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Original Article

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Anorectal Malformations Associated with Esophageal Atresia in Neonates

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Purpose: Anorectal malformations are often associated with other anomalies, reporting frequency with 40-70%. Gastrointestinal anomalies have been known to be relatively less common than associated anomalies of other organ system. This study was performed to assess a distinctive feature of cases associated with esophageal atresia.
Methods: Clinical data (from January 2000 through December 2011) on the 196 subjects with anorectal malformations, managed in our Hospital, were reviewed. Total 14 neonates were identified with accompanying esophageal atresia and retrospective analysis was conducted.
Results: The incidence was 7.1% and there were 8 male and 6 female subjects. Only 2 cases were associated with esophageal atresia without tracheoesophageal fistula. Although variable cases of anorectal malformation in female subjects, almost cases were anorectal malformations with rectourethral fistula in male. Other associated anomalies were identified in all cases, with more than 3 anomalies in 10 cases. There were 4 VACTERL (Vertebral abnormalities, Anal atresia, Cardiac anomalies, Tracheoesophageal fistula, Esophageal atresia, Renal and Limb anomalies) associations accounting for 28.6%, but could not identify chromosomal anomaly. Most cases were managed with staged procedure, usually primary repair of esophageal atresia and diverting colostomy. Overall mortality rate was 21.4%, mainly caused by heart problems.
Conclusion: This study shows that early diagnosis and rational surgical approach with multidisciplinary plan are mandatory in managing anorectal malformations with esophageal atresia, when considering a high frequency of associated anomaly and a relative high mortality. **(Pediatr Gastroenterol Hepatol Nutr 2013; 16: 28～33)**

Key Words: Anorectal malformation, Esophageal atresia, Neonates

INTRODUCTION

Anorectal malformations occur approximately in 1/1,500 to 1/5,000 live births [1,2]. They may occur alone, but they can commonly have other associated anomalies or occur as a part of the combined anomaly. The treatment involved may be complicated by a need to address the associated anomalies, in addition to the

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anorectal malformations. Furthermore, the problems of these associated anomalies could have more of an impact on the morbidity and mortality before and after surgical treatment.

The frequency of associated anomalies in other organs is known to be approximately 40-70% in the decreasing order of urogenital system, musculoskeletal system, and cardiovascular system [3,4]. In addition, anomaly in other parts of the gastrointestinal system can occur concomitantly, and a prompt treatment is required in such situations when the neonate's life is threatened. In particular, when an esophageal atresia accompanies the anorectal malformations, the complex of surgical procedure and the difficulty of situational postoperative management must be considered.

Thus, we conducted the present study to analyze the characteristics of and treatment results in neonates with anorectal malformations associated with esophageal atresia.

MATERIALS AND METHODS

Patients

The subjects of this study were 196 patients who had been diagnosed and managed for anorectal malformations in the neonatal intensive care unit, Pusan National University Children's Hospital, from Jan 1, 2000 to Dec 31, 2011. Among these patients, 14 patients associated with esophageal atresia were selected as the subject patient group.

Methods

A retrospective study was conducted by using the clinical data of the 14 patients. First, clinical aspects such as the type of anorectal malformations and the frequency of other associated anomalies were compared between the groups with and without esophageal atresia. Comparative analysis of the clinical characteristics of anorectal malformations associated with esophageal atresia, as well as the processes of management and the methods, and results for the treatment in neonatal period, were performed.

RESULTS

Comparison of groups with and without esophageal atresia

Among the 196 patients with anorectal malformations, there were 14 patients with esophageal atresia and 182 patients without it; the male to female ratio was 1.3 : 1 (8/6) and 1.2 : 1 (98/84), respectively. Regarding the type of anorectal malformations, there were 2 and 81 cases of low-type malformation, which is correctable through a single procedure, in the group with and without associated esophageal atresia. There were 9 and 100 cases of intermediate- or high-type malformations that require a staged procedure, respectively. Cloacal anomaly was identified in 3 cases and 1 case, respectively (Table 1).

Clinical characteristics of anorectal malformations associated with esophageal atresia

There were 14 neonates with esophageal atresia, accounting for 7.1% of the total subjects. Of them, male was 8 and female was 6; there was no sexual difference in occurrence. According to the classifications of anorectal malformations, there were 7 cases with rectourethral fistula and 1 case with rec-

Table 1. Clinical Aspects according to Accompanying with Esophageal Atresia

Clinical characteristc	ARMs with EA (n=14)	ARMs without EA (n=182)
Sex ratio (Male : Female)	1.3 : 1 (8 : 6)	1.2 : 1 (98 : 84)
Type of ARMs		
Low type (managed by single procedure)	2 (14.3%)	81 (44.5%)
Intermediate & high-type (managed by staged procedure)	9 (64.3%)	100 (54.9%)
Cloaca	3 (21.4%)	1 (0.5%)

ARMs: anorectal malformations, EA: esophageal atresia.

toperineal fistula in the males. In the females, there was a varied distribution of 3 cases in cloacal anomaly, 2 cases in rectovaginal fistula, and 1 case in rectovestibular fistula. In cases of esophageal atresia, there were 2 cases of type A esophageal atresia without tracheoesophageal fistula, but most cases were type C esophageal atresia with tracheoesophageal fistula (Table 2).

Distribution of associated anomalies

Associated anomalies in other organ system were confirmed in all the study cases and more than 3 associated anomalies were observed especially in 10 cases. When considering the frequency by organ system, there were 12 cases involving the cardiovascular system; 8, urogenital system; 5, musculoskeletal system; 3, digestive tract system; 1, central nervous system; and 1, respiratory system. In particular, there were 4 cases (28.6%) presenting as a part of the VACTERL (Vertebral abnormalities, Anal atresia, Cardiac anomalies, Tracheoesophageal fistula, Esophageal atresia; Renal and Limb anomalies) as-

Table 2. Demographic and Clinical Characteristics of Anorectal Malformations Associated with Esophageal Atresia

Case	Sex	GA (week)/BW (g)	Type of ARMs	Type of EA
1	Female	40/2,510	Cloaca	C
2	Male	33/2,100	With rectourethral fistula	A
3	Male	40/3,275	With rectourethral fistula	C
4	Female	41/2,370	With rectovaginal fistula, high	C
5	Male	37/2,720	With rectourethral fistula	C
6	Male	38/2,600	With rectourethral fistula	C
7	Male	37/2,160	With rectourethral fistula	C
8	Male	38/2,600	With rectourethral fistula	C
9	Female	37/2,477	With rectovestibular fistula	C
10	Female	39/2,120	Cloaca	C
11	Female	28/1,070	Cloaca	A
12	Female	38/2,600	With rectovaginal fistula, high	C
13	Male	40/2,850	With rectourethral fistula	C
14	Male	39/3,000	With rectoperineal fistula	C

GA: gestational age, BW: birth weight ARMs, ARMs: anorectal malformations, EA: esophageal atresia.

Table 3. Comparison of Associated Anomalies between Two Types

Organ system	ARMs with EA	ARMs without EA
	No. of cases (%)	No. of cases (%)
Cardiovascular system	12 (85.7)	72 (39.6)
Genitourinary system	8 (57.1)	57 (30.9)
Skeletal system	5 (35.7)	18 (9.8)
Central nervous system	1 (7.1)	5 (2.7)
Other gastrointestinal tract		
DA with malrotation	2 (14.2)	-
Malrotation	1 (7.1)	3 (1.6)
Meckel's diverticulum	2 (14.2)	2 (1.1)
Annular pancreas	1 (7.1)	-
Biliary atresia	-	1 (0.5)
Chromosomal	-	2 (1.1) (down syndrome)
Others	3 (21.4)	-
VACTERL association	4 (28.6)	-

ARMs: anorectal malformations, EA: esophageal atresia, DA: duodenal atresia, VACTERL: Vertebral abnormalities, Anal atresia, Cardiac anomalies, Tracheoesophageal fistula, Esophageal atresia, Renal and Limb anomalies.

sociation, which is the representative example of a complex anomaly; 3 patients were females and 1 patient was a male. There was no abnormal findings in the chromosomal study. However, in anorectal malformations without esophageal atresia, there was a relatively low frequency of associated anomalies, as compared to that in the study subject group; on the other hand, there were a few cases of autosomal abnormalities (Table 3).

Managements and results in the neonatal period

In 10 cases, a primary correction for esophageal atresia and a diverting colostomy were performed concurrently. In 1 case, anoplasty and a primary correction for esophageal atresia were performed concurrently. Diverting colostomy was performed first in 2 cases; one case had a delayed diagnosis of esophageal atresia and the other case had concomitant perforation in the gastrointestinal tract. The remaining one patient was confirmed to be dead due to associated anomalies in the other organs, without having received other surgical treatments (Table 4).

There were 3 mortality cases in 14 patients (mortality rate, 21.4%). A more detailed observation showed that 1 case, a previously described case of death without surgical interventions, was a female neonate with VACTERL association who was born at 28 weeks of gestation with a birth weight of 1,070 g. In the other 2 cases, the cause of death was a heart problem due to associated cardiac anomalies, and 1 of these cases was confirmed to be a male neonate in whom a diagnosis of esophageal atresia was delayed because of a perforation in the gastrointestinal tract. Overall, for the 13 cases with receiving a correction surgery in the neonatal period, 2 cases of death were observed in the postoperative period. The cause of death in these cases was confirmed to be attributable to other associated anomalies rather than the disease of focus in the present study. Meanwhile, in the subjects with anorectal malformations without esophageal atresia, 1 case of death was observed (mortality rate, 0.5%). This was not a case of neonatal period, but due to a heart problem developed in follow-up period after final operation.

Table 4. Management and Clinical Results in Neonatal Periods

Method of management	Result
Primary repair of EA with diverting colostomy: 10	1 death
Primary repair of EA after diverting colostomy: 2	1 death
Primary repair with anoplasty: 1	-
No treatment: 1	1 death
Overall mortality: 3 in 14 cases (21.4%)	

EA: esophageal atresia.

DISCUSSION

In patients with anorectal malformations, associated anomalies in other organs are not uncommon. These associated anomalies may sometimes cause a high rate of morbidity and mortality.

Although it is difficult to directly compare the types of associated anomalies because of their varied natures, cases of associated with esophageal atresia are known to some extent because of their clinical importance. Associated esophageal atresia in patients with anorectal malformations may occur alone or as a part of complex anomaly, and its incidence is reported approximately in 8-11% [3,5]. The incidence rate in the present study was 7.1%, which was not largely different from that in other reports. Moreover, associated anomalies other than anorectal malformations and esophageal atresia were observed in all patient subjects. The majority of these anomalies were problems of the cardiovascular or urogenital systems, and they were not largely different from those reported in previous studies [6]. However, a relatively higher frequency of anomalies was observed in the subjects with esophageal atresia than in those without esophageal atresia. Thus, given that additional associated anomalies were observed in all patients, it is suggested that the management of anorectal malformations associated with esophageal atresia will require more caution and efforts than the management of patients presenting with anorectal malformations alone.

Although many factors may be involved in the occurrence of these anomalies, it may be thought that

anorectal malformations and esophageal atresia are types of midline defects, which present along the body. These defects occur as results of the combination of deficits in mesodermal migration and endodermal defects [7,8]. On the other hand, in VACTERL association, there are two different explanations involving it; genetic factors and external environmental factors. First, the genetic factor model has been supported through animal experiments, and it proposes the formation of anomalies due to genetic mutations that induce signaling pathway abnormalities [9-11]. Second, it is thought that external environmental factors such as maternal diabetes, hormonal exposure during infertility treatments, and exposure to toxic factors negatively influence the morphological development of the fetus, leading to malformations in the fetus [12-15]. In our study, we could not identify any factors, such as chromosomal defects, which may induce this anomaly, but it is necessary to be supposed to think about an adequate investigation of these factors. However, since the incidence of the disease itself is not very high, there are still many limitations to investigate directly.

Generally, associated anomalies occur more frequently in high-type of anorectal malformations than in low-type malformations; the frequency is also higher in males than in females [2-4,16,17]. In our study, for anorectal malformations associated with esophageal atresia, the gender distribution was relatively equal, with a 1.3 : 1 male to female ratio. In the case of male, most of anorectal malformations were intermediate- or high-type with rectourethral fistula (7/8, 87.5%), and mainly low-type or cloacal malformations in female. This findings showed a different distribution in cases of anorectal malformations without esophageal atresia. A relatively high frequency, 28.6%, of the cases occurred as a part of the VACTERL association, which may be considered as result of multiple congenital malformations. In addition, considering the report that the frequency of concomitant gastrointestinal atresia is 4 times as high in VACTERL association than in the cases with a single anomaly of anorectal malformation, this can also be inferred as a result of simple primary malformation due to deficits in the organ formation process, in addition to the previously mentioned disease occurrence process [18-20].

In the management of a complex anomaly, the correlation with life support must be considered primarily in the neonatal period, and it is essential to do appropriately a staged procedure. Ultimately, when considering it's clinical results, the complicated nature of the surgical procedure and appropriate surgical approaches must be considered in managing a case of anorectal malformations associated with esophageal atresia. In this study, the majority of the surgical treatments administered in the neonatal period were a staged procedure with good results, and there were no major differences compared to other reports [21-23]. Although the mortality rates after appropriate treatments are relatively low in the cases of simple anorectal malformations and esophageal atresia, the total mortality rate observed in the present study was 21.4%, a very high frequency compared to that in other gastrointestinal anomalies. In particular, when compared to anorectal malformations without esophageal atresia, it can be concluded that this high mortality rate is attributable to complications associated with other anomalies, rather than the disease itself. Two of the 3 deaths in our study were caused by heart problems during observation after the primary surgery in the neonatal period, and 1 death in VACTERL associations without surgical intervention. Thus, it could be inferred that the influence of other associated anomalies was greater than that of anorectal malformations and esophageal atresia. Meanwhile, diverting colostomy was performed initially in 2 patients. Each case involved a delayed diagnosis of esophageal atresia or concomitant gastrointestinal perforation. Because of these complications, complex surgical procedures were unavoidable, and one case involved with gastrointestinal perforation resulted in a death during the postoperative recovery period. This indicates that a more careful and timely diagnosis based on clinical and radiological findings is necessary before the primary operation.

In conclusion, anorectal malformations associated with esophageal atresia, whether alone or as a part of a complex syndrome, had a relatively high frequency of associated anomalies in other organs, as well as a high mortality rate. It may be suggested that a staged and multidisciplinary approach is essential in the management of neonates with this anomaly. In addition, reasonable treatments considering these possibilities may lead to improved outcomes by preventing delays in the diagnosis of anorectal malformations associated with esophageal atresia, as well as the development of serious complications.

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