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ORIGINAL ARTICLE

FREQUENCY AND CHARACTERISTICS OF MECKEL'S DIVERTICULUM IN TEN-YEAR BIOPSY MATERIAL OF THE INSTITUTE OF PATHOLOGY

UČESTALOST I KARAKTERISTIKE MEKELOVOG DIVERTIKULUMA U DESETOGODIŠNJEM BIOPSIJSKOM MATERIJALU INSTITUTA ZA PATOLOGIJU

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Abstract

Introduction: Meckel's diverticulum is the most common congenital malformation of the gastrointestinal tract, which occurs due to incomplete obliteration of the omphalo-mesenteric duct. The prevalence of Meckel's diverticulum in the general population is 0.3 - 2.9%, with a more frequent occurrence in men. It is mainly lined with typical ileal mucosa, although ectopic tissues may also be present. Complications due to the existence of Meckel's diverticulum occur in about 4 - 16%.

Aim: The aim of this work is to determine the macroscopic and histological characteristics of Meckel's diverticulum, the frequency of the presence of ectopic tissue, the association with other anomalies and the presence of associated complications.

Material and methods: This study includes the analysis of referrals for histopathological analysis and histological preparations of Meckel's diverticulum of patients operated on in the period 2013 - 2022. Sixty samples of Meckel's diverticulum were analyzed, with available data from histopathological referrals: frequency in different age groups, clinical manifestations, distribution by gender, length of diverticulum, frequency of ectopic tissue occurrence, frequency and type of complications.

Results: Meckel's diverticulum was found 3.6 times more often in boys. The median age of patients at the time of surgery was 9.5 years (0.00 - 17.5). In 6 patients (10%), the presence of associated anomalies and/or significant diseases was determined. In 23 patients (38.33%), the following clinical symptoms were found: abdominal pain accompanied by nausea, vomiting and constipation. In 10 (16.67%) patients there was melena, or fresh blood was observed in the stool. Heterotopic tissue was observed in 30 patients (50%). Complications of Meckel's diverticulum were observed in 31 patients (51.67%). No statistically significant association was found between the length of Meckel's diverticulum and the presence of heterotopic tissue.

Conclusion: Although Meckel's diverticulum is a rare anomaly, the frequency of complications is relatively high, so adequate monitoring of patients is of great importance.

Keywords:
Meckel's diverticulum, ectopic tissue, complications, retrospective study

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Sažetak

Uvod: Mekelov divertikulum je najčešća kongenitalna malformacija gastrointestinalnog trakta, koja nastaje usled nepotpune obliteracije omfalomezenterijalnog duktusa. Prevalencija Mekelovog divertikuluma u opštoj populaciji iznosi 0,3 - 2,9%, sa češćom pojavom kod muškaraca. Uglavnom je obložen tipičnom ilealnom mukozom, mada mogu postojati i ektopična tkiva. Komplikacije usled postojanja Mekelovog divertikuluma se javljaju u oko 4 - 16%.

Cilj: Cilj ovog rada je utvrđivanje makroskopskih i histoloških karakteristika Mekelovog divertikuluma, učestalosti prisustva ektopičnog tkiva, udruženosti sa drugim anomalijama i prisustva pridruženih komplikacija.

Materijal i metode: Rad obuhvata analizu uputnica za histopatološku analizu i histoloških preparata Mekelovih divertikuluma pacijenata operisanih u periodu 2013 - 2022. Analizirano je 60 uzoraka Mekelovog divertikuluma, sa dostupnim podacima iz histopatoloških uputnica: učestalost u različitim uzrasnim grupama, kliničke manifestacije, distribucija po polu, dužina divertikuluma, učestalost pojave ektopičnog tkiva, učestalost i tip komplikacija.

Rezultati: Mekelov divertikulum je 3,6 puta češće bio nađen kod dečaka. Medijana uzrasta pacijenata u trenutku operacije bila je 9,5 godina (0,00 - 17,5). U 6 bolesnika (10%) utvrđeno je prisustvo pridruženih anomalija i/ili bolesti od značaja. U 23 bolesnika (38,33%) utvrđeni su sledeći klinički simptomi: bolovi u trbuhu praćeni mučninom, povraćanjem i opstipacijom. U 10 (16,67%) bolesnika postojala je melena ili je primećena sveža krv u stolici. Heterotopično tkivo je uočeno u 30 bolesnika (50%). Komplikacije Mekelovog divertikuluma uočene su kod 31 bolesnika (51,67%). Nije ustanovljena statistički značajna povezanost između dužine Mekelovog divertikuluma i prisustva heterotopičnog tkiva.

Zaključak: Iako je Mekelov divertikulum retka anomalija, učestalost komplikacija je relativno visoka, pa je adekvatno praćenje pacijenata od velikog značaja.

Ključne reči:
Mekelov divertikulum, ektopično tkivo, komplikacije, retrospektivna studija

Introduction

Meckel's diverticulum is the most common congenital malformation of the gastrointestinal tract (1). It is caused by the incomplete obliteration of the omphalomesenteric duct (2). It is a true diverticulum since it contains all the layers of the small bowel wall. It is located on the antimesenteric border of the distal ileum (3). Typically, it is about 61 cm from the ileocecal valve in adults, with an average length of approximately 5.08 cm (4).

The prevalence of Meckel's diverticulum in the general population is 0.3 - 2.9%. The distribution among genders is unequal, with a higher occurrence in males (the male-to-female ratio ranges from 1.5 : 1 to 4 : 1). The majority of patients with symptomatic manifestations and resections of this anomaly are male (5). The Meckel's diverticulum is predominantly lined with typical ileal mucosa. However, ectopic tissues can sometimes be found, such as gastric tissue (20%), duodenal tissue, colon tissue, and pancreatic tissue, as well as Brunner's glands, hepatobiliary tissue, and endometrial mucosa, usually located near the apex of the Meckel's diverticulum (6).

Complications from Meckel's diverticulum occur in about 4 - 16% of cases. The most common complications in the adult population include obstruction (14 - 53%), ulcerations (< 4%), diverticulitis, and perforations. Complications are most commonly found in children under the age of 2 (almost 50%), while the remaining symptomatic cases typically occur in children between 2 and 8 years old. The risk of complications decreases with the patient's age (6). Bacterial proliferation within the Meckel's diverticulum may lead to vitamin B12 deficiency, resulting in symptoms similar to pernicious anemia. Additionally, peptic ulceration in the surrounding intestinal lining may sometimes cause unexplained intestinal bleeding or produce symptoms similar to those seen in acute appendicitis (7).

The treatment of Meckel's diverticulum involves various surgical procedures. The surgical approach may vary depending on the morphology and anatomical variations (short diverticulum with a broad base or fibrous band to the umbilicus, long diverticulum with a narrow base, open vitelline duct, or periumbilical sinus) (8). The conventional methods of choice are: simple excision of the diverticulum (satisfactory in most cases) and resection of the ileum (recommended for edematous, inflammatory and perforated diverticulum) (9). Improvements in laparoscopy have made the diagnosis and treatment of this anomaly much easier, resulting in shorter hospital stays, reduced postoperative discomfort, and improved aesthetic results (10). If there is a significant amount of bleeding, a blood transfusion is necessary (11).

The aim of this work is to determine the macroscopic and histological characteristics of Meckel's diverticulum, the frequency of the presence of ectopic tissue, the association with other anomalies and the presence of associated complications (bleeding, swelling, and similar occurrences).

Materials and methods

This retrospective study analyzed histopathological reports and histological specimens of Meckel's diverticula from the archives of the Institute of Pathology at the Faculty of Medicine University of Belgrade. The patients included were operated on at the University Children's Clinic Tiršova between 2013 and 2022. During the ten-year period, 60 Meckel's diverticula were analyzed. This study examined the available clinical data provided in the referrals for histopathological analysis: sex and age at the time of surgery, clinical manifestations, and associated diseases. The frequency of Meckel's diverticulum was analyzed in different age groups (0 - 5, 6 - 10, 11 - 15, 16 - 18 years), along with the distribution by sex, length of the diverticulum, prevalence of ectopic tissue in the diverticulum, and the frequency and type of complications. The age categorization of patients was based on our assessment to facilitate easier interpretation of the results. Data analysis employed descriptive statistical methods. The χ^2 test and Mann-Whitney U test were used to test for differences, with a statistical significance level of $p < 0.05$.

Results

In a ten-year period, 60 cases of Meckel's diverticulum were identified. The study included 47 (78.3%) males and 13 (21.7%) females, suggesting that Meckel's diverticulum was 3.6 times more prevalent in boys. The youngest patient underwent surgery on their first day of life, while the oldest was 17.5 years old. The median age at the time of surgery was 9.5 years (range: 0.00 - 17.5). No statistically significant difference was found in the distribution of patients by age categories ($\chi^2 = 2.000$, DF = 3, $p = 0.5724$) (**table 1**).

Table 1. Number of patients by age group

Age interval (years)	Number of patients	
0 - 5	18	
6 - 10	17	p = 0.5724
11 - 15	14	
16 - 18	11	

In 6 cases (10%), associated anomalies or significant conditions were detected, whereas 54 cases (90%) were without these occurrences. The associated anomalies and/or significant conditions included: (i) Wast syndrome; (ii) duodenal atresia; (iii) autism, epilepsy, cerebral palsy; (iv) jejunal atresia; (v) mediastinal tumor and pneumoperitoneum; (vi) esophageal and duodenal atresia with esophagotracheal fistula.

In 23 patients (38.3%), clinical symptoms were identified, including abdominal pain accompanied by nausea, vomiting, and constipation. In 10 patients (16.7%), melena was present, or fresh blood was observed in the stool.

In 30 cases (50%), heterotopic tissue was detected, whereas in the remaining 30 cases (50%), no heterotopic tissue was observed. Ectopic gastric mucosa was found in a total of 24 Meckel's diverticula, pancreatic heterotopia occurred in 2 cases, and combined gastric and pancreatic heterotopia was present in 4 cases. Ectopic gastric mucosa can usually be detected macroscopically since it is thicker compared to the usual mucosa of the small intestine type (**figure 1**).

Ectopic gastric mucosa of the corpus type was identified in 15 cases. Combined corpus and antral ectopic gastric mucosa was observed in 9 cases. Ectopic gastric mucosa of the corpus type with pancreatic heterotopia was detected in 2 cases. Ectopic gastric mucosa of both corpus and antral types with pancreatic heterotopia was also noted in 2 cases. Purely pancreatic heterotopia was observed in 2 cases (**figure 2**).

The clinically most significant cases are those with ectopic mucosa of the corpus type, as they are frequently linked to peptic ulcers and their complications (bleeding, perforation, peritonitis) (**figure 3**)

Complications of Meckel's diverticulum were observed in 31 cases (51.67%), while the remaining 29 cases (48.33%) were without complications. Peptic ulceration was present in a total of 15 cases. Peptic ulceration as the

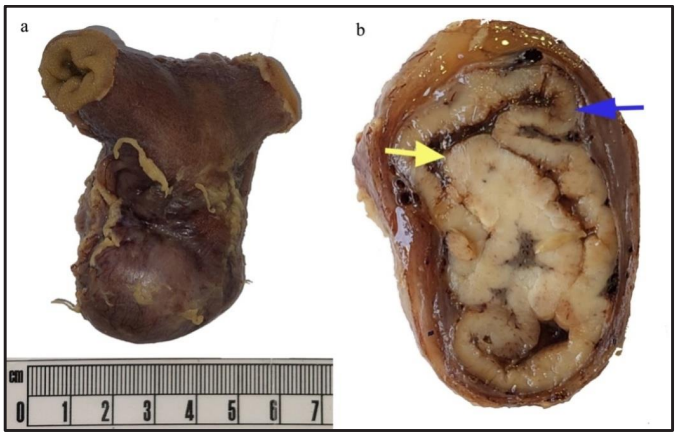

Figure 1. Macroscopic view of Meckel's diverticulum: whole Meckel's diverticulum (a) and transverse section of Meckel's diverticulum - blue arrows indicate small intestine-type mucosa and yellow arrows indicate thickening due to the presence of ectopic corpus-type gastric mucosa (b)

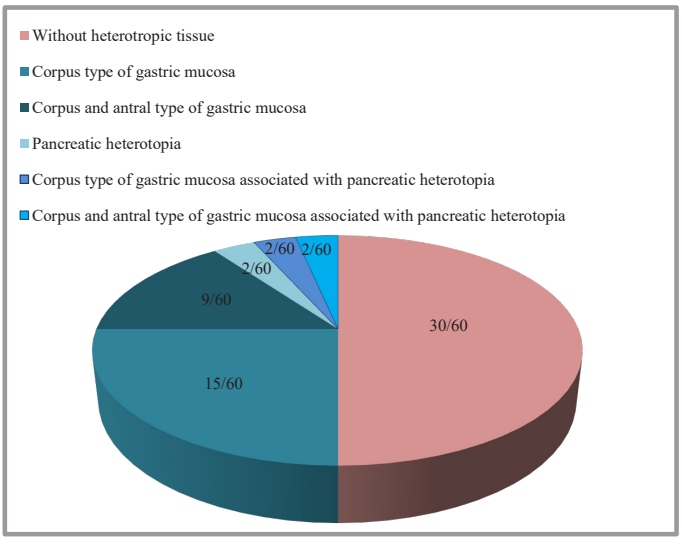

Figure 2. Presentation of the frequency and type of heterotopic tissue

sole complication was identified in 12 cases, while peptic ulceration with diverticulitis occurred in 3 cases, one of which involved perforation with peritonitis. Ischemic lesions of Meckel's diverticulum were noted in 8 cases. Ischemic lesions as the only complication were present in 5 cases, with ischemic lesions and perforation in 1 case, and ischemic lesions associated with diverticulitis and perforation in 2 cases. Diverticulitis as the sole complication was found in 8 cases (**figure 4**).

The length of Meckel's diverticulum varied from 0.3 to 7.5 cm, with a median of 3 cm. A moderately strong statistically significant correlation was observed between the age at the time of surgery and the length of Meckel's diverticulum ($r = 0.3579$, $p < 0.001$). The median length of Meckel's diverticulum in cases without heterotopia was 2.90 cm (range: 0.3 - 5.50). The median length of Meckel's diverticulum with heterotopic tissue was 3.50 cm (range: 1.5 - 7.5). No statistically significant association was found between the length of Meckel's diverticulum and the presence of heterotopic tissue (Mann-Whitney U $z = 0.5241$, $p = 0.6002$).

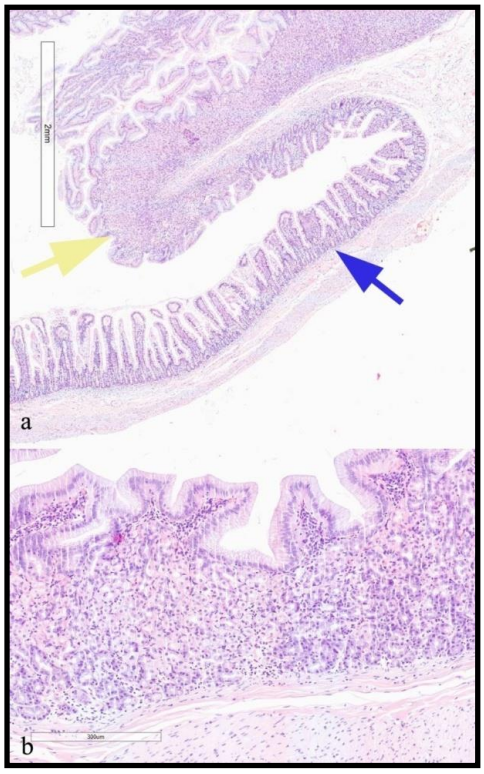

Figure 3. Histopathological preparation of Meckel's diverticulum: typical small intestine-type mucosa (blue arrows) and corpus ectopic gastric mucosa (yellow arrows) (a) and isolated view of corpus-type gastric ectopic mucosa (b)

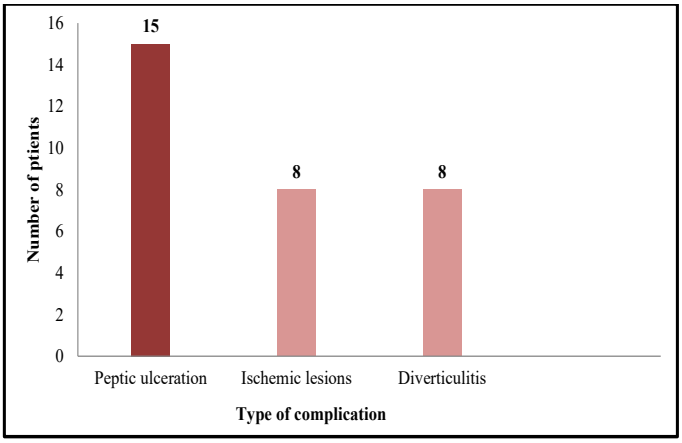

Figure 4. Frequency and type of complications

Discussion

This congenital anomaly is more prevalent in men, occurring up to four times more frequently than in women, according to several large retrospective studies (each involving over 100 patients). Most of the patients who exhibited symptoms related to the presence of Meckel's diverticulum, as well as those who underwent resection, were men. Retrospective studies that included patients of varying ages indicated that the incidence of symptoms due to this anomaly decreases with age, with more than half of the symptomatic patients being under 10 years old (12-14). In this study, there were 47 male patients and 13 female patients, resulting in a gender ratio of approximately 3.61:1, indicating that the majority of those operated on were male (78.3%). The median age of the patients included in this study at the time of surgery was 9.5 years (range: 0.00 - 17.5 years).

Congenital anomalies of the small intestine often manifest with specific symptoms in pediatric patients, though the first signs can also arise in adults. Many of these anomalies are associated with other congenital issues (15). A case presented by Sinzig et al. (16) in 2005 involved a patient with esophageal atresia and a tracheoesophageal fistula, who was surgically treated on the day of birth. The boy also had a bilateral cleft lip and palate, which was surgically addressed at 11 weeks of age. During a surgical intervention at 15 weeks of life, a giant Meckel's diverticulum was detected and resected. Although Meckel's diverticulum is among the most common congenital anomalies of the gastrointestinal tract, a giant variant is rare. As far as the authors are aware, this is the only documented case of a giant Meckel's diverticulum associated with esophageal atresia and tracheoesophageal fistula. The study reports on a patient with Meckel's diverticulum, along with esophageal and duodenal atresia and a tracheoesophageal fistula. The patient underwent surgery on the first day of life, with the Meckel's diverticulum measuring 2.5 cm in length.

A study published in 2022 by Aravind Kumar et al. (17) presented a case of a newborn surgically treated for diagnosed jejunal atresia associated with Meckel's diverticulum and pancreatic heterotopia in the underdeveloped parts of the jejunum. There was no evidence of heterotopic tissue in the Meckel's diverticulum. Our research included one patient with jejunal atresia and Meckel's diverticulum, who underwent surgery on the second day of life. The mucosa of the Meckel's diverticulum displayed typical ileal characteristics, without any detected ectopia.

The study by Aslanabadi et al. (18) reports a case of intestinal malrotation associated with Meckel's diverticulum and duodenal atresia, with an incidence of 3.33%. This retrospective study documents one patient with Meckel's

diverticulum and associated duodenal atresia, without any data indicating the presence of malrotation.

Perforation of Meckel's diverticulum is a rare cause of pneumoperitoneum in neonates. Diagnosis is typically made through laparotomy, and ectopic mucosa is rarely present. In the cited study, ectopic gastric mucosa was found in only 8.5% of cases of pneumoperitoneum due to perforation of Meckel's diverticulum. Pneumoperitoneum primarily occurred during the early neonatal period, which reduces the likelihood of environmental factors playing a role in the etiopathogenesis of pneumoperitoneum, though it does not entirely rule them out (19). Our study documented one case of Meckel's diverticulum with pneumoperitoneum and a mediastinal tumor. The mucosa of the diverticulum was typical of ileal mucosa, with no detected ectopia. The patient was 11 months old at the time of surgery. The diverticulum was discovered incidentally during laparotomy, and the histopathological referral did not provide a clear insight into the etiology of the pneumoperitoneum, whether due to perforation of the diverticulum or an alternative cause.

Meckel's diverticulum is predominantly lined with typical ileal mucosa, similar to that found in the adjacent small intestine. However, ectopic mucosa from the stomach, duodenum, and colon, as well as pancreatic tissue, Brunner's glands, hepatobiliary tissue, and endometrial mucosa, can be detected, typically near the apex of the diverticulum. Of these, ectopic gastric mucosa is the most common, with some studies indicating an occurrence rate of about 20% (6). Yahchouchy et al. (2) reference a study involving 93 patients with symptomatic Meckel's diverticulum, where ectopic gastric mucosa was identified in 62.4% of cases, while Morris et al. (15) reported a prevalence of 50 - 60%. This retrospective study found ectopic gastric mucosa in 24 of 60 cases (40%), with an additional 4 cases featuring associated ectopic gastric mucosa and pancreatic tissue, totaling 28 cases with gastric heterotopia (46.67%). Findings similar to these were reported by Slívová et al. (20), who found gastric heterotopia in 39 out of 88 cases (44.3%).

Ectopic pancreatic tissue is found less frequently in Meckel's diverticulum compared to ectopic gastric mucosa. Research indicates an incidence of pancreatic heterotopia ranging from 0 - 12%, as shown in studies by Hansen et al. (5). In contrast, Yahchouchy et al. (2) reported an incidence of 16.1%. In this study, pancreatic heterotopia was identified in 2 cases (3.33%), along with an additional 4 cases of combined gastric and pancreatic heterotopia, resulting in a total of 6 cases with pancreatic heterotopia (10%).

According to J. F. Meckel, the incidence of complications associated with Meckel's diverticulum was 25%, while later studies report an incidence of 4 - 16% (6). The risk of complications, as noted by Srisajjakul et al. (3), ranges from 4 - 25%. In this study, complications were observed in 31 patients (51.67%).

Diverticulitis occurs as a complication in up to 30% of symptomatic cases, and in more severe instances, an abscess may develop (3). It can clinically mimic acute appendicitis, presenting with abdominal pain and fever (21). Chen et al. (22) reported a total of 56 cases of diverticulitis or perforation of Meckel's diverticulum in a retrospective study of 286 patients (19.58%). In this retrospective study, 8 cases of diverticulitis were recorded as the sole complication. Diverticulitis was associated with peptic ulceration in an additional 2 cases, while one case presented with diverticulitis, peptic ulceration, perforation, and subsequent peritonitis. Ischemic lesions were associated with diverticulitis in 2 cases. This indicates that diverticulitis, either as the only complication or in conjunction with others, was detected in a total of 13 cases (21.67%).

Slívová et al. (20) did not find a connection between the length of Meckel's diverticulum and the occurrence of gastric heterotopia in their research, although the base width of the diverticulum was notably larger in cases with gastric heterotopia. This study recorded a median length of 2.90 cm (0.3 - 5.50) for Meckel's diverticulum without detected heterotopia, while the median length for those with ectopic tissue was 3.50 cm (1.5 - 7.5). There was no statistically significant difference between these two lengths, suggesting that heterotopia was not more common in longer diverticula.

The main limitation of the study was the lack of all necessary data in each of the analyzed histopathological referrals, especially those related to symptoms and signs of complications of Meckel's diverticulum. Nevertheless, this study provides precise and useful data on Meckel's diverticulum, especially those relevant for future clinical research.

Conclusion

In 50% of cases of Meckel's diverticulum there is heterotopic tissue. In about 51% of cases, complications such as peptic ulcers with possible subsequent complications, ischemic lesions and diverticulitis were observed. Although Meckel's diverticulum is a rare anomaly, the frequency of complications is relatively high, so adequate monitoring of patients is of great importance. This study represents the basis for further and more detailed investigations of this character.

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