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ARAŞTIRMA / RESEARCH

Evaluation of congenital anomalies accompanying gastrointestinal system malformation

Gastrointestinal sistem cerrahi patolojilerine eşlik eden konjenital anomalilerin değerlendirilmesi

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Abstract

Purpose: The aim of this study was to review accompanied congenital anomalies to gastrointestinal pathologies.

Materials and Methods: The medical records of patients who were admitted to neonatal intensive care unit with gastrointestinal system surgical pathologies during 2015-2018 were retrospectively evaluated for associated congenital anomalies.

Results: 67 patients were identified during the study period. The most common gastrointestinal system pathology was anal atresia in 15 cases (22.4%), followed by diaphragmatic hernia in 14 cases (20.9%), esophageal atresia (n:10) and ileal atresia (n:10) (14.9%). Thirty two patients (48.8%) have had accompanied congenital anomalies to gastrointestinal system pathologies. Congenital heart disease was the most common anomaly and the most frequent one was atrial septal defect in 18 cases (26.8%). In addition, there was complex congenital heart disease in (n:13) 19.4%. In 12 patients (17.9%), accompanied extracardiac anomalies were detected. Hydronephrosis and sludge in gall bladder were detected in three patients (4.5%). Vesicoureteral reflux or ectopic kidney or polysplenia was detected as a separate anomaly in each case. In our cases, prematurity rate was found in 54%.

Conclusion: Gastrointestinal system pathologies are frequently associated with multiple anomalies, especially with congenital heart diseases. In addition, these patients are likely to be preterm baby.

Keywords: Newborn, gastrointestinal pathologies, congenital anomalies, preterm baby

Öz

Amaç: Bu çalışmanın amacı gastrointestinal sistemin cerrahi patolojilerine eşlik eden konjenital anomalileri değerlendirmektir.

Gereç ve Yöntem: 2015-2018 yılları arasında yenidoğan yoğun bakım ünitesine gastrointestinal sistem cerrahi patolojileri nedeniyle başvuran hastaların tıbbi kayıtları retrospektif olarak ilişkili konjenital anomaliler açısından değerlendirildi.

Bulgular: Çalışma süresince 67 hasta tespit edildi. En sık rastlanan gastrointestinal sistem patolojisi 15 olguda (% 22.4) anal atrezi, bunu 14 olguda (% 20.9) diyafragma hernisi, özofagus atrezisi (n: 10) ve ileal atrezi (n: 10) (% 14.9) izledi. Otuz iki hastada (% 48.8) gastrointestinal sistem patolojilerine eşlik eden konjenital anomali saptandı. Konjenital kalp hastalığı en sık görülen anomaliydi ve en sık birliktelik 18 olguda (% 26.8) atriyal septal defekt idi. Ek olarak, (n: 13)% 19.4'ünde kompleks konjenital kalp hastalığı vardı. On iki hastaya (% 17.9) ekstrakardiyak anomaliler eşlik etmekteydi. Üç hastada (% 4.5) hidronefroz ve safra kesesi çamuru vardı. Vezikoüreteral reflü, ektopik böbrek veya polispleni, her bir olguda ayrı bir anomali olarak tespit edildi. Olgularımızın % 54'ü prematüre olarak doğmuştu.

Sonuç: Gastrointestinal sistem patolojileri sıklıkla konjenital kalp hastalıkları gibi çoklu anomaliler ile ilişkilidir. Ek olarak, GIS patolojilerinin prematüre bebeklerde daha sık görülmesi muhtemeldir.

Anahtar kelimeler: Yenidoğan, gastrointestinal patolojiler, konjenital anomaliler, preterm bebek

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INTRODUCTION

Congenital gastrointestinal system pathologies (GIS) are the most common group of patients required for surgery in newborn infants. The incidence is 1.3 per 1000 live births[1]. GIS pathologies is a significant cause of neonatal morbidity and mortality. Developmental, teratogenic, socioethnic, and genetic factors play a important role in the etiology of congenital malformations and influence the type of these malformations. The most common presenting features were bilious vomiting and abdominal distension. Anomalies accompanying to GIS pathologies might carry risk for high mortality and morbidity, and they can worsen the course. If other system anomalies and problems that may accompany GIS pathologies are known in advance, it is clear that these patients will benefit from follow-up. Previous studies have indicated a high incidence of congenital heart disease (CHD) accompanying to common GIS pathologies[2, 3]. Gastrointestinal system pathologies generally are relatively less well-studied compared to the malformations of other body systems. In this study, the frequency of comorbid associated anomalies from both cardiac and other systems of patients, who were admitted and treated for GIS anomalies, was investigated. The effect of these comorbid anomalies on the prognosis was also emphasized.

MATERIALS AND METHODS

Infants who were admitted to neonatal intensive care unit (NICU) of Selçuk University, Faculty of Medicine Hospital between 01.01.2015-31.05.2018 and required gastrointestinal surgical procedure were evaluated retrospectively. In the NICU of our hospital all neonates with anomalies of any system are screened routinely for associated anomalies of the abdominal and urinary system on ultrasonography (USG), of the central nervous system on cranial USG and of the heart on echocardiography.

All together 80 patients who have GIS pathologies were identified during the study period. Unavailability of adequate records of six patients and incomplete imaging and research in terms of concomitant anomalies in seven patients were excluded. In addition, the twin girls with thoraco-abdominopagus have a lot of gastrointestinal and cardiac anomalies but they were excluded the study.

Etiology for the admission, their demographical data regarding gestational week, birth weight, gender, and physical examination findings, echocardiography results, abdominal and cranial USG findings as well as advanced imaging results and associated anomalies were recorded. The condition at the discharge time was also recorded. Patients with dismorfic features were included the study and their genetic sreening test results evaluated. The probability of the syndrome is increased in patients with two or more major system involvement. When this condition was detected, patients were evaluated for genetic pathologies. In case of need, patients were evaluated by chromosome or FISH analysis.

All cardiac pathologies except patent ductus arteriosus were considered as congenital cardiac anomaly. An atrial septal defect (ASD) of secundum type was diagnosed only when there was an unrestricted left-to-right shunting via an atrial communication. Otherwise it was called as patent foramen ovale and not accepted congenital heart disease. However, any lesion required anti-congestive therapy and/or surgical treatment was considered as complex heart problem. The patients, before discharged were examined for eye examination and hearing pathologies. The study was approved by local ethics committee of the university (2018/215). Since this is a retrospective study, voluntary / patient consent was not required.

Statistical analysis

Statistical evaluation was performed using IBM SPSS Statistics for Windows, Version 20.0 (Armonk, NY, USA) computer program. Data were expressed as number, percentage, mean and standard error of the mean.

RESULTS

The demographic data of the cases are shown in Table 1. The mean time for diagnosis was 4.3 ± 1.2 days and the age at the admission varied between 1-26 days.

The most common GIS pathology was anal atresia in 15 cases (22,4%), followed by diaphragmatic hernia in 14 cases (20,9%), esophageal atresia and ileal atresia in 10 cases (14,9%), Hirschsprung disease in 5 cases (7,5%), omphalocele in 4 cases (6%), gastroschisis in 3 cases (4,5%), intestinal malrotation and pyloric stenosis (n:1) 3%, respectively. In one

case, patent omphalomesenteric duct and intestinal diverticulum was together. In three patients, esophageal atresia and anal atresia were together, whereas in one case gastroschisis and anal atresia was present.

Table 1. Demographic characteristics of cases

Age (days) (mean±SD)	6±2	
Weight (g) (mean±SD)	2561±648,5 g	
Gender	n	%
Female	29	43,3
Male	38	56,7
Gestational Age		
Term	30	44,8
Late preterm	23	34,3
Preterm	14	20,9

From perspective of accompanied congenital anomalies, 32 (48.8%) patients have had CHD together with GIS pathologies. The most common form of non-complex CHDs was isolated ASD, and was diagnosed in 12 cases (17.9%). Complex heart disease was detected in 13 cases (19.4%). Among these pathologies AVSD, Fallot tetralogy, hypoplastic left heart disease, double outlet right ventricle, situs invertus totalis and ectopia cordis were present in our cases. ASD and ventricular septal defect (VSD) were detected together in five cases (7.5%) and VSD was present in four (6%) cases as a single pathology. Accompanied anomalies have been shown on Table 2.

Table 2. Congenital heart diseases accompanying to GIS anomalies

GIS anomalies	**Number of Neonates**		**Number of CHD**		**VSD**	**ASD**	**ASD, VSD**	**Complex heart disease**
	n	**%**	**n**	**%**				
Esophageal Atresia	10	14.9	7	70	2	2	2	1
Anal Atresia	15	22.4	11	73	1	3	2	5
Esophageal Atresia+Anal Atresia	3	4.5	3	100	0	1	1	1
Diaphragmatic hernia	14	20.9	3	21.4	0	1	0	2
Intestinal atresia	14	20.9	9	64.2	0	3	1	1
Hirschsprung disease	5	7.5	3	60	1	0	0	2
Omphalocele	4	6	2	50	0	1	0	1
Gastroschisis	3	4.5	1	33.3	0	1	0	0
Intestinal malrotation	2	3	0	0	0	0	0	0
Pyloric Stenosis	2	3	0	0	0	0	0	0
Patent omphalomesenteric duct	1	1.4	0	0	0	0	0	0

ASD: atrial septal defect of secundum type, VSD: ventricular septal defect, CHD: congenital heart diseases

We also underwent angiography with computed tomography to evaluate complex cardiac disease in our patients. The most common surgical procedure applied to patients who have complicated heart disease was Modified Blalock Tausing shunt.

In the postoperative period, patients with complicated cardiac disease remained in the mechanical ventilator longer than those with or without cardiac disease. The mean duration of mechanical ventilation in patients with complicated cardiac disease was 72 hours, whereas in other patients, this time was 26 hours ($p<0.05$). There was no statistically significant difference in terms of inotropic requirements of the patients in the postoperative period ($p> 0.05$). There weren't experienced mesenteric hypoperfusion or renal insufficiency of the patients because of their cardiac anomaly.

On the other hand, from perspective of accompanied non-cardiac anomalies, 12 cases (17.9%) were identified with additional pathologies. Three cases had extremity anomalies (in two cases focomelia and in one case talipes equinovarus) and two cases had hypospadias and each one has had laryngomalacia, or

cleft lip or mucopolysaccharidosis phenotype, additionally.

Abdominal USG also showed renal agenesis in 5 (7.5%) cases. Hydronephrosis and biliary sludge were detected in three patients (4.5%). Again each case has had either vesicoureteral reflux, or ectopic kidney or polysplenia, additionally.

Cranial USG showed dilation of the third ventricle in 2 cases (3%); and corpus callosum agenesis in one case (1.4%). No eye pathology was detected by ophtalmological examination. Applied hearing tests with patients were normal.

In our study, the most common chromosomal anomaly associated with GIS pathologies was Trisomy 21 in 9 cases (13,6%). One case was diagnosed as DiGeorge Syndrome and the other one was VACTERL association. Hirschsprung's Disease (n: 3) and anal atresia (n: 3) were common GIS pathologies in Trisomy 21.

DISCUSSION

Gastrointestinal pathologies are among the most common surgical cases in newborn period. In addition, congenital cardiac or non-cardiac anomalies accompanying to GIS pathologies are not rare[4]. Sayan et al. found frequency of accompanied lesions in 41.6% of cases and emphasized that these anomalies could increase morbidity and mortality[5].

In our cases, CHD was present in 32 cases 48.8%. In current literature, relation between GIS pathologies and concomitant congenital heart disease has been reported in a range of 17.9% to 62.5% of the cases[1,6-8]. This wide variation may be related to regional differences. However, one should remember that both CHD in GIS anomalies share mesodermal embryogenesis deficiency during intrauterine period, therefore their close relationship is anticipated in many cases[9, 10].

The most common congenital anomalies in the neonatal period are the central nervous system (CNS) and the urinary system pathologies, respectively[11]. However, they are not the most frequent defects associated with GIS pathologies. Therefore, in the present study, CNS and renal pathologies were detected in 3.5% and 28.9% in cases with GIS anomalies respectively. In addition, physical anomalies such as short axis, hypospadias, laryngomalacia and cleft palate were detected in 17.9% of our cases. It is noteworthy that renal pathologies are almost one out of every three patients.

In our study, 19 (28.4%) infants died due to multiple reasons. The highest mortality rate was observed in infants having both intestinal atresia and diaphragmatic hernia. Among those who died, CHD rate was 42%. In the literature, the mortality rate in omphalocele and anal atresia patients associated with heart pathology was reported 20% and 72.7%, respectively[12, 13]. In our study, three patients with omphalocele were passed away. One of these cases, has had complex heart disease. This is consistent with the literature. However, only two of the 15 anal atresia cases died and both cases had multiple non-cardiac congenital anomalies. One infant from this group had no other congenital malformation, but she died due to the complication of short bowel syndrome after malrotation. Gender difference was not observed in terms of mortality but 63% of the cases in mortality group were premature infants less than 37 gestational week.

In our study, anal atresia was the most common GIS malformation (22.4%) and was compatible with the literature[1]. When evaluated in terms of other congenital anomalies associated with anal atresia patients, congenital heart diseases were found to be very common (73%). Only 4 of 15 anal atresia cases had normal cardiac evaluation. Among the detected heart defects, complicated heart disease was seen the most common (45%). This finding is much higher than the literature. Olgun et al. reported anal atresia with complex heart disease 5.8%[1]. However, it is not possible to explain this situation with the existing genetic pathology in the patients (Down Syndrome was present in 4 of 15 patients; and neither cardiac disease nor another system pathology was present in both cases,). In addition, anal atresia was the most common anomaly accompanying other GIS anomalies; three cases of esophageal atresia + anal atresia and one case of gastroschisis + anal atresia were detected. In the study conducted by the EUROCAT Study Group, the rate of multiple congenital anomaly was 60.2% and VACTERL association was 15.4% in patients with anorectal malformation, emphasizing that chromosomal anomalies may also be frequent[14]. In 3 of our cases (20%) renal agenesis was detected; and in one case, an ectopic kidney was present. Also, in one case, the VACTERL association was diagnosed. Cranial ultrasound examinations of 15 patients with anal atresia revealed dilatation of the third ventricle in one

case and agenesis of the corpus callosum in another one.

The rate of abdominal wall defects in our patients was 10.4% (n: 7). Three cases had multiple congenital anomalies and two cases died due to complex heart disease. Stoll et al. found that the incidence of heart disease was 24% and chromosomal anomaly was 11% in patients with abdominal wall defect[15]. In our study, mucopolysaccharidosis was present in one of the 7 patients and the incidence of congenital heart disease was found to be 42.8%, which was found to be more frequent than the literature[16]. This situation can be explained by higher admission rate of such complicated cases to our hospital being a tertiary reference center.

Frequency of congenital diaphragmatic hernia (CDH) was 20.9% in our cases. The incidence of CDH is 1-5 / 10000 among live birth infants and associated congenital anomalies were reported between 37% and 47%[17, 18]. The most important two factors affecting mortality rate in CDH are pulmonary hypoplasia and pulmonary hypertension that have been reported in approximately half of the cases[19]. Mortality rate in our study was 35% among CDH patients. In the literature, CDH is associated with CHD in 8% to 10% of the cases[1, 20]. In present study, this rate was 21.4% which was higher than other reports. No chromosomal pathology was detected in any case. However, frequency of other extracardiac anomalies was 28.5%.

Previous studies showed that esophageal atresia is the second most common pathology in all GIS anomalies and its rate varies between 19% - 28.3%[1, 21]. However, in our study, it was the third one and the rate was 14.9%. In previous studies, overall CHD was reported around 30% of esophageal atresia cases and complex CHD was also reported in 10% of the cases[22, 23]. In our study, CHD rate was 70% (n:7/10); and in one case, complex CHD was present. Extracardiac anomaly was also detected in 40% (n: 4/10) of cases. However 30% of those were composed by associated anal atresia. One case died due to prematurity complications and the other one died due to multiple congenital anomalies.

In our study, 14.9% cases (n: 10) were detected with intestinal atresia. Also, highest genetic abnormalities were found in this group (30%). Our findings were consistent with the literature[24]. These congenital anomalies are common and it is not necessary to have them with chromosomal abnormalities[25]. The incidence of CHD in this group was 50%, but the extracardiac anomaly was detected only in one case. Walker et al. stated that 52% of the patients with intestinal atresia are premature and it affects the mortality[26]. They reported mortality rate 8%. In our cases, the prematurity rate was 55.2%; and half of those died. However, prematurity was very common problem in our patient population.

The limitations of present study include its small number of study patients on account of it being a single-center study. Additionally, because some of the babies who have congenital gastrointestinal pathologies required immediate resuscitation after birth and some of them were dead in the delivery room, they had to be excluded from the study as autopsy had never done.

Gastrointestinal system pathologies are frequently associated with multiple anomalies, especially with CHDs. In addition, prematurity is more common in these patients. As a result, early screening of these patients for concomitant anomalies and follow-up in advanced centers will decrease mortality rate and improve the prognosis.

Yazar Katkıları: Çalışma konsepti/Tasarımı: AS, MK; Veri toplama: MK; Veri analizi ve yorumlama: MG, HS; Yazı taslağı: MK; İçeriğin eleştirel incelenmesi: AS; Son onay ve sorumluluk: MK, AS, MG, HS, SSU; Teknik ve malzeme desteği: SSU; Süpervizyon: HS, MG; Fon sağlama (mevcut ise): yok.
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