



Research Article

Meckel's Diverticulum Does not fit the Rule of Two: A Bicentric Experience

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Abstract

Introduction: Meckel's Diverticulum (MD) is the most common gastro-intestinal congenital malformation. The Rule of Two is largely diffused to describe the characteristics of MD, but in a consistent number of cases, clinic and histology do not fit into the rules. The experience of two referral centers is reported.

Methods: The Rule of Two includes: 2% prevalence, male/female ratio 2:1, <2 years of age, location within 2 feet (60 cm) from the ileocecal Valve (ICV), 2 inches' length (5 cm), 2 types of ectopic mucosa. Patients with MD admitted between 2010 and February 2022 were analyzed. Appendectomies, performed in the same period, were considered as the reference population. Data on prevalence, gender, age, position along the intestine, MD length, histology were analyzed.

Results: Seventy-three patients were identified, of whom 43 symptomatic (59%). Appendectomies were 2289, the prevalence was 2.9%. Male/female ratio was 2.65; 8.5 in case of gastrointestinal bleeding. Mean age at onset 5.48 ± 4.34 years (range 0.08-14); 60.5%>2-year-old. Mean distance from IVC 45.10 ± 16.66 cm: 11% were >2 feet. Mean MD length $3.13\text{cm} \pm 1.49$. Ectopic tissues, found in 19, were all gastric mucosa except for 1 case of gastric-pancreatic mucosa.

Conclusions: The diagnosis of MD should be included throughout all the pediatric age and the intestinal examination extended until 100 cm from IVC, especially in older children. According to our results, the Rule of Two seems too limited to describe the characteristics of MD.

Keywords: Gastrointestinal malformation; Meckel diverticulum; Omphalomesenteric duct

Introduction

Meckel's Diverticulum (MD) is the most common gastrointestinal malformation caused by the persistence of the omphalomesenteric duct [1]. This duct is supposed to obliterate during late pregnancy and failure of closure process leads to different congenital anomalies such as a residual fibrous cord, umbilical sinus or cyst, omphalomesenteric fistula, and MD [2]. MD is a fully formed diverticulum representing 85% of

the omphalomesenteric duct anomalies, usually located on the antimesenteric border, except for some rare cases [3]. MD is covered by ileal mucosa, but islets of gastric ectopic mucosa are not infrequent, being the pancreatic, colic, endometrial, and hepatobiliary tissue much rarer [4]. MD is symptomatic in less than 5% of cases [1] and often it is incidentally found during abdominal surgery performed for other reasons. The spectrum of clinical manifestations, listed in decreasing order, includes episodic and painless lower gastrointestinal bleeding, occlusion, diverticulitis with or without perforation, and cancers [5]. The "Rule of Two" (RoT) has been used to describe the main features of MD [5] (Table

1). However, in a variable number of cases, the characteristics and clinical pictures do not follow the rule. The experience of two referral pediatric surgical centers is herein reported with the aim to verify the validity of RoT.

Rule of Two	
Prevalence	2%
Age at the onset of symptoms	<2 years
Male: Female	02:01
Ectopic mucosa	2 types (gastric and pancreatic)
Distance from the Ileo-cecal valve	<60 cm (2 feet)

Table 1: Rule of Two's criteria.

Material and Methods

Pediatric patients with ICD-9 code diagnosis of "Meckel Diverticulum", admitted to two pediatric referral centers, between April 2010 and January 2022, were included. Both centers routinely perform the search of MD during appendectomies and specimens are sent for histology. The number of acute and incidental appendectomies was also retrieved to have a reference population and estimate MD prevalence. MDs were divided into two groups, based on presence (S-patient) or absence (A-patient) of symptoms. Symptoms were classified into 3 macro-categories: intestinal occlusion, intestinal bleeding, and inflammation. Records of all cases were collected focusing on gender, age of presentation, macro and micro characteristics, and location of MD along the intestine. Data were analyzed with Pearson correlation coefficient for the age-related position from the ileocecal valve and t-test to compare the mean length of MD in symptomatic and asymptomatic patients.

Results

A total of 73 children were identified. Two of them were umbilical sinus and no histology was performed.

Epidemiology

The characteristics of patients with MD are reported in Table 2. The appendectomies performed in the same period were 2289, and the prevalence in the normal population was 2.9% (73/2289). The overall male to female ratio was 2.65:1 and the same male dominance was observed in symptomatic patients (2.9:1). In the asymptomatic patients the ratio was 2.33:1. In particular, gender difference was much higher in children with lower gastrointestinal bleeding (8.5:1). Patients presenting with inflammation were mainly males (4:1) and no gender difference was observed in case of occlusion (1.37:1).

Patients	All	S-Patients	A-Patients
Age (years)	6.84 ± 4.00	5.48 ± 4.33	8.20 ± 3.67
Male: female	8.5:1	1.37:1	04:01
Bleeding	19	19	
Occlusion	19	19	
Inflammation	5	5	
MD length (cm)	3.13 ± 1.49	3.55 ± 1.59	2.55 ± 1.10
Heterotopic mucosa	19	17	2
Distance from ileo-cecal valve (cm)	45.10 ± 16.66	48.75 ± 17.45	
Total	73	43	30

Table 2: Characteristics of symptomatic and asymptomatic patients. S-patients: Symptomatic patients; A-patients: Asymptomatic patients; MD: Meckel diverticulum.

Clinical Presentations

Forty-three cases were symptomatic (S-patient, 59%) with a mean age of 5.48 ± 4.33 years and 32 were asymptomatic (A-patient, 41%) with a mean age of 8.20 ± 3.67 years. S-patients presented with intestinal bleeding (44%), occlusion (44%), and inflammation in 12% of the cases. The reasons for intestinal occlusion were intussusception, Meckel band, torsion of MD, and intestinal volvulus (Figure 1) while symptoms of inflammation included diverticulitis and omphalitis. The mean age of patients presenting with bleeding and occlusion was similar (5.30 ± 4.57 years and 5.80 ± 4.36 years, respectively), while those presenting with inflammation were younger (5.02 ± 4.60 years). Overall, 60.5 % of S-patients were older than 2 years of age and 21 % of the latter were older than 10 (Figure 2).

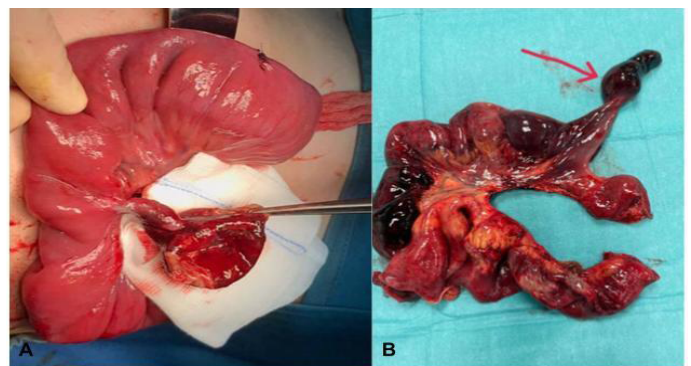


Figure 1: Torsion of MD in 3 years old boy (A); Intestinal volvulus on MD in 6 years old girl (B).

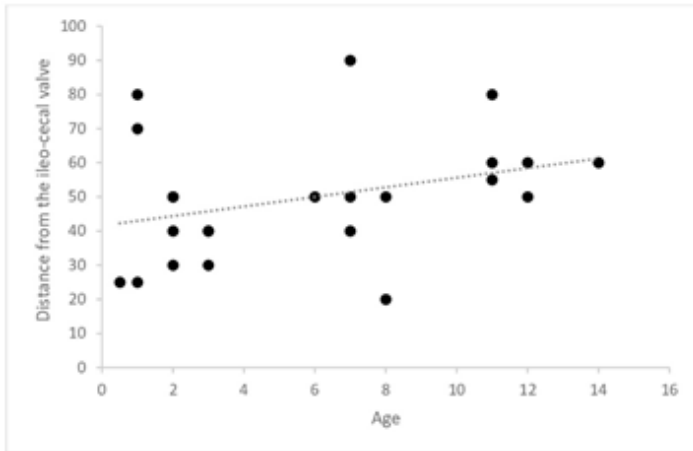


Figure 2: Age distribution of symptomatic patients.

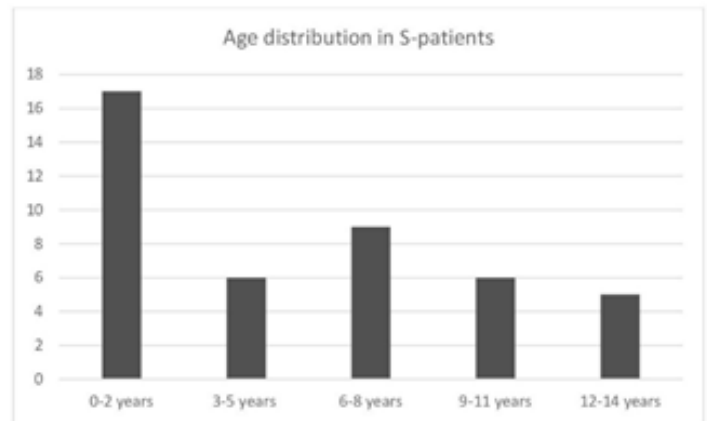


Figure 3: Scatter chart showing the weak correlation between age and the position of MD along the intestine ($r=0.13$).

Histology

All but 2 specimens were sent for histology. The mean length of MD, calculated in 63 cases, was 3.13 ± 1.49 cm (range 0.8-7 cm). Thirty-seven/63 MD belonged to S-patient and 26 to A-patient. The mean length of S-patient and A-patient was 3.55 ± 1.59 cm and 2.55 ± 1.10 cm, respectively and the difference was statistically significant ($p=.0076$). Nineteen/73 MD (26%) presented ectopic mucosa, being gastric in all but 1 A-patient who showed both gastric and islets of pancreatic tissue. S-patients had ectopic mucosa in 39.5% and the presence of gastric mucosa was predominantly associated with intestinal bleeding (72%). Moreover, the ectopic tissue was strongly associated to male sex with a male to female ratio of 8.5:1.

Position From The Ileocecal Valve

The mean distance of MD from the ileocecal valve (ICV), calculated in 46 patients, was 45.10 ± 16.66 cm. In 5/46 cases (11%) the distance of MD from the valve was over 60 cm. Furthermore, there was a weak correlation between age and position along the intestine ($r=0.13$; $p=.38$) (Figure 3). The main results and the results of the study compared with RoT are summarized in Table 2.

Discussion

Meckel diverticulum was first identified by Hildanus in 1598 and further characterized by Johann Friedrich Meckel in 1809, who established its embryological origin [6]. Historically, the main characteristics of MD are summarized according to RoT [5,7]. However, in the present study, only some characteristics of MD corresponded to RoT and all the others were discordant. The presence of MD is estimated to be between 0.3% and 2% considering the general population [8] and 1.2% reported in autopsy-studies [4]. Based on a different reference population, Ueberrueck et al. detected 2.9% of MD during appendectomies [9]. Our results showed the same percentage (2.9%) calculated over the appendectomies performed in the same analyzed period. Even so, the real percentage is likely higher in the general population, considering that around 95% of MD remain asymptomatic and undiagnosed during life [10]. The most common clinical onset of MD are intestinal obstruction, hemorrhage, and inflammation [11]. In our series, gastrointestinal bleeding was the most frequent, followed by occlusion and inflammation. The male: female ratio for MD is reported to be 2:1 and the male predominance is showed by several authors [12-14]. This gender difference is even higher

in case of symptomatic patients, as demonstrated by Jung Hee Rho et al (male 7.5:1 female) [15]. In the study by Karaman et al, the ratio was 2.25:1 in asymptomatic MD and 5.4:1 in the symptomatic patients [16]. Our data confirmed especially the higher percentage of males for gastrointestinal bleeding (8:5:1). In addition, 90% of cases of heterotopic mucosa were males. The higher frequency of symptomatic MD in males can be explained also by the hyper-acidity theory, according to which, males have more elevated levels of gastrin and acid that cause a greater stimulation of the ectopic gastric mucosa [17]. Altogether, these findings can explain why the gastrointestinal bleeding episodes occur most frequently in boys. Conversely, in our series no gender difference was detected in patients who presented with intestinal occlusion. Usually, MD is suspected in children younger than 2 years with painless rectal bleeding. However, in several studies the mean age at onset was higher [13,15,18-22]. Indeed, Jung Hee Rho [15] reported only 24.9% of patients younger than 2 years of age and most of them in the range 5-10 years. Huang et al. [12] showed similar results: 65% of children older than 2 years with a mean age of 5.32 ± 4.74 . According to them, the mean age of symptomatic patients in our series was in the range between 5 and 6 years. Another population-based study [23], that also included adults, found that 48% of patients older than 20 years were symptomatic, mainly intestinal obstruction, and with high postoperative mortality. Furthermore, our data showed no age differences comparing patients with intestinal bleeding and occlusion. On the contrary, it has been reported a younger mean age in children with intestinal obstruction, probably caused by the increased peristalsis due to the greater number of Auerbach plexus fibers present in young children [24]. The possibility to find an ectopic mucosa in the symptomatic MD is reported to be as high as 65-90% [25]. Gastric and pancreatic mucosa are the most frequent type of tissue and the gastric one also represents a risk factor [5]. Sli'vova' et al. [18] shows that the presence of ectopic mucosa and a large base of the diverticulum are predictive factors for the development of complications and to decide whether to perform an intestinal resection. We observed the ectopic mucosa, mainly gastric, being present in a lower percentage (39.5%) of symptomatic cases. The length of MD has been correlated with a higher chance of complication [26]. Indeed, we registered a significant statistical correlation between longer MD and symptomatic patients. According to RoT, MD should be located within 2 feet (60 cm) from the ileocecal valve, and it is a common practice to search the diverticulum at least up to this length. Rho JH et al [15] reported MD located at a mean distance of 47.0 cm from the ileocecal valve and Lee et al. [27] described a mean distance of 45.9 cm. Our data are globally concordant with the literature, even if 11% of MD were found beyond 60cm, suggesting the search of MD extended at least up 100 cm. At a variant of the literature [24,28], we could not demonstrate a correlation between age and distance from the ileocecal valve.

Conclusion

MD have several and diversified characteristics regarding age and symptoms onset, histology, length, and position along the intestine. RoT is very often considered the benchmark to describe the characteristics of MD, but this retrospective study demonstrates its limits. Prevalence of MD in our series population was greater than 2%, more than half symptomatic patients were older than 2 years, and in 11% of the cases MD was located beyond 60cm from the ileocecal valve. Therefore, RoT may be no longer suitable to describe the main characteristics of MD.

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