



Demystifying Meckel's diverticulum – a guide for the gastroenterologist

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Purpose of review

Meckel's diverticulum (MD) is a common congenital ileal diverticulum. Whilst mostly asymptomatic, 4–9% develop complications, such as small bowel obstruction, diverticulitis or bleeding. In 1933, Charles Mayo wrote that MD is 'frequently suspected, often looked for and seldom found', and it continues to pose a diagnostic challenge today. With advancements in small bowel imaging and endoscopy, this review outlines the gastroenterologist's approach to MD.

Recent findings

There are a number of strategies for diagnosing MD. Meckel's scan has a sensitivity of 80–92% in children but 62–88% in adults. The diagnostic yield of small bowel capsule endoscopy (SBCE) is only up to 50%. Device-assisted enteroscopy (DAE) has a sensitivity of 84–100% for MD but is invasive. The definitive treatment for symptomatic MD is surgical resection, but the management of asymptomatic cases are controversial. A recent systematic review favoured resection of incidental MD.

Summary

A high index of suspicion and a multimodality combination of SBCE, Meckel's scan, CT and DAE is often required to diagnose MD. Complicated MD is treated by surgical resection. Management of incidental MD remains debated, although current evidence appears to favour resection.

Keywords

capsule endoscopy, device-assisted enteroscopy, Meckel's diverticulum, neuroendocrine tumour, small bowel

INTRODUCTION

Meckel's diverticulum (MD) is a common diverticulum of the ileum with a reported prevalence of between 0.3% and 4% [1–3,4^a,5]. It is caused by a persistent remnant of the congenital omphalomesenteric (vitelline) duct and was first described by the German anatomist, Johann Friedrich Meckel in 1809 [6]. MD is a true diverticulum, involving all layers of the small bowel wall. It is commonly described in surgical textbooks by the 'rule of twos': it occurs in 2% of the population (often around the age of two), affects males twice as commonly as females, lies two feet (61 cm) from the ileo-caecal valve and is two inches (3 cm) long [7]. MD is often asymptomatic and found incidentally. Complications of MD occur in 4 to 9% over a lifetime and include overt bleeding, anaemia and intussusception [1–3,4^a,5]. Whilst the majority are lined by ileal mucosa, heterotrophic mucosa can exist with the most common ectopic tissue being gastric, followed by pancreatic. Rarely, ectopic duodenal, colonic, hepatobiliary and endometrial mucosa have been

described [1]. The presence of ectopic gastric mucosa can be associated with bleeding complications such as anaemia and gastrointestinal (GI) haemorrhage.

PRESENTATION

Symptomatic MD can present at any age but is most commonly seen in children; more than 50% of patients present under the age of 10 [1]. The mean time from presentation to diagnosis is 19.4 months (range 7.4–42.9 months) [8,9,10^a]. Most paediatric patients present with obstruction or GI haemorrhage.

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KEY POINTS

- Meckel's Diverticula are often diagnosed asymptotically and incidentally, however complicated Meckel's diverticulitis can present symptomatic with obstruction, acute or chronic gastrointestinal bleeding, abdominal pain due to inflammation or perforation, and synchronous ileal neoplasia.
- Device-assisted enteroscopy is a highly sensitive but invasive diagnostic modality. A combination of small bowel capsule endoscopy with Meckel's scan could improve the diagnosis of Meckel's diverticulum (MD), particularly in children.
- H2 receptor antagonist and proton pump inhibitors may play a peripheral role in the diagnosis and management of bleeding Meckel's diverticula.
- Complicated MD is treated by surgical resection and resection of incidental MD remains debated, although current evidence appears to favour resection.

MD is the most common cause of GI haemorrhage in children [1,2]. In a large retrospective study of 1476 patients by Park *et al.* the authors concluded that overall 84% of patients are asymptomatic and Meckel's diverticulum are discovered incidentally [11]. 50% of paediatric patients presented with obstruction; however, the authors defined a paediatric patient as younger than 11 years, so allowing for this, bleeding was more common. In another large study, including 815 paediatric patients, the most common presentation was obstruction [12]. Two systematic reviews found that overall obstruction was the most common presentation in children, in up to 50% [1,2].

Obstruction is usually caused by volvulus against the redundant diverticular mucosa or intussusception into the small intestine lumen [1,2]. Acid secretion from ectopic gastric mucosa can lead to Meckel's diverticulitis and inflammation of adjacent small bowel mucosa. MD and the adjacent ileum can become ulcerated causing GI haemorrhage and, in some cases, Meckel's diverticulitis can lead to perforation and peritonitis [1,2]. Up to 19% of children and 29% of adults with symptomatic MD present with inflammation. Of those symptomatic, 7 out of the 17 (41%) paediatric patients with Meckel's diverticulitis developed perforation, compared to 18 out of the 50 (36%) adult patients [11].

Otherwise, adult patients present similarly to children, but more commonly with GI haemorrhage, often before the age of 40 [1–3,1]. Presentation ranges from overt signs of GI bleeding (haemorrhagic shock, rectal bleeding and melaena)

to iron deficiency anaemia [1,2,11]. The greater occurrence of GI bleeding during adulthood is hypothesized to be due to the growing length of the MD. Growth occurs quickly within the first 3 years of life then more slowly thereafter, displacing the heterotopic gastric mucosa distally towards the base of the diverticulum, where ulceration and bleeding occur more commonly [13].

Neoplasia is occasionally seen within MD, with a reported incidence of 0.5 to 3.2% [14,15]. However, data is limited mainly to case series and case reports. Where malignancy is found, it is most commonly a neuroendocrine tumour (NET) (Fig. 1). Other pathologic types include leiomyosarcoma, gastrointestinal stromal tumour, adenocarcinoma and lymphoma. Rare subtypes such as pancreatic carcinoma have also been reported [14–16]. The median age of presentation is 58 years [14]. Most cases are found incidentally during surgery or diagnosed pathologically after removal of a symptomatic MD [14,16]. Clinical presentation of these synchronous pathologies can vary depending on the tumour subtype; for example, a NET may in itself present with intermittent abdominal pain, gastrointestinal bleeding, obstruction, or rarely, symptoms of carcinoid syndrome [15,16]. A 2011 study by Thirunavukarasu *et al.* compared malignancy in MD ($n=163$) to other ileal malignancies ($n=6214$). Despite the low incidence of MD, the risk of malignant transformation is high (1.44 per 10 million inhabitants), which is 70 times higher than other ileal malignancies unrelated to Meckel's diverticula. Risk of malignancy within MD increases with age [16]. The mechanism of neoplasia in MD is not fully understood. It has been suggested

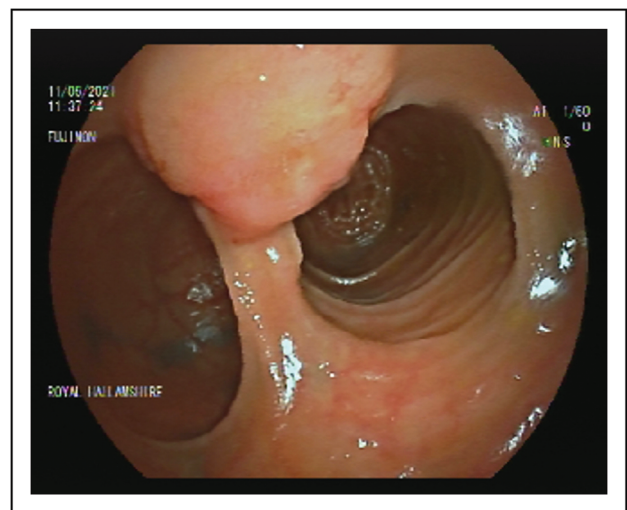


FIGURE 1. Retrograde double-balloon enteroscopy showing a submucosal mass adjacent to a Meckel's diverticulum, found to be a grade 1 neuroendocrine tumour post operatively.

that adenocarcinoma could be related to ectopic tissue within the diverticulum, which may have increased malignant potential compared to normal bowel mucosa. Another postulated mechanism is *Helicobacter pylori* infection, which has been implicated in the pathogenesis of gastric adenocarcinoma and mucosa-associated lymphoid tissue (MALT) lymphoma [15].

DIAGNOSIS

Identification of MD is challenging. Complicated Meckel's has a wide variety of presentations, with symptoms overlapping with other acute abdominal pathology. For instance, Meckel's diverticulitis can often present similarly to acute appendicitis. A multimodality combination of imaging and endoscopic modalities aids diagnosis and ultimately a decision towards surgery.

IMAGING

Imaging has a low diagnostic yield for MD, especially in asymptomatic cases. MD can be seen on small bowel ultrasound and computed tomography (CT) scanning as a cyst or blind pouch or 'cul-de-sac' termination diverging from the ileum, although ultrasound is rarely utilised for this purpose in clinical practice [17]. Small bowel fluoroscopy may detect MD as a blind-ending diverticulum or identify a triradiate fold pattern, which most likely represents the exit of the omphalomesenteric duct [17]. As these signs are difficult to detect and require local expertise, fluoroscopy is seldom used. Complications such as obstruction or diverticulitis may be

found on ultrasound or CT, but their sensitivity for Meckel's is low [1,17].

CT angiography may identify Meckel's at the time of GI haemorrhage; the sign of the vitelline artery branching off the superior mesenteric artery is pathognomonic but not commonly seen [18–21]. Other findings, such as contrast extravasation in the right lower quadrant or haematoma formation in adjacent small bowel mucosa (Fig. 2b), may be seen. Whilst the most common location for the MD is proximal to the ileocaecal valve, it can also be identified in the midline or left lower quadrant (Fig. 2). In the context of acute GI bleeding, an interventional radiologist may proceed to digital subtraction angiography with a view to embolization if a bleeding point is identified on CT angiography. A retrospective study of 165 cases over 10 years examining the use of CT in diverticulum versus nondiverticulum causes of small bowel bleeding demonstrated that Meckel's diverticula were more common (23%, $n=32$) than duodenal (4.4%, $n=6$), jejunal (4.4%, $n=6$) and other ileal (8.0%, $n=11$) diverticulum [22^{***}]. Contrast extravasation as a feature of active bleeding was more commonly found in patients with diverticular bleeding (91.5% vs. 18.6%, $P=0.001$). Unsurprisingly, review of the CT images by senior radiologists identified a higher rate of active bleeding (48.3% vs. 34.5%, $P=0.02$) and a greater detection rate of potential bleeding lesions (94% vs. 66.2%, $P<0.001$) overall, which supports the use of a multidisciplinary team approach to identify MD bleeding. Cases of Meckel's in this study were more commonly distinguished by a tubular appearance compared to other diverticula (78.1% vs. 11.5%, $P<0.001$) [22^{***}].



FIGURE 2. Abdominal CT scan demonstrating (a) arterial phase and (b) venous phase axial slices of a Meckel's diverticulum (astericks). A blush of contrast suggesting active bleeding (single arrow) is seen in the arterial phase and haematoma formation in the adjacent small bowel (double arrow) is seen in arterial then venous phase; (c) coronal reformat of Meckel's diverticulum in the left lower quadrant.

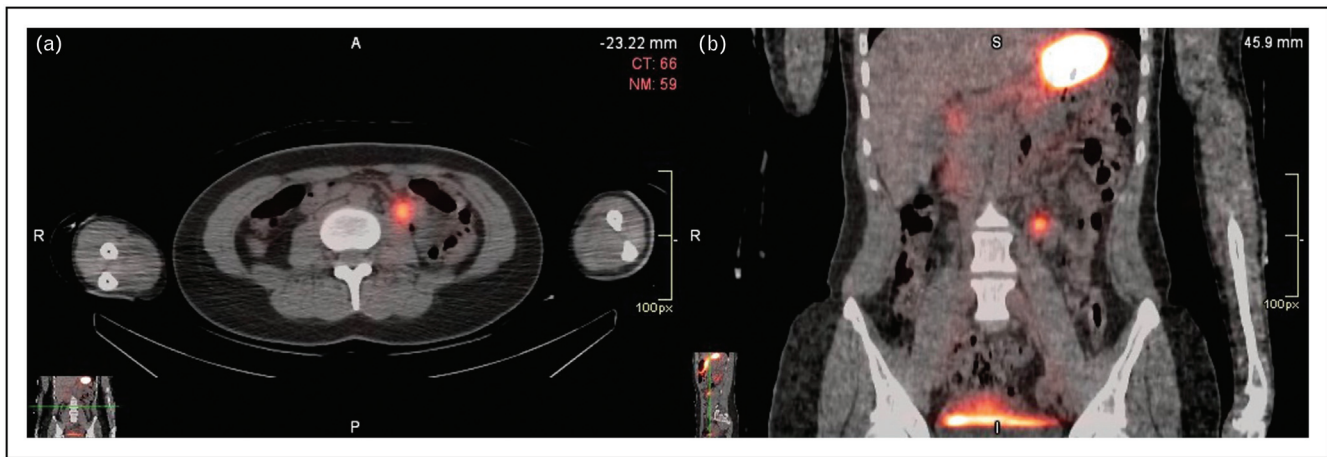


FIGURE 3. Tc-99m scintigraphy: Fused (a) axial image showing uptake in left lower quadrant, and (b) coronal image showing uptake in stomach and left lower quadrant. Uptake corresponds to the bleeding point seen on CT.

Technetium-99m pertechnetate (Tc-99m) scintigraphy ('Meckel's scan') is often utilized when MD is suspected by other means to demonstrate the presence of heterotopic gastric mucosa. Tc-99m pertechnetate accumulates in mucin-secreting cells of the stomach and ectopic gastric mucosa within MD (Fig. 3). Overall, ectopic gastric mucosa has been described in 35% of patients (between 4.6 and 71%) with symptomatic MD [1,16]. The Meckel's scan is moderately sensitive in children; a recent systematic review and meta-analysis of 1115 paediatric patients from sixteen studies found that sensitivity was 80% and specificity was 95% [23[¶]]; sensitivity has previously been reported to be as high as 92% [24]. There are few large studies of Meckel's scan in adults, but sensitivity appears to be much lower (21.4–62%) [25,26], as fewer cases contain ectopic gastric tissue [1,16,27]. A systematic review of 40 studies suggested that the sensitivity of the Meckel's scan is higher in patients using H2RA as premedication (92% vs. 84% without), children (92% vs. 82% in adults), and in those with gastrointestinal bleeding presentations (95% vs. 75% without) [24]. On the other hand in cases of active bleeding it is believed that extravasation of the tracer may lead to an unreliable examination [1]. It is suggested that H2 receptor antagonists may delay the release of Tc-99m from mucosa and parietal cells, and so reduce the dilutional effect of severe bleeding [28]. H2 receptor antagonists are not considered necessary for a high-quality scan, and are therefore not routinely used. However, in patients with a negative Meckel's scan but significant recent GI bleeding and a high clinical index of suspicion, a repeated study using H2 receptor antagonist premedication may be helpful [29].

ENDOSCOPY

Small bowel capsule endoscopy (SBCE) has become a gold standard investigation in the evaluation of small bowel bleeding, after negative bi-directional endoscopy [30,31]. The diagnostic yield of MD in SBCE however only ranges from between 7.7% and 50% in adults [9,32,33]. Typical SBCE findings of MD are the double-lumen sign with a visible entrance into the MD (Fig. 4a), a thickened bridge between the MD and ileal lumen, and mucosal webs and bulges within the diverticulum (Fig. 4d) [9,31,32]. Occasionally tufts of ectopic tissue can be distinguished from the background diverticular mucosa (Fig. 4c). Whilst the double-lumen sign is a pathognomonic finding in MD, it should be interpreted with caution. This sign can also be seen transiently when viewing both directions of a normal small bowel loop when the capsule is located at a bend, and in cases of external small bowel adhesions or intussusception where pseudosacculation occurs. A recent European multicentre study of 69 patients with MD described that a combination of findings is likely to be more supportive of a diagnosis of MD, with 69.6% of patients having two or more findings [34^{¶¶}]. Here, the majority of patients had SBCE performed for overt GI bleeding or iron deficiency anaemia. In combination with typical findings above, 52.2% had ulceration. Ulceration appeared to be limited to within the MD or the adjacent small bowel segment, mostly surrounding the opening of the diverticulum (Fig. 4b) [33].

There are a few studies on the application of SBCE in children with MD. A recent small study of 11 paediatric patients highlights the challenges in diagnosing Meckel's; of the 9 patients who underwent SBCE, 5 had a normal examination [10[¶]]. A patient with jejunal ulceration was initially



FIGURE 4. Features of Meckel's diverticulum on small bowel capsule endoscopy: (a) the double lumen sign (white asterisks), (b) ulceration of mouth of diverticulum, (c) ectopic gastric mucosa (white arrows) seen within the diverticulum with a background pseudocolonic appearance and (d) mucosal webs and patch of ectopic gastric mucosa.

diagnosed with Crohn's disease, and another patient with a polypoid lesion on SBCE had a differential diagnosis of Peutz-Jeghers syndrome or malignancy. Interestingly, of the 9 patients who had a Meckel's scan, the test was negative in 6, which is much lower than the reported sensitivity of 82–90% in children; however, the study specifically selected a 'challenging' subset of patients with atypical presentations, which may explain this discrepancy [10[¶]]. A larger retrospective study by Li *et al.* evaluated fifty-eight children with confirmed MD [35[¶]]. All children presented with overt GI bleeding. 51.7% had double-lumen sign and 20.7% had other typical

MD signs on SBCE. Of the twenty-four patients who also had Meckel's scan, the diagnostic coincidence rate was 91.7%. In eight cases, Meckel's scan was negative but SBCE was positive [35[¶]]. Whilst further research is needed, a combination of SBCE with Meckel's scan could improve the diagnostic rate of MD in paediatric patients, especially since MD in children is more likely to have ectopic gastric tissue [1].

Several factors make diagnosis of MD via SBCE endoscopy challenging. In uncomplicated MD, the typical double-lumen sign can be overlooked by fast transit and suboptimal luminal cleanliness.

Complicated MD with significant diverticulitis might be identified on SBCE as ulcerated villous oedema with or without a bulge masquerading as a wide differential diagnosis of neoplastic or inflammatory conditions. The location and appearance of ulceration can help to differentiate MD from other conditions; ulcers associated with MD are predominantly located in or adjacent to the diverticulum and are usually longitudinal or circumferential rather than aphthous [34[■]]. The mean small bowel transit time for the first indicative image of MD is usually beyond 50% of transit [34[■]].

Device-assisted enteroscopy (DAE) has high sensitivity and specificity for MD [8,26,36]. In one retrospective study of 74 patients, DAE showed a diagnostic yield of 84.6% [26]; in another study, MD was found in 100% ($n=54$) of patients who completed DAE, all of whom had prior negative CT, Meckel's scan or SBCE [37[■]]. A recent retrospective case-series of 66 adults with MD diagnosed on DAE found that patients with MD undergoing DAE for suspected small bowel bleeding (SSBB) were significantly more likely to have MD-associated ulceration [38[■]]. The ulcers were seen within the diverticulum in 23/35 cases. Strictures within the diverticula were seen in 11 cases of which ulceration was associated with the intradiverticular stricture in 10 cases. In contrast, 1 of 15 cases of MD seen in those without SSBB had erosive lesions on the orifice edge [38[■]]. However, whilst highly sensitive, DAE is invasive and therefore should be used as second line investigation. In unclear cases of SSBB, an antegrade approach is preferred, as the majority of bleeding lesions such as angioectasia are found proximally. If there is a strong suspicion of GI bleeding due to MD, a retrograde approach could be utilised [34[■]].

MANAGEMENT

The definitive treatment for symptomatic Meckel's diverticulitis is surgical resection. At surgery, Meckel's diverticula typically arise from the anti-mesenteric border of the middle to distal ileum. However, as has been the mysterious journey of diagnosing MD thus far, rare cases of mesenteric MD have been described at surgery, with differential diagnoses being the less common intestinal duplication cysts. These may also contain ectopic gastric mucosa or communicate with the intestinal lumen [39].

MD resection can be performed laparoscopically or open, with the laparoscopic approach being more common. Options include diverticulectomy, wedge ileal resection, or segmental ileal resection. The procedure chosen depends on the integrity of the

diverticulum base, and the presence and location of ectopic tissue within the MD [1,13[■]].

Whilst surgery is the definitive treatment for complicated MD, several case reports suggest that proton pump inhibitors (PPIs) and H2 receptor antagonists are associated with temporary symptom resolution in bleeding MD, delaying the need for urgent surgery. On the other hand there is no evidence for the use of antibiotics, although it may be sensible in the setting of incipient perforation. Secretion from ectopic gastric tissue within MD can erode adjacent intestinal mucosa, closely resembling peptic ulceration, and medications aimed at acid suppression, such as PPIs and H2 receptor antagonists, are theorized to act on this mechanism [40]. One case report describes a 72-year old patient who declined surgery and was maintained on oral PPI for seven months, remaining asymptomatic [41] and another reports that bleeding Meckel's diverticulitis responds to intravenous pantoprazole [42]. However, acid suppression should only be used as bridge to definitive surgical management.

MD is asymptomatic in the majority of cases. Resecting MD found incidentally at surgery is controversial. Postoperative morbidity following prophylactic resection is reported as 1–5.7% [4[■],5,7], compared with a 4–9% risk of complicated MD [1,5]. Many historical studies concluded that the risk of complications from resection outweighed the risk of developing complicated MD, but these referred to a hypothetical scenario of operating solely for the purpose of removing an incidental, asymptomatic MD, which is not advocated [4[■]]. A recent systematic review examining the risk of resecting incidental MD found at surgery concluded that the risk of morbidity (defined as short- and long-term postoperative complications) was 5.7% after reviewing 2934 cases. Of the 571 cases where mortality data was available, there were five cases of fatalities. Four were described as unrelated to MD resection; one patient's death was attributed to the MD resection, although the exact cause of mortality is not stated. The authors therefore concluded that the evidence to date would appear to favour resection due to increased safety of surgery and anaesthesia, a better understanding of the risk of complications, and the risk of cancer, albeit small [4[■]]. Additionally, there is no significant advantage to leaving an incidental MD in situ. However, given the lack of a controlled study due to the sporadic incidence and under-reporting of asymptomatic MD, the decision should still be individualized to the patient. Factors felt to increase the likelihood of developing complications are male sex, age under 50 years, diverticulum length over 2 cm, and the presence of ectopic tissue [1,4[■],13[■]].

CONCLUSION

MD is a congenital ileal diverticulum. It is mainly asymptomatic. Symptomatic patients present with obstruction, acute or chronic GI bleeding, or abdominal pain due to inflammation. Whilst previously considered a disease of childhood, MD can present at any age. Preoperative diagnosis is challenging, and high index of clinical suspicion is needed to yield a diagnosis. MD can be detected by using complementary imaging modalities, such as CT and Meckel's scan, and endoscopic modalities, such as SBCE and DAE. Where obstruction or inflammation is suspected, CT should be used first line. SBCE would be more appropriate in cases of SSBB, although CT angiography is more readily available and appropriate in patients with significant haemorrhage. Meckel's scan should be considered in tandem with a suspicious SBCE, depending on clinical presentation and local availability. DAE has a high sensitivity and specificity for MD but as it is invasive, it should be utilized as a second line investigation of SSBB. There is often a significant delay from presentation to diagnosis, and two or more modalities are needed to diagnose MD in many cases. Complicated MD is treated by surgical resection. Management of incidental MD remains debated, and although evidence appears to favour resection, management decisions should be individualized to the patient.

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Conflicts of interest

There are no conflicts of interest.

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