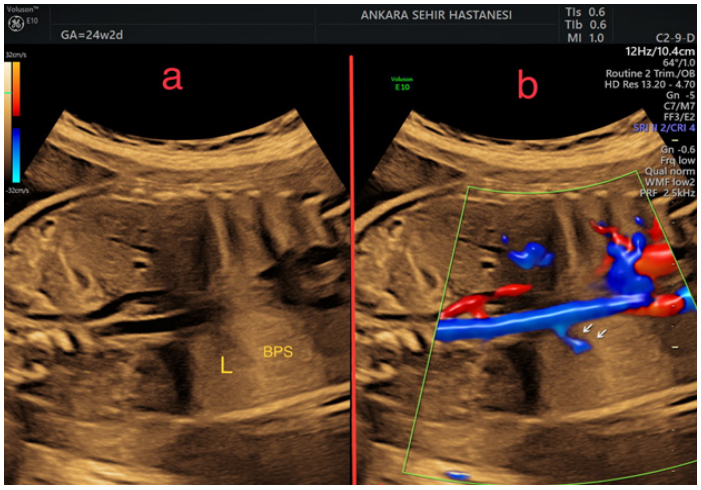

Figure 3 Bronchopulmonary sequestration. a Coronal sonographic image at 24 weeks of gestation shows a hyperechoic wedge-shape mass (BPS) at the posterioinferiorleft lung . The normal intermediate echogenicity lung parenchyma (L) is visible. b Power Doppler US image of the same iamge shows a feeding vessel (arrow) from the descending thoracic aorta supplying the bronchopulmonary sequestration

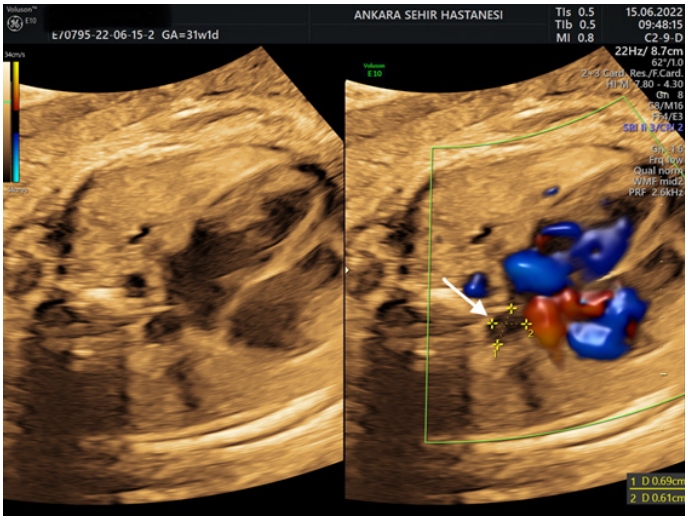

Figure 4. Bronchogenic cyst. Transverse sonographic (left) and transverse color Doppler US image (right) of the same fetus through the fetal chest at 31 weeks. A round, anechoic, avascular cyst (arrow) is present in the midline behind the heart, compatible with a bronchogenic cyst.

Material and Methods

We conducted a review of all pregnancies complicated by a prenatally diagnosed CPAM, BPS, BC at 21-33 weeks of gestation between September, 2020 and December, 2022 in Ankara City Hospital, Department of Obstetrics and Gynecology, Division of Perinatology, Ankara, Turkey. Approval was granted by the local Institutional Review Board for this retrospective cohort study (E2-23-3952). Freely-given informed consent to participate in the study was obtained from all participant pregnant women. Literature search was also carried out to compare our data with those of previous series.

Pregnancies with additional anomalies that could impair lung capacity (e.g. congenital diaphragmatic hernia) were excluded, and subdiaphragmatic BS and esophageal duplication cysts were also excluded since our aim was to investigate the effect of only pulmonary lesions in thorax on perinatal outcomes.

Baseline maternal demographic information and clinical data were obtained from review of stored electronic medical records. Imaging records for all cases were assessed to confirm diagnosis and to calculate the CVR value of cases without records. CVR was calculated by multiplying the three dimensions of the lung mass with 0.52 and dividing by the head circumference according to previously published formula.[3] Thirteen cases for which no or insufficient images had been stored were excluded from the cohort. To perform this study, the following variables were evaluated: Maternal age, gravidity, parity, previous miscarriage, living child, gestational week at diagnosis, location of lesion, initial CVR values, whether the presence of ascites, pleural effusion, hydrops, mediastinal shift and associated structural/chromosomal abnormalities, gestational age at delivery, gender of neonates, birth weight, Apgar scores at first and fifth minutes, NICU admission, mortality due to pulmonary lesion and short term (postnatal first three months) outcome.

The data were collected using an Excel 2007 spreadsheet (Microsoft Corp., Redmond, WA, USA). For statistical analysis, continuous variables were presented as mean& standard deviation (SD) or median and range values according to the normally distributed by using the Kolmogorov–Smirnov test. Categorical variables were expressed as numbers and percentages.

Results

During the study period, 41 pregnancies were evaluated and distribution of congenital thoracal lesions and flowchart illustrating study population selection is presented in Figure 5. Of 41 pregnancies complicated by fetal congenital

thoracal lesions during the study period, 6 cases were excluded from further analysis: three with a coexistent congenital diaphragmatic hernia, two subdiaphragmatic sequestrations, one esophageal duplication cysts, since our aim was to investigate the effect of pulmonary lesions on perinatal outcomes alone. Actually, there were 3 cases with BC, but preliminary diagnosed case was seen as an esophageal duplication cyst during surgical excision and died due to postoperative infection, so it was excluded. Finally, we included 34 cases in the study analysis. According to prenatal sonographic data, 27.5% of cases were microcystic, 31% were macrocystic and 41% of cases were unspecified.

Demographics and characteristics of the study population is presented in Table 1. Maternal mean standard deviation (SD) age was 29.41±4.88 and mean SD gestational week at diagnosis of the pulmonary lesions were 25.03±3.4. Ten of thirty-four pregnant women (29.4%) had maternal disease and/or obstetric complication and all of those except one were present in patients diagnosed with CPAM. There were two cases of twin pregnancy (1dichorionic-diamniotic, 1monochorionic-diamniotic) and in both, only one of the fetuses had CPAM. In both twin pregnancies, fetuses had macrocystic CPAM and were born at 32nd and 34th gestational week. Both newborns underwent thoracic surgery in the first three months postnatally and the prenatal diagnosis was confirmed pathologically. Table 1 outlines the characteristics of the lesions on the basis of prenatal sonographic appearance. Fourteen fetuses (41%) had right- sided lesions, 18 (53%) had left-sided lesions, and 2 fetus (those with BCs) had median

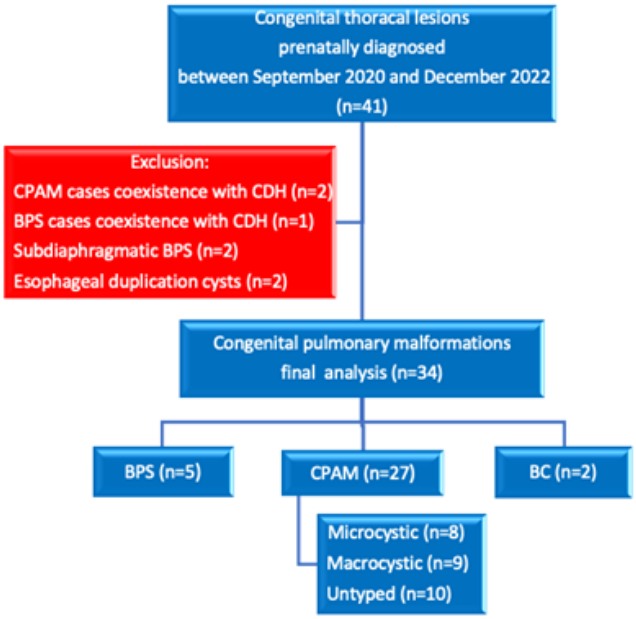

Figure 5. Flowchart illustrating study population selection

Table 1. Demographics and characteristics of congenital pulmonary lesions

	All (n=34)	CPAM (n=27)	BPS (n=5)	BC (n=2)
Maternal age (mean, SD)	29.41±4.88	28.5 ±4.6	33.8 ±5.1	29,31
Gravidity (median, min-max)	2 (1-6)	2 (1-4)	3 (2-6)	2,1
Parity (median, min-max)	1 (0-4)	1 (0-3)	2 (1-4)	0,0
Previous miscarriage (median, min-max)	0 (0-3)	0 (0-1)	0 (0-3)	1,0
Living Child (median, min-max)	1 (0-3)	1 (0-3)	2 (1-3)	0,0
GW at diagnosis (mean, SD)	25.03±3.4	25.04 ±3.4	23.2 ±2.1	28,31
Maternal disease and/or obstetric complication	10/34 (29.4%)	10/27 (37%) 3 GDM 1 GDM+MKDA+PTB 1 asthma 1 placenta previa 1 DKDA+ cerclage 1 GHT 1 hypothyroidism 1 hx of gastric bypass	1/5 (20%) 1 GDM	0
Location of lesion (n, %)				
Right Lung	14/34 (41%)	14/27 (52%)	0/5 (0%)	-
Left Lung	18/34 (53%)	13/27 (48%)	5/5 (100%)	-
Median	2/34 (6%)	-	-	2/2 (100%)
Initial CVR	0.39±0.37	0.39±0.4	0.42±0.17	
CVR>1.6	1/34	1/27	0/5	
Ascites& Hydrops	1/34	1/27	0/5	0/2
Pleural effusion	4/34	4/27	0/5	0/2
Mediastinal shift	8/34	7/27	1/5	
Associated structural and/or chromosomal anomalies	8/34 (23.5%)	6/27 (22.2%) 1 umbilical vein varix 1 single umbilical a. 1IUGR+oligohydramnios 2 polyhydramnios 1 VSD	0/5	2/2 (100%) 1polihidramnios 1DORV+EDC

CPAM: Congenital Pulmonary Airway Malformation; BPS: Bronchopulmonary Sequestration; BC: Bronchopulmonary Cyst; CVR: CPAM Volume Ratio; DORV: Double Outlet Right Ventricle; EDC: Esophageal Duplication Cyst; n: Number; SD: Standard Deviation; MKDA: Monochorionic Diamniotic Twin pregnancy; PTB: Risk of Preterm Birth; DKDA: Dichorionic Diamniotic Twin Pregnancy; GHT: Gestational Hypertension; IUGR: Intrauterine Growth Retardation; VSD: Ventricular Septal Defect; GW: Gestational Week.

lesions identified. In subgroup analysis, we identified that CPAM lesions were predominantly in right lung (52%) and all BPS lesions were in left lung (100%). The mean CVR at initial diagnosis, available in all CPAM and BPS cases, was 0.39 (± SD of 0.37, range 0.04-1.62). Mediastinal shift was evident in 8 of 34 cases. In our cohort, hydrops was identified only in one case; a right-sided microcystic CPAM with ascites, subcutaneous edema, bilateral pleural effusion, mediastinal shift and elevated CVR (1.62). This female fetus underwent placement of thoraco-amniotic shunt at 32th week subsequently resolved and were delivered at 38th week weighing 2020 gr and underwent right lower lobectomy. Histopathological analysis of the resected lobe identified features of macrocystic CPAM. Eight of all 34 cases (23.5%) had other structural anomalies while none of cases with BPS had additional structural anomalies. Six of twenty-seven cases with CPAM (22.2%) had associated anomalies (umbilical vein varix, single umbilical artery, VSD, polyhydramnios and intrauterine growth retardation).

The two cases with BC had other structural anomalies (1 case with double outlet right ventricle and esophageal duplication cyst, 1 case with polyhydramnios). BC case with polyhydramnios was underwent surgical resection and BC with DORV+EDC is still in follow-up, and she is waiting for simultaneous resection with DORV surgery at postnatal 6th month. Actually, there were 3 cases diagnosed with BC and preliminary diagnosed BC case was seen as esophageal duplication cyst during surgical excision.

Only a small minority of cases underwent genetic amniocentesis (n = 4) and all of which returned normal karyotypes.

Table 2 outlines the fetal and neonatal outcomes of congenital pulmonary lesions. None of the pregnancies underwent termination and all thirty-four (100%) of fetuses survived. Most cases were delivered at term, median gestational week at delivery was 38 (range, 32-40) and mean standard deviation (SD) birthweight was 3165±530 gr. Eight of thirty-four neonates (23.5%) were admitted to the NICU following delivery based on local generalized practice irrespective of respiratory status. Majority of congenital pulmonary lesions (64.7%) were resolved late antenatally or postnatally with expectant management. Surgery was performed in 8 of 34 cases (23.55%) and 4 of 34 (11.8%) cases are still being followed. Survival rate in the first three months of neonatal period was 100%.

Discussion

In consistent with the previously and recently published literature, our experience further confirms that CPMs are with benign outcome, which is not usually associated with structural, chromosomal or fetal growth defects.[5-6-7] This study demonstrated that with careful follow-up during pregnancy and after birth, the majority of the pregnancies with congenital pulmonary malformations were delivered at term, without NICU admission, with only 11% need for thoracic surgery during the first 3 months of life. Consequently, survival rate in the first three months of neonatal period was 100%, even in complicated cases with hydrops.

Since most of our cases resolved spontaneously (64.7%), pathological confirmation was only possible in patients who underwent thoracic surgery. However, thanks to the ultrasonographic improvements, all of the postnatal computed tomography performed in the postnatal period were concordant with our prenatal diagnoses, except for two case. In one of the three fetuses followed up prenatally with BC, esophageal duplication cyst was seen on gross examination during surgical excision, and we excluded this case from our study. The other discordant case was confirmed as CPAM postnatally, which we diagnosed as hybrid lesion prenatally. Despite antenatal diagnosis of congenital cystic lung lesions

Table 2. Fetal and neonatal outcomes of congenital pulmonary lesions

	All (n=34)	CPAM (n=27)	BPS (n=5)	BC (n=2)
Termination of pregnancy	0	0	0	0
Fetal thoraco-amniotic shunt procedure	1/34	1/27	0	0
GA at delivery (median, min-max)	38 (32-40)	39(32-40)	38(37-40)	36, 39
Birthweight (gram, mean, SD)	3165±530	3138±530	3421±349	2470, 3320
Gender (n, %)				
Male	18 (53%)	15 (55%)	3 (60%)	
Female	16 (47%)	12 (45%)	2 (40%)	2/2 (100%)
Apgar at 1st minute (median, min-max)	7 (5-7)	7 (5-8)	7 (7-7)	7,9
Apgar at 5th minute (median, min-max)	9 (7-9)	9 (7-9)	9 (8-9)	7,9
5th minute Apgar < 7	0	0	0	0
NICU admission (n, %)	8/34 (23.5%)	6/27 (22.2%)	1/5 (20%)	1/2 (50%)
Short term outcome (n, %)				
Spontaneous resolution	22/34 (64.7%)	19/27 (70.4%)	3/5 (60%)	0/2
Expectant management	4 /34 (11.8%)	3/27 (11.1%)	0/5 (0%)	0/2
Thoracic Surgery	8/34 (23.55)	5/27 (18.5%)	2/5 (40%)	1/2
Planned for surgery				1/2
Mortality due to pulmonary lesion	0 (0%)	0 (0%)	0 (0%)	0 (0%)

CPAM: Congenital Pulmonary Airway Malformation; BPS: Bronchopulmonary Sequestration; BC: Bronchopulmonary Cyst; NICU: Neonatal Intensive Care Unit; GA: Gestational Age

reaches 85.7% due to sonographic improvements,8 the ultrasonographic appearance of CPMs in our study was indistinguishable as reported before and only color Doppler ultrasound made the definition between CPAM and BPS demonstrating their unique and different blood supply.[9] Prenatal magnetic resonance imaging (MRI) was reported to have high sensitivity and specificity in the detection of pulmonary lesions and consistent with surgical pathology in 82–91% of cases while this consistence was 82-83% by ultrasonography. However, as it appears more cost-effective that prenatal management and prognostication based on lesion size than prediction based on suspected final histology, MRI did not demonstrate any added value in terms of diagnosis and prognosis compared to the ultrasound.[10],[11] As previously reported that the prognosis of CPMs was associated with elevated CVR, mediastinal shift and presence of hydrops fetalis, also supports the cost-effectiveness of ultrasound in prenatal diagnosis [3],[12] Supporting the literature, we had the only one case with elevated CVR (1.62), and that was the only case who developed hydrops. Fetal management was carried out by placement of a thoraco-amniotic shunt.

Literature about thoraco-amniotic shunt placement reported periprocedural complications including premature preterm rupture of membranes (PPROM), preterm labor, chorioamnionitis, shunt occlusion, and fetal dislodging of the shunt requiring a new shunt placement with the same risks, and postnatal complications including rib deformities in 77% of the neonates.[13],[14] Fortunately, although our case was complicated with IUGR and oligohydramios, she was delivered at 38th gestational week without periprocedural complications.

The surgical management in neonates and infants with CLMs is consensual for symptomatic patients while postnatal management of asymptomatic patients is controversial. Some propose prophylactic surgery in the asymptomatic infant to avoid possible infection and malignancy that could develop later in life.[15],[16] However, some clinicians recommend for conservative management of asymptomatic prenatally CPAMs and BPSs.[16] In a meta-analysis of 1,070 neonates with CPAM and BPS, approximately 50% remained asymptomatic into infancy, and only 3% of the asymptomatic infants eventually became symptomatic while being observed or awaiting for surgery.[17] Our clinicians applied expectant management in asymptomatic cases, as highlighted in table 2, surgery was performed in 23.5% of all cases.

Congenital pulmonary malformations could be associated with other congenital malformations. Associated abnormalities seen in 3-12% of CPAMs and those present up to 50% of BPSs.[18] However, it is noteworthy that in our study, no associated abnormalities were observed in any of the 4 BPSs cases.

Our study has some limitations. The main limitations were retrospective design and the lack of long-term outcomes. Additionally, the impact of corticosteroids as therapy on the perinatal outcomes of fetal CPMs could not be assessed, as this information was not readily available. It may depend on the fact that it is used according to the initiative of the physician. It is not included in the routine protocols in our clinic as it cannot be proven due to small sample sizes. Finally, histopathological diagnosis was only available in a minority of cases due to local preference for conservative management and the high spontaneous resolution rates of lesions.

Conclusion

The findings from our center in last two years reflect overall favorable outcomes for all congenital pulmonary malformations, even in complicated cases with appropriate management. The role of ultrasound in the diagnosis and management of congenital pulmonary malformations is important and cost-effective during perinatal period rather than fetal MRI and other diagnostic tools. However, esophageal duplication cysts should be taken into consideration in the differential diagnosis of cases prenatally diagnosed with BC by ultrasonography. Serial ultrasounds should be performed to evaluate the malformation, to assess the fetus for associated anomalies and to plan for delivery and future treatment. Although the vast majority regressed spontaneously, a multi-disciplinary team should play a vital role in ensuring that the mother and fetus receive current and recommended treatment and are managed antenatally and postnatally. Even in asymptomatic cases, or those with ultrasounds suggestive of a regressed lesion, they should still undergo investigation with a postnatal follow-up because of the risk of long-term sequelae and malignancy.

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Conficts of Interests

The authors have no relevant financial or non-financial interests to disclose.

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Data Availability Statement

Data available on request due to privacy/ethical restrictions. The data used in this study can be shared on demand if any concern rises due to the reliability of the data but according to the ethical and legal regulations in Turkey the authors can not share the data via a data repository.

Authors contributions

All authors contributed to the study conception and design and meet the ICMJE criteria for authorship. Material preparation, data collection, study design and analysis were performed by [Aysegul Atalay]. The first draft of the manuscript was written by [Aysegul Atalay]. [Dilek Sahin] critically revised and commented on previous versions of the manuscript and study supervision. All authors read and approved the final manuscript.

Ethical approval

Ethics approval was obtained from the institutional review board. The study was conducted in accordance with the Declaration of Helsinki.

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