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Outcomes of fetal non-cardiac thoracic abnormalities: a single center experience

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ABSTRACT

Aims: This study planned to evaluate fetal non-cardiac thoracic anomalies, which are less common than other organ systems, in terms of diagnosis, incidence, therapy and prognosis.

Methods: The data of 66 cases who were evaluated in a perinatology department between January 2021 and July 2023 with diagnosis of fetal non-cardiac thoracic abnormalities were analyzed retrospectively.

Results: A total of 66 cases were in our study with a mean maternal age of 28.61±4.9 years and a median gestational week of first assessment at our center of 24 weeks (15-38 weeks). The most common non-cardiac thoracic malformation was congenital diaphragmatic hernia (30 cases, 45.4%), followed by congenital pulmonary airway malformation (CPAM) (17 cases, 25.7%). Termination of pregnancy was performed in 4 cases (6.06%). While genetic testing was carried out in a total of 9 cases (13.9%), no chromosomal abnormality was found in any of these cases. In utero interventional procedure was performed in 5 cases (7.57%) and success was achieved in 3 cases. Ten (58.8%) cases with CPAM lesions were resolved during the late antenatal or postnatal period with expectant management. Surgery was performed in 2 (11.8%) of 17 cases with CPAM.

Conclusion: Deliveries of the FNTA cases should be planned in tertiary centers where necessary intervention and care can be provided. A multi-disciplinary team could demonstrate a crucial role in assuring that the pregnant woman and fetus obtain appropriate treatment and are managed during the antenatal and postnatal periods. US plays a crucial role in the diagnosis and management of FNTA cases during the prenatal period rather than fetal MRI and other diagnostic tools. More than half of the CPAM lesions regressed spontaneously with expectant management.

Keywords: Congenital thoracic malformations, prenatal ultrasound, postnatal treatment

INTRODUCTION

Fetal non-cardiac thoracic abnormalities (FNTA) are reported to occur in 1/10000-1/35000 pregnancies that originate from lung parenchyma, airways or vascular structures. These abnormalities develop as a consequence of diverse embryologic abnormalities. However, because of the similar physiopathologic mechanisms, these anomalies might potentially have a devastating effect on normal fetal development and perinatal outcomes.[1]

FNTA are increasingly being detected using prenatal ultrasound nowadays.[2] FNTA take a place in a wide range from asymptomatic and small-sized pathologies to covering most of the thorax, accompanied by other anomalies and requiring urgent intervention. Intrauterine recognition of thoracic anomalies and knowing their possible complications play a decisive role in pregnancy follow-up strategy, delivery method and perinatal care.[3]

The main method of examination is ultrasonography (USG). Magnetic resonance imaging (MRI) can be considered in addition to USG in cases where USG is not sufficient. USG appearances of some pathologies are very similar and prenatal definitive diagnosis is often not possible. Especially, MRI is used as an auxiliary method in cases where diagnosis is difficult and in calculating lung volüme comes into play.[4] The most important predictor of perinatal survival in a fetus with a lung mass is the presence or absence of fetal hydrops. The mortality rate can reach%90 in the presence of hydrops.[5]

The most common thoracic anomalies in fetuses are congenital diaphragmatic hernia (CDH), congenital pulmonary airway malformation (CPAM) and hydrothorax. Congenital bronchogenic cysts, esophageal duplication cysts, bronchial atresia, and arteriovenous malformations are rare anomalies.[6,7]

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In this study, FNTA cases of our maternal-fetal medicine unit were classified according to their origin and presented based on USG findings.

METHODS

Ethics

The study was carried out with the permission of Başakşehir Çam and Sakura City Hospital Clinical Researches Ethics Committee (Date: 11.10.2023, Decision No: 462). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This retrospective study was conducted by evaluating a total of 66 cases referred from the external center or diagnosed for the first time with the diagnosis of prenatal FNTA between January 2021 and July 2023 in the Perinatology Department of Çam and Sakura City Hospital. Our hospital serves as a tertiary reference center of the region.

Fetal USG examination and prenatal diagnosis were made by maternal-fetal medicine specialists using ultrasonic equipment with the option of color and pulsed Doppler USG. After the diagnosis of the fetal anomaly, all cases were re-evaluated and discussed by the multidisciplinary perinatal team, which consists of medical specialists involved in perinatal care, including maternal-fetal medicine specialists, obstetricians, neonatologists, paediatric surgeons, paediatric intensive care specialists, and clinical geneticists. Following this, information was given to parents about the significance of the diagnosis, whether surgical or non-surgical treatment modalities would be required after birth, the expected short and long-term prognosis of the cases, and the option of termination of pregnancy.

All examinations were performed using ultrasonic equipment with the option of color and pulsed Doppler with Arietta 850 USG (Hitachi, Japan). The confirmation of diagnosis was assessed by postnatal follow-up in the first months of life, and/or by autopsy in cases of termination of pregnancy.

Maternal age, gestational week at diagnosis, the presence of consanguineous marriage, the diagnosis before referral to our clinic, the presence of chromosomal anomalies, and prenatal and postnatal treatment procedures were recorded in detail.

Statistical Analysis

IBM SPSS Statistics for Windows, Version 26.0 (Chicago, IL, USA) was used for statistical analysis of the data. Our analysis was confined to descriptive statistical methods and encompassed the utilization of mean±standard deviation, or median (minimum-maximum), and percentage distributions to delineate the demographic and clinical features of the participants. A p-value less than 0.05 was considered statistically significant.

RESULTS

A total of 1124 pregnant women with a major fetal abnormality were assessed in our center during the study period. The total number of fetuses diagnosed with FNTA or whose FNTA diagnosis was confirmed before referral was 66 (5.87%) in our center during this period of more than 2 years. The antenatal prevalence of FNTA in our study cohort was 5.87%. The median gestational age at first evaluation at our center was 24 weeks (minimum 15 weeks, maximum 38 weeks) and the mean maternal age was 28.61±4.9 years.

Table 1 shows prenatal and postnatal diagnostic lesions and types of malformations of cases in our study. As can be seen in Table 1, seven different types of FNTA were detected prenatally. These are CDH (n=30, 45.4%), CPAM (n=17, 25.7%), esophageal atresia (n=6, 9%), idiopathic hydrothorax (n=5, 7.5%), bronchopulmonary sequestration (n=5, 7.5%), congenital bronchogenic cysts (n=1, 1.5%), Cantrell pentalogy (n=1, 1.5%), and congenital high airway obstruction syndrome (CHAOS) (n=1, 1.5%). Postnatal information of 39 patients (59%) who were followed up and delivered in our hospital out of a total of 66 cases was obtained. Information about the remaining 23 cases that were not delivered in our hospital could not be obtained.

Table 1. Types of fetal noncardiac thoracic malformations

	Prenatal diagnosis	Postnatal diagnosis
Congenital diaphragmatic hernia, n (%)	30 (45.4%)	18
Congenital pulmonary airway malformation, n (%)	17 (25.7%)	7
Esophageal atresia, n (%)	6 (9%)	6
Idiopathic hydrothorax, n (%)	5 (7.5%)	2
Bronchopulmonary sequestration, n (%)	5 (7.5%)	5
Congenital bronchogenic cysts, n (%)	1 (1.5%)	1
Cantrell pentalogy, n (%)	1 (1.5%)	-
Congenital high airway obstruction syndrome, n (%)	1 (1.5%)	-
Total	66	39

Demographic and clinical characteristics of the cases are shown in Table 2. Chromosomal analysis was performed in 9 of the cases (13.64%); of which 6 fetuses had a CDH, and three had idiopathic hydrothorax. However, no chromosomal abnormality was found in any of these cases. Parents opted for termination of pregnancy (TOP) in 10 cases; of which, 4 fetuses had a CDH, 2 had CPAM, one had esophageal atresia, one had pulmonary sequestration, one had Cantrell pentalogy, and one had

CHAOS. Termination of pregnancy was performed in a total of 4 cases with fetal hydrops; of which two fetuses had CPAM, one had CDH, and one had Cantrell pentalogy. Two patients who opted for pregnancy termination but did not choose this option (one fetus had CDH, and one had CHAOS) experienced spontaneous intrauterine fetal demise. In total, intrauterine fetal death was observed in 4 cases (6.06%) during the follow-up visits in the intrauterine period; of which, two fetuses had CPAM, one fetus had CDH, and one had CHAOS. Three cases received intrauterine treatment during the follow-up period. Neonatal death was observed in 8 cases (12.12%).

Table 2. Demographic and clinical characteristics of the cases

Maternal age, years (mean±std.)	28.61±4.9
Gravida, median (min-max)	2 (1-11)
Gestational week at diagnosis, median (min-max)	24 (15-38)
Chromosomal analysis, n (%)	9 (13.64%)
Diaphragmatic hernia, n	6
Idiopathic hydrothorax, n	3
Intrauterine treatment, n (%)	5 (7.57%)
Termination of pregnancy, n (%)	4 (6.06%)
Congenital pulmonary airway malformation, n	2
Diaphragmatic hernia, n	1
Cantrell pentalogy, n	1
Intrauterin fetal death, n (%)	4 (6.06%)
Congenital pulmonary airway malformation, n	2
Diaphragmatic hernia, n	1
Congenital high airway obstruction syndrome, n	1
Neonatal death, n (%)	8 (12.12%)

In our study, we did not feel the need for MRI in any of the cases. Pleuroamniotic shunt procedure was performed in 5 of the total cases diagnosed as hydrothorax in the prenatal period and they were followed up. Of these 5 cases, the procedure was successful in 3 cases and the shunt remained until birth in these patients. At the end of the pregnancy, healthy fetuses were born without any further problems. However, in the remaining 2 cases, the shunt was found to be dislocated in the USG examination performed on the 7th day after the procedure and the shunt was removed. Because of the failure of this procedure, hydrothorax reoccurred in these cases. Prenatally, no procedure was performed for diagnoses other than hydrothorax in cases with FNTA.

Five (29.4%) of 17 cases with CPAM were resolved late antenatally with expectant management. These patients were subsequently excluded from follow-up. Also, 5 cases with CPAM were lost to follow-up. Seven of 17 cases with CPAM were delivered at our center. Of this, 5 cases with CPAM were resolved during the postnatal period with expectant management. In total, 10 (58.8%) cases with CPAM lesions were resolved during the late antenatal or postnatal period with expectant management. Surgery was performed in 2 (11.8%) of 17 cases with CPAM.

As mentioned above, of the 66 fetuses with a prenatal diagnosis of FNTA, 39 were delivered in our center. The prenatal FNTA diagnosis of all of the cases was confirmed after birth. Congenital diaphragma hernia cases were confirmed by X-ray radiography. Esophageal atresia cases were confirmed by orogastric tube. All CPAM and bronchopulmonary sequestration cases were confirmed by computerized tomography.

Postnatally, surgery was performed in 18 cases with a diagnosis of CDH, in 2 cases with a diagnosis of CPAM, in 6 cases with a diagnosis of esophageal atresia, and in 5 cases with bronchopulmonary sequestration.

DISCUSSION

For lung maturity of the fetus, sufficient thoracic space, intrapulmonary fluid and diaphragm innervation are necessary. Most of the masses in the fetal thorax can be detected by USG examination as early as the 16th week of pregnancy. All thoracic masses should be considered potentially life-threatening, because the pressure on developing lungs may cause pulmonary hypoplasia. Development of hydrops in a fetus with lung mass is an indicator of poor prognosis, regardless of the type of mass. After accurate prenatal diagnosis, planning in utero interventional procedures, delivery, and immediate postnatal surgery is very important for FNTA.[8,9]

As USG technology continues to improve, the diagnosis of fetal thoracic lesions increases. Much still needs to be learned about the in-utero natural history and pathophysiology of these fetal thoracic lesions. These lesions may affect the development of the pulmonary parenchyma, causing lung hypoplasia. Large lesions may obstruct venous return, causing hydrops fetalis.[10]

Accurate prenatal diagnosis of a chest mass is important because the natural history, treatment, and prognosis vary depending on the etiology. The USG is a noninvasive, inexpensive, and widely available modality to assess fetal anatomic structures. Thus, the USG examination is routinely used to screen for fetal anomalies and can provide real-time studies without ionizing radiation. Most USG scans are diagnostic for these abnormalities.[11-13] In recent years, with the ultrafast sequences technology evolution, MRI has been considered a beneficial diagnostic procedure complementary to the USG. Recio Rodríguez et al.[14] reported that fetal MRI can provide further information useful in predicting prognosis and in neonatal management of FNTA. However, as there seemed to be that prenatal management and prediction according to the lesion size was more cost-effective than

prediction according to the suspected final histology, MRI did not show any further benefit regarding diagnosis and prognosis compared to the USG.[15] Based on this knowledge, we did not perform an MRI in any of the cases to confirm the diagnosis, management, and prognostication.

In the literature, the most common FNTA is CDH, which accounts for approximately 40% of cases.[16] CPAM is the second most common congenital lung lesion and accounts for 25% of FNTA cases.[17] In our study, likewise in other studies, the most common fetal chest masses were CDH (45.4%), and CPAM (25.7%). Also, similar to the literature, the prevalence of esophageal atresia, bronchopulmonary sequestration (BPS), and idiopathic hydrothorax is relatively rare than CDH and CPAM.[6,7,10,18]

Most CPAM cases can be managed with maternal support, planned termed delivery, and postnatal resection. However, once these lesions have been identified, they must be followed carefully because the lesion may involute in utero or increase in size. With progressive increasing size, there may be associated fetal hydrops, which are believed to be indicative of impending fetal demise.[18] In our study, the CPAM lesion regressed with expectant management in 29.4% of the cases during the antenatal period and in also 29.4 of the cases during the postnatal period. Postnatal surgery was required in 14.3% (n= 2) of our cases whose postnatal information was accessed. In their study, Kaya et al.[19] included 37 cases (71.2%) diagnosed with CPAM and 15 cases (28.8%) with bronchopulmonary sequestration. The presence of bronchopulmonary malformation was demonstrated radiologically in 23 cases (59%) in the neonatal period, and 18 of the cases (78.3%) with CPAM and bronchopulmonary sequestration were operated on in the first year of life. When the cases were analyzed separately, 14 cases with bronchopulmonary sequestration and 4 cases with CPAM (10.8%) were operated in their first year. Similarly, Atalay et al.[15] revealed that 64.7% of congenital pulmonary malformation cases resolved spontaneously. Thus, we consider that CPAM cases demonstrated favorable outcomes with appropriate management.

In utero therapies for FNTA are variable but there are no large randomized trials to compare risks and benefits. Fetal endoscopic tracheal occlusion therapy for diaphragmatic hernia, radiofrequency thermal ablation for CPAM and thoracoamniotic shunting for hydrothorax are current intrauterine treatment approaches.[20-22] In our clinic, only thoracoamniotic shunting procedure was performed for only 5 patients with a diagnosis of hydrothorax among these treatment approaches. After this shunt procedure, healthy fetuses were born in these 3 patients without the need for any other prenatal or postnatal surgery. In the remaining 2 patients, the shunt procedure failed and these patients refused to have the shunt reinserted, and the fetuses died during follow-up. Unfortunately, the Fetal endoscopic tracheal occlusion therapy and Laser procedure could not be performed in our clinic due to the lack of an experienced specialist and the lack of necessary equipment for these procedures.

Limitation

The main limitation of this study is the retrospective design of this research and the absence of long-term postnatal outcomes. Also, the inability to confirm the diagnosis of the cases with autopsy who experienced pregnancy termination or intrauterine fetal demise is the other crucial limitation of our study.

CONCLUSION

Although the incidence of thoracic anomalies, which we see less frequently than other organ systems has not changed much over the years, treatment approaches and postpartum prognosis have improved over the years. Deliveries of the FNTA cases should be planned in tertiary centers where necessary intervention and care can be provided. A multi-disciplinary team could demonstrate a crucial role in assuring that the pregnant woman and fetus obtain appropriate treatment and are managed during the antenatal and postnatal periods. US plays a crucial role in the diagnosis and management of FNTA cases during the prenatal period rather than fetal MRI and other diagnostic tools. More than half of the CPAM lesions regressed spontaneously with expectant management.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Başakşehir Çam and Sakura City Hospital Clinical Researches Ethics Committee (Date: 11.10.2023, Decision No: 462).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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