Journal of Pediatric Surgery 53 (2018) 1137–1141

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

The Distended Fetal Hypopharynx: A Sensitive and Novel Sign for the Prenatal Diagnosis of Esophageal Atresia

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ARTICLE INFO

Article history:
Received 24 February 2018
Accepted 27 February 2018

Key words:
Esophageal atresia
Prenatal diagnosis
Distended hypopharynx
Esophageal pouch

ABSTRACT

Background/Purpose: Although advances have been made in the prenatal diagnosis of esophageal atresia (EA), most neonates are not identified until after birth. The distended hypopharynx (DHP) has been suggested as a novel prenatal sign for EA. We assess its diagnostic accuracy and predictive value on ultrasound (US) and magnetic resonance imaging (MRI), both alone and in combination with the esophageal pouch (EP) and secondary signs of EA (polyhydramnios and a small or absent fetal stomach).
Methods: We retrospectively reviewed fetal US and MRI reports and medical records of 88 pregnant women evaluated for possible EA from 2000 to 2016. Seventy-five had postnatal follow-up that confirmed or disproved the diagnosis of EA and were included in our analysis.
Results: Seventy-five women had 107 study visits (range 1–4). DHP and/or EP were seen on US and/or MRI in 36% of patients, and 78% of those patients had EA. DHP was 24% more sensitive for EA than EP, while EP was 30% more specific. After 28 weeks of gestation, DHP had a predictive accuracy for EA of 0.929 ($P = 0.001$).
Conclusions: DHP is a sensitive additional prenatal sign of EA. More accurate diagnosis of EA allows for improved counseling regarding delivery, postnatal evaluation, and surgical correction.
Type of Study: Diagnostic.
Level of Evidence: Level II.

Esophageal atresia (EA) is a relatively common congenital anomaly with an incidence ranging from 1 per 3500 to 4500 live births. The prenatal diagnosis of EA has been reported using both fetal ultrasound (US) and magnetic resonance imaging (MRI) [1–6]. As direct visualization of the primary finding of a blind-ending esophageal pouch (EP) is difficult, the prenatal recognition of esophageal atresia more often relies upon secondary signs, such as polyhydramnios and a small or absent stomach. Unfortunately, these signs are not always present or recognized on prenatal imaging, and many patients are not diagnosed until after birth. Reported rates of prenatal diagnosis by US and/or MRI range from 16 to 36% [7–13]. Patients who are diagnosed prenatally tend to have higher morbidity related to a higher incidence of pure EA, without tracheoesophageal fistula (TEF), in this cohort [10,11]. Pure EA is more likely to be associated with a persistently absent stomach on prenatal imaging due to the lack of amniotic fluid egress through a TEF. EA with TEF is associated with a small stomach, but this finding is only observed in approximately 1/3 of fetuses [7,14].

Type C EA with TEF is the most common presentation of EA, and most patients with this anatomical variant are not diagnosed prenatally because they may have a normal sized fluid-filled stomach and normal amniotic fluid volume. In a recent report from the French National Registry, more than 80% (332/405) of patients with Type C EA/TEF born between 2008 and 2010 were diagnosed after birth, and not in utero [10].

A visualized esophageal pouch (EP) has been shown to have a very high positive predictive value for EA, and is seen in approximately 1/3 of patients with a prenatal diagnosis of EA [10,15]. The EP sign, representing dilation of the blind-ending upper esophagus, seen in the neck or mediastinum during fetal swallowing, was first described in 1983 by Eyheremendye et al. [16]. Subsequently, other authors described the EP, which is identified typically in the third trimester with fetal US or MRI [17–23]. Visualization of a distinct EP is a more specific finding for EA than polyhydramnios or a small fetal stomach, which

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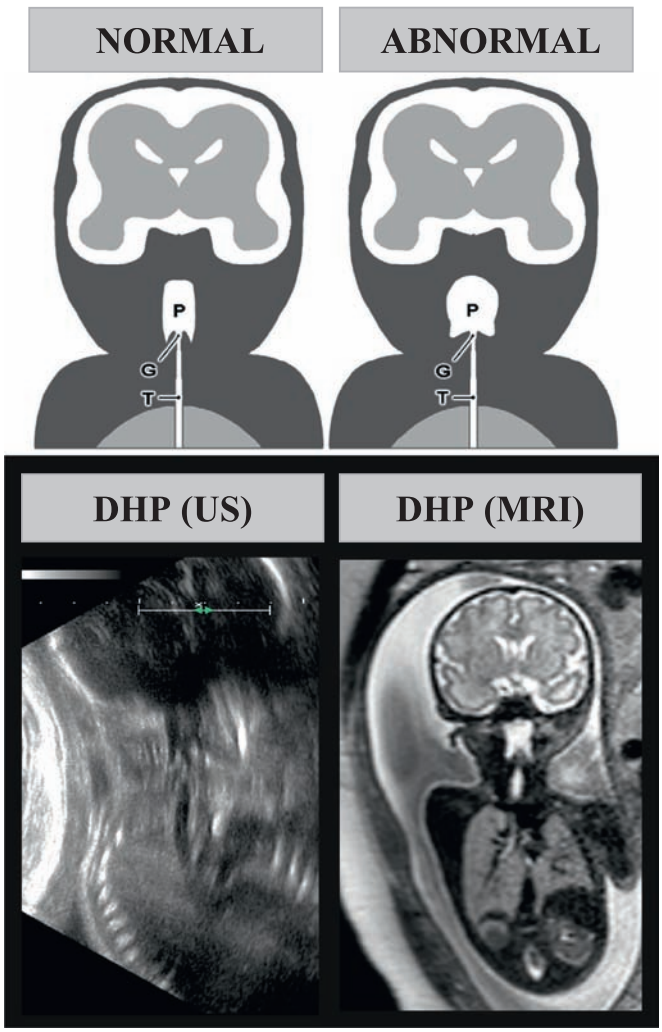
https://doi.org/10.1016/j.jpedsurg.2018.02.073
0022-3468/

can both be seen in other settings. Although more widespread use of fetal MRI at multidisciplinary centers holds promise for improving the prenatal diagnosis of EA, US remains the most widely available and cost effective fetal imaging modality worldwide. As such, a novel and reliable US finding that could improve the overall sensitivity and specificity for the diagnosis of EA would be useful.

In this paper, we analyzed the added value of seeing the distended fetal hypopharynx (DHP), a novel sign that was first described in 2003 in one case of esophageal atresia by fetal MRI [24]. We have been using this additional sign in our center for over 15 years. Anatomically, the hypopharynx is the portion of the pharynx that extends inferiorly from the horizontal plane of the top of the hyoid bone to a horizontal plane extending posteriorly from the inferior border of the cricoid cartilage. In fetuses with EA, swallowing is obstructed, and amniotic fluid is forced upward into the oral cavity, passing retrograde through the hypopharynx and causing its distension. This dynamic process can be observed on both real time fetal sonography and cine mode fetal MRI.

On US and MRI, the hypopharynx is best assessed at the level of the glottis, in the coronal plane of the fetal neck. Fetal imagers can evaluate this region with US by locating the fetal cervical spine in the sagittal or axial plane, then turning the probe 90 degrees into the coronal plane. Convex (rather than straight or concave) hypopharyngeal walls are considered abnormal (Fig. 1). The sagittal plane is best for seeing an EP. The EP sign is a blind-ending fluid-filled structure in the neck or chest, typically located inferior and posterior to the hypopharynx, behind the trachea.



P = hypopharynx, G = glottis, and T = trachea.

Fig. 1. Coronal views of the DHP sign depicted with graphic illustration, US and MRI.

1. Material and methods

This retrospective review focused on a cohort of patients from a larger institutional review board-approved study conducted by our group evaluating the prenatal diagnosis of EA, with or without TEF (IRB-P00024063). We examined all pregnant women from January 2000 through July 2016 who were referred to the Advanced Fetal Care Center (AFCC) at Boston Children's Hospital with a concern for EA based on imaging findings of polyhydramnios and/or small or absent stomach. We also included women with imaging findings suggestive of EA at the time of fetal evaluation for other anomalies. Only patients with prenatal imaging and postnatal follow-up at our institution were included in this report. Data collected prenatally from clinical notes and US and/or MRI reports included: gestational age (GA) at imaging, fetal gender, fetal position, amniotic fluid volume, absence or presence and size of any stomach bubble, presence of any primary sign of EA (EP and/or DHP) and any associated anomalies. Data collected postnatally included: any confirmation of EA diagnosis and type and any confirmation of associated anomalies and syndromes. Diagnosis of EA was confirmed with operative or autopsy reports.

Noncontrast MRI studies were performed on 1.5 T GE (Fairfield, CT, USA) or Philips (Amsterdam, Netherlands) magnets using 3- to 5-mm-thick slices from 2000 until mid-2013, and 3.0-T Siemens (Berlin, Germany) magnets using 2- to 3-mm-thick slices from mid-2013 through 2017. Standard MRI sequences of axial, coronal and sagittal views were obtained with three methods: (1) single-shot fast spin echo (SS-FSE, T2 weighted, GE) and half-Fourier acquisition single-shot turbo spin echo (HASTE, Siemens); (2) steady-state free precession (SSFP, T2 weighted), fast imaging employing steady-state acquisition (FIESTA, GE), and TruFISP (Siemens); and (3) echo-planar imaging (EPI).

All categorical variables were compared by Fisher's exact test or chi-square. Continuous variables (GA) were expressed as medians and interquartile ranges owing to lack of normality (or departure from normal bell shape) and groups were compared using the nonparametric Mann–Whitney *U*-test. Sensitivity analysis was performed to assess the relationship between prenatal signs and EA. Receiver operating characteristic curve analysis was used to calculate area under the curve, or c-index, for each prenatal sign in predicting EA. We analyzed study visits ≤28 weeks GA and >28 weeks GA to determine whether a later window of imaging would be associated with better performance of the diagnostic signs [25]. Multivariable logistic regression with backward selection was used to establish independent predictors of EA. We selected two covariates: one or more primary sign (DHP and/or EP) and both secondary signs (polyhydramnios and small or absent stomach) [26]. Wald chi-square was used to assess significance in our logistic regression analysis [27]. Combinations of our two covariates led to four conditions, for which we derived predicted probabilities with a 95% CI. Statistical analysis was performed using IBM SPSS Statistics (version 23.0, IBM, Armonk, NY) and two-tailed values of $p < 0.05$ were considered statistically significant.

2. Results and discussion

To our knowledge, this is the largest review to date of fetuses referred with a suspicion of EA who were screened for both primary and secondary signs of EA with MRI and US. It is also the first time a statistical model has been developed using combinations of prenatal imaging findings to predict, with reasonable accuracy, the risk for EA in a fetus.

During the study period, 96 fetuses were referred for suspicion of EA, and of those, 88 had US and/or MRI at our institution. 75/88 (85%) had postnatal follow-up and were included in our analysis. Of these 75 patients, 39 (52%) had EA confirmed at birth. 45/75 (60%) were male. 57/75 (76%) had additional anomalies identified on prenatal and