CASE REPORTS

RJME
Romanian Journal of Morphology & Embryology
http://www.rjme.ro/

Esophageal atresia with distal fistula – unusual case series. Considerations related to epidemiological aspects, malformative associations, and prenatal diagnosis

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Abstract

Background: Esophageal atresia (EA) is the most frequent and severe congenital anomaly of the esophagus, occurring in 1:2500–1:4500 live births. Five types of EA have been described, EA with tracheoesophageal fistula (TEF) being the most frequent. *Aim*: The aim of this paper is to evaluate epidemiological aspects, malformative associations, and prenatal diagnosis in an unusual case series of EA with distal TEF. *Case presentations*: The authors are analyzing a series of seven cases of EA with distal TEF. The seven cases of EA with TEF presented occurred during a period of two years, resulting in an unusually increased rate – 1.1:1000 live births. Except a late suspicion of EA (one day before delivery), EA was not diagnosed during prenatal scans despite association with polyhydramnios in two cases and single umbilical artery in four cases. None of the two cases of unilateral renal agenesis or anorectal malformations were diagnosed on prenatal ultrasound scans. In two of the cases, EA was part of VACTERL (vertebral defects, anorectal malformations, heart defects, EA with or without TEF, renal anomalies/dysplasia, and limb defects) association. Despite lack of prenatal diagnosis, postnatal diagnosis of EA was suspected at birth in four cases, at two hours in one case. *Conclusions*: An increased index of suspicion for congenital structural defects, particularly for EA, should be maintained in the presence of a single umbilical artery and/or polyhydramnios on prenatal ultrasound scan. Prenatal diagnosis of EA offers the chance for parental counseling, planned birth and transfer for corrective surgery and decreases the risk for postnatal aspiration pneumonia associated with early feedings.

Keywords: esophageal atresia, tracheoesophageal fistula, prenatal diagnosis, polyhydramnios, congenital structural defects.

Introduction

Esophageal atresia (EA) is a relatively frequent congenital abnormality, the most frequent and severe anomaly of the esophagus [1, 2], reported in 1:2500–4500 live births, without gender preference [3, 4]. Different anatomical varieties were described but the most often type seen is EA with distal fistula (approximately 85% of the cases) [3, 5]. Esophageal atresia may occur as an isolated defect but in more than 50% of the cases is associated with other congenital defects [3, 6–8] or is a part of congenital syndromes [9]. The exact etiology of the EA is not completely elucidated, most of the cases occurring sporadically [2, 3].

During pregnancy, EA, isolated or with tracheo-esophageal fistula (TEF), is suspected in the presence of the association between polyhydramnios, dilated superior esophageal pouch, and small or absent gastric bubble after the 18th week of gestation [5, 10]. Prompt diagnosis of EA, before the first feeding, allows prevention of aspiration pneumonia. A failed attempt to pass a catheter into the stomach, abundant foamy oral secretions, cough, drowning with saliva, or by episodes of cyanosis and/or apnea during feeding attempts should raise the suspicion of EA [8, 11]. Thoracic radiography with air contrast confirms EA; TEF is suggested by air presence in the stomach [2, 6, 12]. Prompt diagnosis, stabilization, and transfer to pediatric surgery for surgical intervention are vital for survival and improved short and long-term prognosis. Low birth weight and complex congenital heart defects are the most important risk factors for unfavorable prognosis [13, 14]. Currently, the survival rate after surgical correction

is approaching 95% in centers offering the best neonatal care [15–18].

The paper presents an unusual case series of EA with FTE, occurring in a very short period of time. The cases are discussed in the light of the current knowledge regarding EA epidemiology, etiology, associated anomalies, prenatal and postnatal diagnosis, and short-term prognosis.

Case presentations

An unusual series of newborns with EA, born or admitted in a short period of time in the Maternity Hospital of the Emergency County Hospital of Sibiu, Romania is presented. The seven cases presented were submitted for surgical correction to Department of Pediatric Surgery, "Grigore Alexandrescu" Clinical Emergency Hospital for Children, Bucharest, Romania. Information was extracted form maternal and neonatal charts.

Case No. 1

Female newborn, birth weight of 2600 g, delivered by cesarean section at 35 weeks gestation, in a level II maternity hospital (Apgar score of 8 at one minute), was submitted in our Department at four hours of life for respiratory distress syndrome (RDS). Maternal, paternal, and pregnancy history were insignificant except polyhydramnios. The cesarean section was performed for polyhydramnios. Immediately after admission, the newborn presented a severe apnea needing intensive resuscitation, followed by mechanical ventilation for 12 hours. The attempt to insert a nasogastric tube for feeding failed, raising the suspicion of EA. Thoracic and abdominal radiography confirmed EA with TEF. Persistent *foramen ovale* (PFO) and *ductus arteriosus* (PDA) were seen on echocardiography. Laboratory investigations showed congenital anemia and transient renal failure. After stabilization, the newborn was submitted to pediatric surgery for surgical correction. Surgical correction was performed without complications; with gastro-esophageal reflux (GER) and tracheomalacia (laryngeal stridor was noted since birth).

Case No. 2

Female newborn, birth weight of 3080 g, was delivered at 38 weeks gestation by cesarean section (after previous cesarean section delivery) after a physiological pregnancy and a prenatal diagnosis of single umbilical artery, and had a good general condition at birth (Apgar score of 10 at one minute). Immediately after birth, the infant presented abundant foamy secretions and a vomiting soon after the first attempt of breastfeeding associated with decreased oxygen saturation with rapid normalization (peripheral oxygen saturation was maintained at 96–98% in room air). An obstacle was felt at 10–11 cm while attempting to insert a gastric tube and, together with persistent foamy oral secretions, raised the suspicion of EA. The infant was submitted to the Neonatal Intensive Care Unit (NICU) for investigations, monitoring, and treatment. Thoracic and abdominal radiography confirmed EA with distal TEF. No other defects were diagnosed except PFO. After stabilization, the newborn was submitted to pediatric surgery. Immediate post-operative development was favorable but the infant was lost at follow-up.

Case No. 3

Female newborn, birth weight of 2320 g, was vaginally delivered, in vertex presentation, at 40 weeks gestation and had perinatal asphyxia (Apgar score of 5 at one minute) needing neonatal resuscitation including positive ventilation with T-piece resuscitator. The parents were healthy; no significant pathology was reported during pregnancy. Few minute after delivery, the newborn presented abundant foamy oral secretions and insertion of a gastric tube failed raising the suspicion of EA, confirmed by thoracic radiography. The clinical examination also revealed anal imperforation with recto-vaginal fistula, fused L5–S1 vertebrae, and single umbilical artery (Figure 1). Ventricular septal defect (VSD), PFO, and PDA were demonstrated by Doppler echocardiography. The spectrum of congenital defects fulfilled criteria for VACTERL (vertebral defects, anorectal malformations, heart defects, EA with or without TEF, renal anomalies/dysplasia, and limb defects) association. Surgical correction of the esophagus and anal defects was performed without significant postoperative complications. Tracheomalacia and GER were diagnosed after surgery but the child has a normal growth and development.

Case No. 4

Female newborn, 1420 g birth weight, from an *in vitro* fertilization obtained pregnancy complicated with thrombophilia, thalassemia minor, and pregnancy-induced hypertension was delivered by cesarean section at 33 weeks gestation due to severe arterial hypertension and proteinuria with Apgar score of 8 at one minute. Single umbilical artery was noted at prenatal ultrasound. A gastric tube could not be inserted at birth and thoracic and abdominal radiography confirmed EA with TEF. Investigations were done to find associated abnormalities and, aside PFO and PDA, right kidney agenesis, and transient acute renal failure were diagnosed. After stabilization of RDS with continuous positive airway pressure support, the preterm infant was submitted for surgical correction. Despite successful repair of the malformation, the infant died three weeks after surgery due to severe renal failure.

Case No. 5

Male newborn, vaginally born in vertex presentation, at 35 weeks gestation, with a birth weight of 2110 g, from healthy parents, and an uneventful pregnancy, had a good condition at birth (Apgar score 9 at one minute) but developed a minor RDS immediately after birth. Continuous positive airway pressure support on nasal cannula was administered and the infant was submitted to NICU for care and monitoring. Insertion of an umbilical venous line failed. An attempt was done to insert a gastric tube for feeding also failed and, since more than usual oral secretions were noted, a suspicion was raised for EA. Radiography demonstrated EA with TEF. Subependymal hemorrhage was found on head ultrasound. No other defects or conditions were found except PDA and PFO. After stabilization, the infant was submitted to pediatric surgery for operative intervention. No complications were seen immediately after surgery; GER diminished in time and disappeared up to one-year evaluation, the child having a normal growth and development.

Case No. 6

Female newborn, birth weight of 2440 g, delivered by cesarean section for maternal lumbosciatica at 37 weeks gestation, from healthy parents and after a physiological pregnancy, had a good condition at birth (Apgar score 9 at one minute) but developed foamy abundant oral secretions soon after birth. Insertion of a gastric tube failed after an obstacle was encountered at approximately 10–11 cm from mouth. The suspicion of EA with TEF was confirmed by radiography. PFO and PDA were diagnosed by echocardiography. Congenital anemia was also associated. The infant was submitted for surgical correction after stabilization. Surgical correction went uneventfully; the infant has a favorable postoperative development, with mild GER.

Case No. 7

Female preterm infant, birth weight of 2420 g, was extracted by cesarean section for prenatal diagnosis of hydrocephalus, at 35 weeks gestation, and needed neonatal resuscitation at birth (Apgar score of 6 at one minute). Prenatal diagnosis of polyhydramnios, hydrocephalus, and single umbilical artery was at 25 weeks gestation but suspicion of EA was raised just one day before delivery due to lack of visualization of the stomach. The suspicion of EA was confirmed immediately after birth, since insertion of a gastric tube failed. Radiography confirmed EA with distal TEF (Figure 2). No relevant health problems could be identified in parents and during pregnancy. The infant was initially cared for in the NICU, while investigating the child for associated abnormalities. Aside communicating hydrocephalus, PFO, PDA, single left kidney, and anorectal malformation with rectovestibular fistula were diagnosed. The infant was submitted in good conditions for surgical correction, the surgical correction went uneventfully but the immediate postoperative was complicated by bilateral recurrent hydrothorax and evolving hydrocephalus.

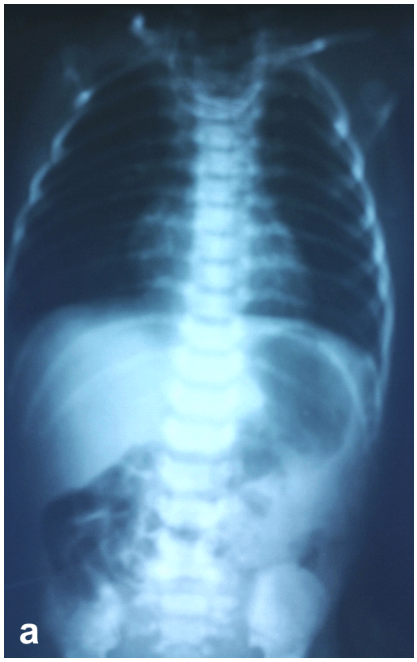
A summary of the case reports is presented in the Table 1.

Discussion

The term EA defines a group of congenital abnormalities including a lack of continuity of the esophagus with or without a persistent communication with trachea [15], the most frequent and serious congenital anomaly of the esophagus [1, 15]. The first case was described by Thomas Gibson, in 1697, but the first successful surgical correction was reported only in 1941, by Cameron Haight [13, 15].

The seven consecutive cases of EA with distal TEF (Table 1) occurred in a short period of time, between June 2, 2014 and July 5, 2016, from a total of 6121 births. Thus, EA occurred with a prevalence of 1.1/1000 live births, considerably higher than the numbers reported in the literature – 1/2500–1/4500 live births [9, 11, 13, 15, 19–21]. Important regional differences were noted by the *European Surveillance of Congenital Anomalies (EUROCAT) Working Group*, when reporting for EA a prevalence of 2.4/10 000 births after evaluating data from 23 European registries of congenital anomalies [16]. No explanations were found for the increased rate of EA in our region or predominant occurrence in female neonates.

Five anatomical varieties of EA were described but the most often type seen is EA with distal fistula (approximately 85% of the cases), followed by EA without fistula (6–8% of the cases), TEF without EA (H-type, 4–5% of the cases), EA with proximal TEF (3% of the cases), and EA with proximal and distal fistula (<1% of the cases) [2, 3, 5, 11, 15]. The fact that EA with distal TEF was seen in all of our cases is probably due to the short time frame when these cases occurred.



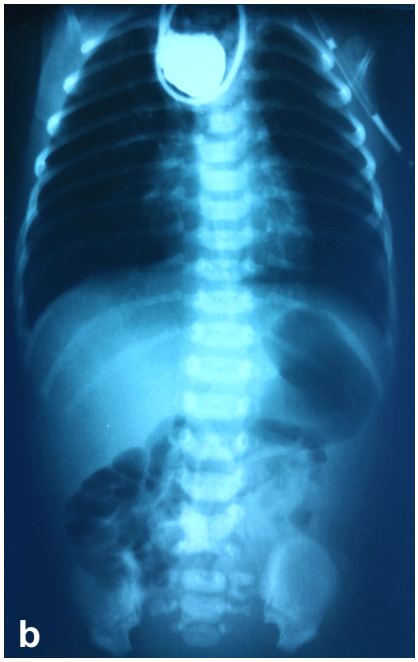


Figure 1 – ***(a and b) Esophageal atresia with distal fistula and fused L5–S1 vertebrae (Case No. 3). Thoracic-abdominal radiography with air and contrast substance.***

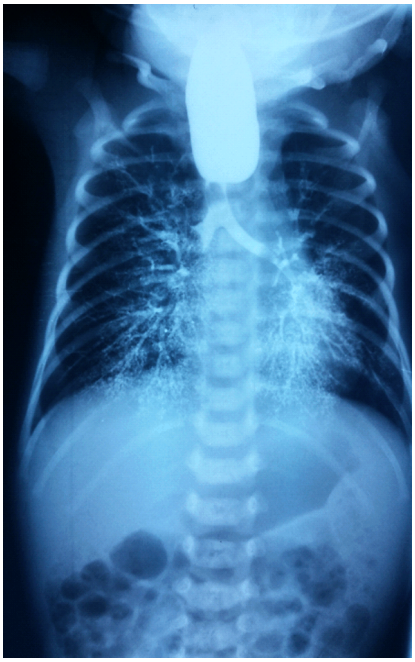


Figure 2 – ***Esophageal atresia with distal fistula. Thoracic-abdominal radiography with contrast substance.***

Table 1 – ***Summary of the maternal and neonatal data***

	Case No. 1	Case No. 2	Case No. 3	Case No. 4	Case No. 5	Case No. 6	Case No. 7
Mother							
Maternal age [years]	18	29	30	39	36	23	24
No. of pregnancies	1	2	1	1	1	1	2
No. of deliveries	1	2	1	1	1	1	1
Maternal history	–	–	–	thalassemia, thrombophilia	–	lumbosciatica	–
Pathology during pregnancy	hydramnios	–	–	pregnancy-induced hypertension	risk for preterm birth	risk for preterm birth	hydramnios
Drugs during pregnancy	–	–	vitamins	enoxaparin antihypertensive drugs	progesterone	–	antibiotics antispastic drugs
Pregnancy type	natural	natural	natural	*in vitro* fertilization	natural	natural	natural
Prenatal diagnosis	hydramnios	single umbilical artery	single umbilical artery	single umbilical artery	–	–	hydramnios, hydrocephalus, single umbilical artery
Newborn							
Gender	female	female	female	female	male	female	female
Gestational age [weeks]	35	38	40	33	35	37	35
Birth weight [g]	2600	3080	2320	1420	2110	2440	2420
Weight centiles	P50–75	P50–75	<P10	P10	P25–50	P10–25	P50–75
Type of esophageal atresia	EA with distal TEF	EA with distal TEF	EA with distal TEF	EA with distal TEF	EA with distal TEF	EA with distal TEF	EA with distal TEF
Associated heart defects	PDA PFO	PFO	PDA PFO VSD	PDA PFO	PDA PFO	PDA PFO	PDA PFO
Other congenital defects	tracheomalacia	–	anal imperforation with recto-vaginal fistula, vertebral defects; VACTERL association	unilateral kidney agenesis	–	–	hydrocephalus, anorectal malformation with recto-vestibular fistula, left kidney agenesis; VACTERL association
Other perinatal pathology	mild RDS, transient renal failure, congenital anemia	–	–	mild RDS, transient renal failure, subependymal hemorrhage, congenital anemia	mild RDS, subependymal hemorrhage	congenital anemia	mild RDS
Age at diagnosis	7 hours	2 hours	at birth	at birth	6 hours	at birth	at birth
Corrective surgery	yes	yes	yes	yes	yes	yes	yes
Survival	yes	yes	yes	no	yes	yes	yes

P: Percentile; EA: Esophageal atresia; TEF: Tracheoesophageal fistula; PDA: Persistent *ductus arteriosus*; PFO: Patent foramen ovale; VSD: Ventricular septal defect; VACTERL: Vertebral defects, anorectal malformations, heart defects, EA with or without TEF, renal anomalies/ dysplasia, and limb defects; RDS: Respiratory distress syndrome.

The etiology of EA is still incompletely understood, appreciated as multifactorial, involving genetic and environmental factors [15, 22–24]. Most of the reported cases are occurring sporadically [2, 15], genetic factors having a minor role [9]. A 2.5-fold increased incidence of EA was noted in twins [21, 25]. Analyzing of the maternal and neonatal data in the reported cases, we found no explanations for the increased rate of EA in our population in the latest two years. In the absence of genetic clues, environmental factors may have played the main etiological role in our cases.

Interestingly, six of the seven cases occurred in singleton female newborns, contrary to data in the literature that suggests that esophageal atresia has no gender preference [3, 4].

A multi-institutional retrospective cohort study reported that 37% of the EA patients were born preterm [26]. The mean gestational age of our reported cases was 36.1±2.3 weeks (33–40 weeks), four out of seven (57.1%) infants being born preterm. This is in accordance with the mean gestational age of 37±3 weeks reported by Schneider *et al.* [27], in a study of 301 patients with EA. The mean birth weight of our cases was 2341.4±505.2 g (1420–3080 g) and two of the seven (28.6%) cases had birth

weights lower than the 10th percentile for the gestational age (small for gestational age). David & O'Callaghan [28] also reported that one-third of the infants with EA were small for gestational age in their study.

No etiology or risk factors could be found in the history of the parents or of the pregnancies, except in one case – the infant born from a pregnancy obtained after *in vitro* fertilization. A three-fold increased risk for alimentary atresia is cited for pregnancies obtained after *in vitro* fertilization, some authors speculating that this excess risk is a direct consequence of the *in vitro* fertilization procedure [29]. Reefhuis *et al.* [30] reported an adjusted odds ratio for EA of 4.5 [95% confidence interval (CI) 1.9–10.5] in pregnancies following assisted reproductive techniques, and this increased risk was confirmed by Källén *et al.* [31] and Midrio *et al.* [32].

Prenatal diagnosis of EA may improve the outcome by offering the chance to optimize the prenatal and postnatal care [22]. Lack of visualization of the gastric bubble associated with polyhydramnios are suggestive but not specific signs for the prenatal diagnosis of EA [5, 8, 10, 22, 25, 33, 34] since both of these signs may occur in association with many congenital defects [33, 35] and due to increased subjectivity of echographic appreciation of the stomach size [22, 36, 37]. Also, polyhydramnios, even though frequently seen in pregnancies complicated with various congenital defects, is usually developing later in pregnancy, in the third trimester [22, 38]. A positive predictive value between 44% and 56% for EA was reported for the lack of visualization of the gastric bubble associated with polyhydramnios [25, 33, 39]. The reported sensibility of prenatal ultrasound diagnosis of EA varies between 8.9% and 42% [39, 40–42]. A more specific sign is the visualization of the blind esophageal pouch filled with fluid during fetal deglutition[10, 43, 44], a sign described starting 23–26 weeks gestation [43, 45] but this sign is rarely reported [43, 46] due to technical difficulties, time limitation of the ultrasound examination, or absent fetal deglutition during examination [22, 25, 41]. The rate of prenatal diagnosis of EA is low, around 44% in the study published by Brantberg *et al.* [38]. While prenatal ultrasound was performed in all the cases, a prenatal diagnosis of EA was done just in the Case No. 7 and only just one day before delivery (14.2%). Polyhydramnios was diagnosed in two of the cases, correctly, in the Case No. 7 in association with hydrocephalus and single umbilical artery at 25 weeks gestation. Although, unilateral renal agenesis escaped prenatal diagnosis in the Case No. 7 and polyhydramnios, known to occur in association with digestive tract atresia, should have prompted towards a more detailed ultrasound examination of the digestive tract [22]. All four cases of prenatal diagnosis of single umbilical artery were correctly diagnosed before birth. Single umbilical artery occurs in 0.4–1% pregnancies [47–50] and is often cited in association with renal agenesis [50], as it was seen in both our cases in which unilateral renal agenesis was found after birth. In 2005, Entezami *et al.* [51] raised the problem of the association between single umbilical artery and esophageal atresia after studying 362 fetuses with single umbilical artery. Dane *et al.* [49], in a study of 45 newborns with single umbilical artery, reported that in 45% of the cases diagnosed with single umbilical artery, at least another congenital defect was found and in two of these cases esophageal atresia was reported. The association between single umbilical artery and EA was noted by other authors too [22, 52, 53]. La Placa *et al.* [53] noted that single umbilical artery was the most frequent congenital anomaly (61.5% of the cases) after congenital heart and vertebral defects in a series of 15 VACTERL cases that included EA. Bourne & Benirschke [52] also reported an renal agenesis in association with single umbilical artery, as it was in the Cases Nos. 4 and 7 of our series. The fact that four out of seven (57%) infants had been diagnosed with single umbilical artery on prenatal ultrasound examination suggests that an increased index of suspicion for associated congenital defects should accompany the discovery of a single umbilical artery and a more detailed prenatal scan should be performed in these cases. Prenatal diagnosis of EA offer the chance for parental counseling, planned birth and transfer to pediatric surgery, avoiding the risk of feeding the infant and aspiration pneumonia.

Esophageal atresia may occur as an isolated defect but in 40–65% of the cases is associated with other congenital defects [2, 3, 6–9, 15, 22, 27, 39, 40, 54]. Cases of EA are seen in association with syndromes with know genetic etiology or as a part of congenital syndromes or associations – as VATER (vertebral defects, anal atresia, TEF with EA, radial and renal dysplasia), VACTERL association, CHARGE (coloboma of the eye, heart defects, atresia of the choanae, retardation of growth and development, and ear abnormalities and deafness) or Feingold syndromes [3, 15, 50, 55]. Other congenital defects are most often seen in EA with TEF (65% of the cases) and more rarely reported in TEF without EA (10% of the cases) [3, 7, 15, 56]. Congenital heart defects are most frequently seen in association with EA (23–35% of the cases, most often ventricular septal defect and Fallot tetralogy), followed by musculoskeletal defects (18% of the cases, most often vertebral defects), anorectal and gastrointestinal anomalies (13–16% of the cases, mainly duodenal atresia, imperforated anus, and malrotation), genitourinary tract defects (14–15% of the cases, mostly renal agenesis/dysplasia), head and neck defects (10% of the cases), mediastinal defects (8% of the cases), and chromosomal abnormalities (4–5.5% of the cases) [2, 15, 53, 57, 58]. More than one associated congenital defect was reported in 83.5% of the cases in the study of 3479 patients with EA performed by Sulkowski *et al.* [26] while in the much smaller study published by Czerkiewicz *et al.* [22], isolated EA was reported in 46 out of 62 (74.2%) cases. In two out of seven (28.5%) cases, isolated EA with distal TEF was diagnosed. Also, in our cases, except PDA and PFO, which are recognized as delayed cardiac adaptation and not structural congenital defects in neonates, a ventricular septal defect was the only congenital cardiac defect diagnosed (14.2%). After single umbilical artery (57% of the cases), the most frequent congenital abnormalities seen in our case were anorectal malformations (imperforate anus with rectovaginal fistula in the Case No. 2 and anorectal malformation with rectovestibular fistula in the Case No. 7), and unilateral renal agenesis (Cases Nos. 4 and 7). Most probably, the discrepancies between the rates of different types of congenital defects between the studies in the literature and our study are due to the very small number of cases analyzed by us. Also, our reported

cases were only EA with distal TEF, known to occur more rarely as an isolated defect [3, 7, 15, 56]. In two of the cases, EA was isolated.

Approximately 10% of the cases of EA are part of the syndromatic association, most often VATER or VACTERL association [3, 55]. A new similar syndromatic association – VACTERL-H – was suggested by Solomon [59], since cases associating hydrocephalus secondary aqueductal stenosis to VACTERL spectrum were also reported. Definition of VACTERL association can be used to define cases of EA associated with at least two other abnormalities from VACTERL spectrum. In our series, the definition can be applied to the Cases Nos. 3 and 7 (28.5%). Head ultrasound could not define the etiology of hydrocephalus in the Case No. 7; therefore, definition of VACTERL-H cannot be used to describe this case. The rate of VACTERL association found in our series is higher than described in most of the studies in the literature but closer to the rate reported by La Placa *et al.* [53] – 28.8% (15 cases of EA included in VACTERL association of the total of 52 cases of EA studied). We have no explanation for these increased rate except the association of these cases with single umbilical artery – both our VACTERL cases were associated with single umbilical artery –, an association highly recognized in VACTERL cases and even proposed to be included in VACTERL spectrum of congenital defects by some authors [52, 60]. Laryngeal stridor, suggesting tracheomalacia, was diagnosed at birth in Case No. 1 of our series. No reports of tracheomalacia before corrective surgery were found, most of the authors are citing tracheomalacia as a postoperative complication [8, 15, 27, 61].

Chromosomal abnormalities – mostly trisomy 18, 21, and 13q deletions [3, 4, 9, 10] – are seen in 4–5.5% of EA cases [2, 15, 53, 57, 58]. Diagnosis of chromosomal abnormalities is a negative prognostic factor, increasing the mortality risk up to 70% [4]. We cannot speculate about the incidence of chromosomal abnormalities in our series since postnatal chromosomal analysis was not performed in our cases. However, a prenatal karyotyping was performed and normal in the Case No. 4. None of our cases presented phenotypic features suggesting a chromosomal abnormality.

Prenatal diagnosis is important for parental counseling. Several classifications were developed in order to evaluate the outcome based on risk factors [2, 15, 62, 63]. Spitz classification [13] can be used even before birth if EA and associated congenital defects are diagnosed on prenatal scan. According to Spitz *et al.* [13], for the group 1 of EA – birth weight greater than 1500 g and no major congenital cardiac defects – the survival rate is almost 100%, for the group 2 – birth weight less than 1500 g or a major congenital heart abnormality – the survival rate is approximately 82%, while for the group 3 of EA – birth weight less than 1500 g and a major congenital heart abnormality – the survival rate is approximately 50%. Cases Nos. 3 (VSD) and 4 (birth weight <1500 g) can be classified in the group 2 after Spitz, none of the cases meeting the criteria for the lowest chances for survival group 3. Death occurred in the Case No. 4 due to severe postoperative renal failure, most probably unilateral renal agenesis being an important contributor risk factor. An unfavorable prognosis is also expected for the Case No. 7 due to association with evolving hydrocephalus and prolonged postoperative need for mechanical ventilation (due to recurrent bilateral hydrothorax).

Prenatal diagnosis and prompt postnatal diagnosis, before the first feeding, are extremely important as early feedings are associated with aspiration pneumonia that may delay corrective surgery or complicate postoperative course, with negative impact on the outcome [3, 5]. In the absence of a prenatal diagnosis or suspicion of EA, EA should be suspected after a failed attempt to insert a gastric tube for more than 10–12 cm for gastric aspiration at birth during neonatal resuscitation, in order to empty the stomach in infants delivered by cesarean section, or to feed preterm or sick term infants. In the rest of the cases, suspicion is raised by abundant foamy oral secretions, cough, drowning with saliva, or episodes of cyanosis and/or apnea during feeding attempts [8, 11, 12, 15, 21, 25, 41]. These symptoms are due to aspiration of the excess fluid from the esophageal pouch into the trachea [3, 5]. Repeated aspiration of the secretions – saliva from the upper esophageal pouch or acidic secretion of the stomach through the inferior esophageal pouch – leads to progressive installation of respiratory distress (tachypnea, retractions) [11]. A more gradual occurrence of these symptoms in association with abdominal distension and recurrent respiratory infections constitutes the clinical picture of TEF without EA [3, 5]. Therefore, experts are recommending insertion of a gastric tube in order to verify esophageal patency in all the neonates delivered from pregnancies complicated with polyhydramnios and in the newborns with abundant, foamy, aerated oral secretions, persistent in the first hours after birth [5, 15]. In the presented cases, EA was suspected at 2.1±3.0 hours after birth, in four of the seven cases at 5 minutes after delivery due to failed attempt to insert a catheter for gastric aspiration. In the Case No. 1, despite a prenatal diagnosis of polyhydramnios, EA diagnosis was delayed to due postnatal transfer form a lower level unit. At admission, the infant presented a severe apneic episode needing extensive resuscitation maneuvers and even mechanical ventilation. Esophageal atresia was suspected when a catheter was inserted for enteral feeding, at seven hours after birth. In the Case No. 2, the newborn developed abundant foamy secretions, vomiting, and transient cyanosis after the first feeding that prompted verification of the esophagus patency due to clinical suspicion of EA, so that radiography confirmed the diagnosis at two hours after birth. In the Case No. 5, development of a respiratory distress syndrome immediately after birth was first attributed to delayed clearance of the amniotic fluid due to prematurity (35 weeks gestation) but EA diagnosis was still done before the first feeding since gastric tube feeding is recommended for infants with tachypnea [64]. Thoracic and abdominal radiographs with air or contrast substance confirmed EA with TEF in all our cases and early diagnosis allowed stabilization, inventory of associated malformations, and transfer in good conditions in all our cases. Respiratory distress syndrome was addressed and solved before transfer in three of the four cases, and transient renal failure was corrected in both Cases Nos. 1 and 4. Preoperative avoidance of mechanical ventilation is associated with a better postoperative prognosis [2]. Respiratory support during transfer was needed only in the smallest preterm infant, the Case No. 4, the only infant in

our case series that died. A subependymal hemorrhage was diagnosed by head ultrasound in the Cases Nos. 4 and 5 (both preterm infants), while congenital anemia was noted in the Cases Nos. 1 and 6, none of these with impact during preoperative period.

Conclusions

The unusually high incidence of EA with TEF in the Sibiu and Alba Regions (Romania) during the latest two years could not be explained after analyzing the maternal and pregnancy data of our case series. An unexpectedly increased association of EA with single umbilical artery suggests that more detailed prenatal ultrasound scan should be performed in fetuses with single umbilical artery. Prenatal diagnosis of EA and associated congenital defects may help for family counseling, for a better planning of delivery and surgical correction, influencing the short and long-term outcome. Despite lack of prenatal diagnosis, obeying experts recommendations – as mandatory check of the esophagus patency if polyhydramnios is noted at prenatal ultrasound scan or at birth, or if a newborn develops abundant foamy oral secretions, associated with cough and/or drowning with saliva gastric, or mandatory tube feeding of infants with respiratory distress syndrome – may also help for a prompt diagnosis of EA and avoidance of aspiration pneumonia.

Conflict of interests

The authors declare that they have no conflict of interests.

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Received: November 15, 2016 *Accepted: August 1, 2017*