Meckel’s diverticulum (MD) is the most common malformation of the digestive system, due to the incomplete closure of the omphalomesenteric duct. It is usually asymptomatic and less than 6% of patients develop complications. In adults, the most frequent symptoms are bowel obstruction and inflammation, gastrointestinal bleeding is much more common in the pediatric age group. Although symptomatic MD is an uncommon diagnosis after childhood, when observed, urgent diagnosis and surgical treatment is often required. MD preoperative diagnosis may be challenging.

The study reports two cases of gastrointestinal hemorrhage with diagnostic difficulties in identifying a source of pathology, which turned out to be Meckel’s diverticulum containing bleeding ectopic gastric mucosa (with gastrointestinal stromal tumor within one of them).

Staggering improvement of noninvasive diagnostic methods, including capsule endoscopy (CE), double-balloon endoscopy (DBE), CT-angiography, Tc-99m pertechnetate scintigraphy, allow for a visualisation of the small intestine and detection of active bleeding source. Nevertheless, there are still cases when all those methods are not sufficient for making a proper diagnosis. Nowadays, explorative laparoscopy, as minimally...
invasive, reduced the applications of laparotomy, and is considered as a method of choice in cases with gastrointestinal hemorrhage with undetermined source. Once the underlying pathology has been determined, an exploratory laparoscopy may be also continued as a therapeutic procedure.

Although infrequent, MD should be considered as a possible source of rectal bleeding in adults as well as children. It should be looked for in all cases of an acute abdomen of uncertain etiology. Surgical resection of symptomatic MD shall be the treatment of choice.

**BACKGROUND**

Meckel’s diverticulum (MD) is the most frequently occurring congenital anomaly of the gastrointestinal tract with the incidence ranging from 0.3% to 1.7% and a male-female ratio of 3:2 (1, 2, 3). MD is located on the antimesenteric border of the ileum, about 40-130 cm proximal to the ileocecal valve. It ensues from the failure of the omphalomesenteric duct to obliterate. Ectopic gastric mucosa is the most frequent finding MD microscopy. This condition is usually asymptomatic and less than 6% of patients develop complications, such as gastrointestinal bleeding, obstruction, diverticulitis, or umbilical abnormalities (4). The majority of symptomatic diverticula arise in the pediatric age group. Although symptomatic MD is an uncommon diagnosis in adults, when observed, emergency surgery is often required. The usual presentation is that of small bowel obstruction or inflammation. Gastrointestinal hemorrhage after childhood is even more infrequent. MD preoperative diagnosis may be challenging. When digestive tract bleeding is massive and cannot be properly controlled by conservative methods, making a precise diagnosis as soon as possible is extremally important. Staggering improvement of noninvasive diagnostic methods over the last decades, including capsule endoscopy (CE), double-balloon endoscopy (DBE), CT-angiography, Tc-99m pertechnetate scintigraphy, has revolutionized the diagnostic approach to the small intestine. The new methods allow for a visualisation of the entire alimentary tract and detection of the source of bleeding. Exploratory laparoscopy, with conditional MD surgical resection, remains a gold standard in emergency situations, that need to be resolved immediately.

**AIM**

The aim of this study is to evaluate the role of diagnostic laparoscopy for detection and treatment of bleeding Meckel’s diverticulum, basing on two cases of MD containing ectopic gastric mucosa with difficulties in identifying the source of recurrent gastrointestinal hemorrhage.

**CASE PRESENTATION 1**

In 1988, a 29-year-old male was admitted to emergency department with a history of weakness and abdominal pain, accompanied by multiple bloody diarrhea. His past medical history revealed similar episodes of upper abdominal pain for 3 years. There was no history of medication or drug abuse. Radiological examination of the stomach and duodenum did not show any pathologies. On admission, the patient’s blood pressure was 130/80 mm Hg, pulse 80 beats per minute, haemoglobin concentration was 5.5 g/dl and hematocrit was 28%. On physical examination, he had a soft, flat abdomen with midline rebound tenderness. Digital rectal examination revealed black stool masses. Gasctroscopy was performed and revealed no abnormalities in upper gastrointestinal tract.

On the second day, patient manifested fever and persistent, severe pain in the right lower abdomen, with guarding and rigidity of abdominal muscles and positive Blumberg sign. Leukocyte count rose from 6.1 L 10^3/mm^3 to 9.4 L 10^3/mm^3. The patient was scheduled for urgent laparotomy. Appendicitis with a small perforation and local peritonitis was found at surgery. Patient underwent appendectomy, then MD was found approximately 50 cm from the ileocecal valve and resected. The patient made uncomplicated recovery. Postoperative gastroscopy revealed no abnormality in the upper gastrointestinal tract. Histopatological examination confirmed 3.5 cm-long MD with ulceration in heterotopic gastric mucosa and pancreatic tissue nearby.

**CASE PRESENTATION 2**

In 2014, a 22-year-old male presented to the surgical department with complaints of recurrent abdominal pain and melena. He denied taking any medications. He had not travelled outside of the country recently or eaten unusual or spoiled food. The review of systems was negative. On physical examination, the vital signs were within normal limits. His abdomen was soft, with mild tenderness in the right ilias fossa and nondistended. Normactive bowel sounds were heard. Rectal examination revealed melena with traces of fresh blood. The admission hemoglobin concentration was 10.0 g/dL with a decrease from 14.0 g/dl from the previous day.

The patient’s past medical history revealed several similar episodes of gastrointestinal bleeding over last 5 years in his native country of Portugal. At the age of 17, he underwent colonoscopy and no abnormality was identified. Afterwards, a 99m-Tc pertechnetate
gamma camera imaging of the abdomen and pelvis revealed a focus of atypical tracer deposition in the right hypogastric region concomitant with the appearance of gastric activity in left hypochondrium. Based on this, MD with ectopic gastric mucosa was suspected. Capsular endoscopy was performed to confirm the diagnosis, but it failed to identify the source of bleeding. During that time the patient had been repeatedly reporting to Emergency Room with complaints of abdominal pain. Further investigation with the use of ultrasonography and double balloon endoscopy did not revealed any pathologies.

Symptoms of digestive tract bleeding recurred in 2013. There were still no abnormalities observed on ultrasonography of the abdomen. Upper gastrointestinal tract endoscopy, reaching the second portion of the duodenum, was negative. Even angiotomography was performed but it was also unsuccessful in identifying any active bleeding. The patient continued to have bloody diarrhea necessitating blood transfusions. Hemoglobin concentration decreased to 7.0 g/dl currently and he had received 4 units of red blood cells concentrate and 2 units of fresh frozen plasma. The real diagnostic dilemma began.

After admission to the ward, another angiotomography scan and gastroscopy were performed, which still revealed no pathology. On the second hospital day, patient was taken to the operating room for an exploratory laparoscopy. Intraoperatively, a 3.5 cm-long, 2.5 cm-wide Meckel’s diverticulum was found, located about 60 cm from the ileocecal valve. It was resected with mechanical staplers (fig.1, fig.2). There was blood both proximal and distal to the lesion. The rest of the bowel was explored and did not reveal any signs of inflammation or bleeding. Histopathological examination of the specimen confirmed the presence of MD with bleeding gastric mucosa and totally excised gastrointestinal stromal tumor (GIST) within (fig.3). It was 4 cm in diameter, CD 117 – positive, mitotically inactive (zero per high-power field), with Ki67 index reaching 3% indicating a low relapse risk after resection according to AFIP-NCCN criteria (tab.1)(5). Accordingly, no further oncological systemic therapy with tyrosine kinase inhibitor (imatinib) was offered. Patient was discharged after 3 days with no recurrent episodes of bleeding and no other complications postoperatively.

**DISCUSSION**

The incidence of Meckel’s diverticulum is reported at about 2% among gastrointestinal anomalies of the general population (male more frequent than female, predominantly in the age range between 11-87 months) (3, 6). Just under half of MD are symptomatic in adults. The most frequent symptoms are bowel obstruction (22-50%) and inflammation (20%), bleeding is much more common in the pediatric age group. Digestive tract hemorrhage is reported to occur in 11.8% of all MD, but accounts for 25% of symptomatic cases (7). The majority of patients will develop bleeding symptoms before the age of 20. Past medical history often reveals recurrent gastrointestinal hemorrhage in up to 40% of them.

As per literature, less than 5% of gastrointestinal bleeding originates from small intestine (3). Dumpre et al. reviewed 1489 patients with lower intestinal hemorrhage from 1989 to 1993 and identified 10 cases of bleeding originating from the small bowel (0.7%). Only 4 of them (0.26%) were caused by MD (9). Due to the rarity of cases in adults, the diagnosis of MD may be extremely difficult to arrive at preoperatively. This is particularly true in patients presenting with symptoms other than bleeding. Kusumoto et al. reported a study of 776 patients with MD in which 88% presenting as bleeding had a correct preoperative diagnosis versus 11% with symptoms other than bleeding (10).

MD is an embryonic defect due to the incomplete closure of the omphalomesenteric duct. Since cells lining the yolk stalk are pluripotent, heterotopic mucosa may be present in MD and is responsible for occurrence of complications like hemorrhage, chronic peptic ulceration and perforation. The incidence of heterotopic mucosa reaches 60% of MD cases. The most commonly found is gastric mucosa (61%), pancreatic mucosa (6%), both gastric and pancreatic (5%), jejunal (2%), Brunner’s glands (2%), gastric and duodenal (2%) (11, 12). Bleeding is associated with ectopic gastric mucosa in 96% of cases. In those rare cases of MD diagnosed in adulthood, bleeding is uncommon and often due to perforation of MD itself (13). Main mechanism of bleeding is the acid secretion from ectopic mucosa, leading to ulceration of adjacent ileal mucosa. The pathogenic role of Helicobacter pylori in the development of gastritis and bleeding in the ectopic tissue is still debatable. Also NSAIDs’ effect on it is yet to be proved (3). Heterotopia makes 99m technetium-pertechnetate taken-up by ectopic gastric mucus secreting cells the most commonly performed functional imaging for localization of MD. Although this scan is 85-90% sensitive in diagnosing symptomatic MD in pediatric population, the diagnosis is not readily established in adults (sensitivity up to 60%), as ectopic gastric mucosa is found much less frequently in the diverticulum in this age group (11, 12).

The incidence of heterotopic cells is a predictive factor for the occurrence of neoplastic changes originating from the gastric tissue (14). The tumors within the MD are observed infrequently and are known to occur only in 0.5–3.2% of cases (15, 16). Most of them are benign tumours like leiomyomas, angiomas and lipomas. Malignant neoplasms include adenocarcinoma, sarcoma, carcinoid tumour and gastrointestinal stromal tumor (GIST). GISTs are rare neoplasms which account for 0.1–1% of gastrointestinal malignancies. The majority of GISTs (60% to
70%) have been reported to arise in the stomach, whereas 20% to 30% originate in the small intestine, and less than 10% in the esophagus, colon and rectum. They also occur in the extra-intestinal abdominopelvic sites such as the omentum, mesentery, or retroperitoneum. GISTs arising from Meckel’s diverticulum are extremely rare. However, 12% of all neoplasms arising within MD turn out to be GIST (14). The most common presentation of a neoplasm of MD is intussusception followed by melaena (17, 6). With regard to GIST molecular markers, detection of Ki-67 and CD117 is routinely performed. The Ki-67 protein exists in actively proliferating cells. Ki-67 index reflects the proportion of cycling cells in a given population. Certain studies have reported that Ki-67-positive expression is closely associated with aggressive biological behaviour of tumor cells. Whereas, CD117 has been found to be located at the tumor cell membrane and cytoplasm and the positive rate recorded was up to 95% in GISTs. CD117-negative expression is believed to be associated with an early postoperative GIST recurrence (19). Other neoplasms arising from the gastrointestinal tract, including lipoma, leiomyoma, leiomyosarcoma are typically CD117 – negative.

Nowadays, progress in diagnostic methods, including DBE and CE, provides the opportunity for improved small intestine visualisation and identification of a source of active bleeding. Nevertheless, there are still cases where those methods are not sufficient for obtaining a diagnosis. Because of the distance between the diverticulum and the ileocecal valve (ranging from an average distance of 34 cm in children (<2 years) to 67 cm in adults), a typical colonoscope cannot usually reach the part of small intestine in which MD is located. It is usually impossible to diagnose bleeding from MD during colonoscopy, except in cases with bleeding seen distally to the ileocecal valve. Capsular endoscopy may be indicated for patients with gastrointestinal blood loss when other diagnostic methods such as upper and lower endoscopy have failed to localize the source of bleeding (18). There were only few cases of detecting MD after capsular endoscopy in adults reported in the literature. The method is especially dedicated to the pediatric age group. CE and DBE can play complementary roles in preoperative diagnosis of bleeding MD. Detection rates of abnormalities in small intestine range from 65% for CE to 53% for DBE (20). As the source of bleeding can not be indentified by endoscopy, angiography with 99mTc-labelled red blood cells can be performed. Traditional CT scans are usually unhelpful in diagnosing MD because of difficulty in distinguishing it from intestinal loops. Angiography can show the bleeding site but it can be negative in patients with intermittent bleeding. Animal studies have demonstrated that a bleeding rate of 0.5 mL/min is necessary in order for angiography to be positive (21).

As in the reported cases, an explorative laparotomy has been preferred for patients with symptoms either of an acute abdomen of uncertain etiology or a digestive tract bleeding of long duration. Despite the passing of time, surgery is still the procedure of choice when the diagnosis is not available via clinical diagnostic methods or when doubts remain. With the increasing availability of sophisticated imaging modalities and other investigative techniques, the indications for and scope of exploratory laparotomy have shrunk over time. The increased availability of laparoscopy as a minimally invasive means of inspecting the abdomen has further reduced the applications of exploratory laparotomy. Once the underlying pathology has been determined, an exploratory laparoscopy also may be continued as a therapeutic procedure. It is worth noting that surgical resection is the only way to unambiguously confirm the diagnosis via histopathological examination.

CONCLUSIONS

Meckel’s diverticulum requires a high level suspicion. Although rare, MD should nevertheless be considered as a possible source of bleeding in adults as well as children. Hemorrhage is generally associated with the presence of ectopic gastric mucosa. The character of heterotopic cells also is a predictive factor for the occurrence of neoplastic changes. MD should be looked for at laparotomy in cases of acute abdomen. Even the use of several up-to-date diagnostic methods does not provide certainty of correct diagnosis in some cases. Then, exploratory laparoscopy with surgical resection remains the method of choice for not only recognition but also treatment at the same time, as minimally invasive, quicker and more efficient in comparison to laparotomy.

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MEDtube Science Vol.II (3); 8-12.

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Fig. 3

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TAB. 1  AN APPRAISAL OF RELAPSE RISK AFTER SURGICAL RESECTION OF PRIMARY GIST. AFIP-NCCN CRITERIA

<table>
<thead>
<tr>
<th>mitotic activity</th>
<th>size</th>
<th>stomach</th>
<th>duodenum</th>
<th>jejunum or ileum</th>
<th>rectum</th>
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<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<td>low</td>
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<td>high</td>
<td>mediate</td>
<td>high</td>
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<tr>
<td></td>
<td>&gt;10 cm</td>
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HPF - high power field (× 400)

BIBLIOGRAPHY