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Dilated azygos arch mimicking an aortic arch anomaly during thoracic surgery

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ABSTRACT

Cardiovascular malformations are frequently associated in patients with esophageal atresia (EA). We observed *azygos continuation* mimicking an aortic arch anomaly in four newborns with type III EA. They presented concomitant rib anomalies indicating a common developmental defect. Foreknowledge is important for planning thoracotomy or interventional cardiac catheterization in this population.

1. Background

Cardiovascular malformations are the most frequent associated anomalies in patients with esophageal atresia (EA) as part of a complex spectrum of axial mesodermal dysplasia [11,15]. Several studies are reporting caudal pharyngeal arch neurocristopathies like aortic arch anomalies, carotid anomalies, aberrant retroesophageal right subclavian artery, conotruncal heart defects or persistent left superior vena cava (SVC) [1,11,15,23]. Therefore, during the preoperative echocardiographic evaluation, sonographers should pay attention to establish the laterality of aortic arch and its anomalies. Otherwise, also some venous anomalies should be ruled out for various motivations. First one, azygos vein (AV) anomalies are reported to be associated with a wider gap between the esophageal pouches, with higher morbidity and mortality [9]. Second, an absent AV makes more difficult during intervention the identification of the distal tracheoesophageal fistula [1,21]. And third, a dilated azygos arch, as an expression of systemic circulatory alteration, can mimic a right aortic arch during intervention inducing the surgeon to an erroneous approach. We report the clinical features of these rare systemic venous anomalies with emphasis on the practical implications of the diagnosis and the importance of preoperative assessment of patients with EA.

2. Methods

A retrospective chart review was performed on all newborns admitted to the neonatal intensive care unit for type III EA between January 1, 2013 and October 31, 2016. Data from routinely preoperative X-ray, ECG, echocardiogram, abdominal ultrasound (US), operation report, clinical course, and genetical testing were collected. Univariate analyses were performed by open source statistical R Commander "Palermo software package" [17] using the Fisher's exact test for categorical variables and the two-sample *t*-test for continuous variables; $p < 0.05$ was considered significant.

3. Results

Over this four-year period, dilated AV due to *azygos continuation* of the inferior vena cava (IVC) in *situs solitus* was evidenced by color-Doppler US in 4/20 (20%) newborns with type III EA. The dilated AV was lying behind the right renal artery and intra-thoracically was entering the superior surface of the right atrium or SVC as a dilated right bluish arch. This evidence was confirmed during thoracotomy and the surgeon did not perform the AV division, as it is frequently practiced [21] during the tracheoesophageal fistula repair and esophageal anastomosis. We did not find AV agenesis or duplication, venous thrombosis, associated malrotation (demonstrating normal position of superior mesenteric vein and artery by US and/or normal cecal position by enemas) or other signs of isomerism (normal atria, liver, spleen, stomach, pancreas, and biliary tree by US).

The four outborn infants with *azygos continuation* were born at term without prenatal diagnosis of EA, despite the evidence of polyhydramnios. They presented rib number anomalies ($p = 0.003$) and other associated malformations as listed in Table 1. Particularly, an associated azygos accessory lobe was evidenced on thoracic CT in patient 1. There was no significant difference in means or frequencies between

Abbreviations: AV, azygos vein; EA, esophageal atresia; IVC, inferior vena cava; SVC, superior vena cava; US, ultrasound

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Table 1
Mean values and frequencies observed in newborns with and without *azygos continuation* in the type III esophageal atresia (EA/III) population.

EA/III	Birth weight, g (range)	Rib number anomaly, % (rib pairs)	Congenital heart diseases, %	Other non-cardio-vascular anomalies, %	Related syndrome, %	Discharged home, days
Azygos continuation (n = 4)	2886 (2040–3955)	100	50	75	50	39
Pat. 1	2300	(11)	LSVC, PDA	Hemisoma, SUA, anemia, azygos lobe, postsurgical chylothorax		64
Pat. 2	3955	(11)		Macrosomia, laterocervical tumor	Down	23
Pat. 3	2040	(13)	Subaortic VSD	IUGR, anemia, hypothyroidism,		25
Pat. 4	3250	(13)	HOCM	ARM, absent coccyx, anemia, hydronephrosis	VACTERL	44
Non-azygos continuation (n = 16)	2283 (580–3625)	12.5	50	56	56	33
p-Value	0.28	0.003	1	0.49	0.82	0.63
Prevalence ratio (95% CI)		8 (2.19, 29.25)	1 (0.33, 2.99)	1.42 (0.65, 2.72)	0.89 (0.30, 2.59)	

Abbreviations: ARM, anorectal malformation; HOCM, hypertrophic cardiomyopathy; IUGR, intrauterine growth restriction; LSVC, persistent left superior vena cava; PDA, persistent ductus arteriosus; SUA, single umbilical artery; VSD, ventricular septum defect.

newborns with and without *azygos continuation* with regard to maternal age (33.5 vs 36 years), gestational age (38 vs 36 weeks), birth weight percentile (31° vs 26°), gender (75 vs 44% female), twinning (0 vs 12.5%), omphalocele (0 vs 6%), left SVC (25 vs 0%), single umbilical artery (25 vs 0%), kidney disorders (25 vs 19%), related syndromes (50 vs 56%), gap-distance (1.7 vs 1.7 cm), time to achieve full enteral nutrition (26 vs 19 days), surgical complications (25 vs 6%), infections (0 vs 25%) or mortality (0 vs 18.7%).

4. Discussion

In all patients, the sonographic evidence of *azygos continuation* was confirmed during thoracotomy. This asymptomatic developmental variation, secondary to interruption of at least the hepatic segment of the IVC, should be considered part of the clinical spectrum of the polymalformative complex EA with rib disorders. Although other AV anomalies have been reported in patients with EA [9,21,24], to best of our knowledge, there are only few reports of *azygos continuation* in infants with EA, all associated to left-isomerism [5,7,12].

Embryologically, the cardinal venous system with its anastomoses is the precursor of the IVC, the AV and the hemi-AV. Normally, the AV originates at the junction of the right ascending lumbar and subcostal veins, entering the thorax through the aortic hiatus. It ascends along the anterolateral surface of the thoracic vertebrae and arches ventrally just cephalad to the right main bronchus at T5–6, draining into the SVC or, more rarely, into the right brachiocephalic vein, right subclavian vein, intrapericardial SVC or right atrium [3,8]. Abnormal fusion between the hepatic and the prerenal segments of the IVC results in the infrahepatic hypoplasia or interruption of the IVC with *azygos continuation* and compensatory enlargement [19]. In that case, during EA repair it is important to do not perform a routine AV division in order to do not interfere with the inferior body venous drainage. Severe sequelae after AV division have been reported [4,13]. A similar surgical challenge exists during patent ductus arteriosus ligation and concomitant *hemiazygos continuation* on the left body side [22]. In light of this, it is reasonable the proposal of sparing the AV always during surgery to prevent early postoperative edema and leakage by maintaining physiological esophageal venous drainage [20].

The dilated azygos arch is a potential mimicker of aortic pathologies (dissection, aneurysm or rupture) [2] not only during thoracotomy, when the enlarged AV can mimic in caliber and course a right aortic arch, but also during imaging studies in more advanced ages in life. This anomaly may be isolated or associated with other anomalies, including abnormal cardiac situs and left-isomerism, bilateral SVC, atrial and ventricular septal defects, pulmonary stenosis, anomalous pulmonary venous return, pulmonary anomalies, like azygos/hemiazygos accessory lobe [3], or imperforate anus [6].

The incidence in patients with congenital heart disease undergoing cardiac catheterization is up to 1.3% [3]. During fetal echocardiography, the anomaly was encountered in 0.5%, but reaches higher proportion (20.6%) in case of associated omphalocele [14]. The exact reason for our high incidence is not known. The anomaly is in general underdiagnosed because asymptomatic unless it is not associated to laterality defects, arrhythmias, or venous thrombotic events. In the type III EA population, it can be misinterpreted as right aortic arch or its diagnosis can be missing or trivial and not reported because a vessel that looks bigger will however not be tied. However, little importance is given to asymptomatic vascular malformations, but represent a significant part of genetic diagnostic assessment. Asymptomatic pleural bounding azygos (hemiazygos) pulmonary lobe, as a discriminant for *azygos continuation*, might be not identifiable in newborns on anteroposterior or lateral X-ray due to normal neonatal thymus presence, like not the *azygos continuation* itself [16]. Color Doppler echocardiography is the most suitable non-invasive technique in detecting IVC interruption with *azygos continuation* [2,14], because the more sensitive CT is not recommended for routine vein or pulmonary screening exam. Furthermore, since the prenatal diagnosis of type III EA is quite difficult and based on indirect aspecific signs (polyhydramnios, altered gastric dimension), it should be examined whether the AV anomalies can represent an additional soft marker for gastrointestinal malformations.

Patients with IVC interruption have higher risk of thrombosis because of both impaired circulation and factor V deficiency [18]. There is still controversy whether an absent IVC is a developmental anomaly or the result of perinatal IVC thrombosis causing regression and disappearance of previously present IVC [10]. The IVC interruption is a hallmark for laterality defects. However, Mlczoch and Carvalho [14] debated that failure of IVC formation is not a situs abnormality in patients with omphalocele, despite frequently encountered in situs abnormalities. We support this theory, considering that our patients did not encompass at least three requested diagnostic categories for laterality defects [12]. Although low statistical power because of small study size, we think that the described association of rib anomalies, *azygos continuation* and EA arises from an early developmental disruption mechanism.

5. Conclusions

Despite of the associated rib number anomalies, the intraoperative possible confusion with aortic arch anomalies and the avoidance of surgical division, the *azygos continuation* of the IVC did not have a

relevant clinical implication in the neonatal age. If during fetal US, the IVC is interrupted with azygos continuation to the SVC (right or left-sided), the diagnosis of isomerism should be considered and the possibility of an associated gastrointestinal abnormality should be investigated. The *azygos continuation*, unlike AV agenesis, has not been associated with wider esophageal gap or surgical complications. However, the foreknowledge of *azygos continuation* is important in case of thoracic surgery or interventional cardiac catheterization and should always be sought in the preoperative sonographic approach. Long-term follow-up may elucidate for associated thrombosis risk in patients with *azygos continuation* and EA.

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