A rare case of extensive ileo-caecal intussusception due to small bowel adenocarcinoma with neuroendocrine differentiation

Authors: Dr S Malekout, Dr G Reiff, Dr K Hulley, Dr M Alhilani, Dr M Persad, Dr R Amin, Mr A Gueroult, Dr S Khaleeq, Dr S Lee, Dr N Patel, Dr A Dawood, Mr D Tsironis, Dr A Wale

St George's University Hospital NHS Foundation Trust

IMAGING RESEARCH GROUP
ST GEORGE'S HOSPITAL

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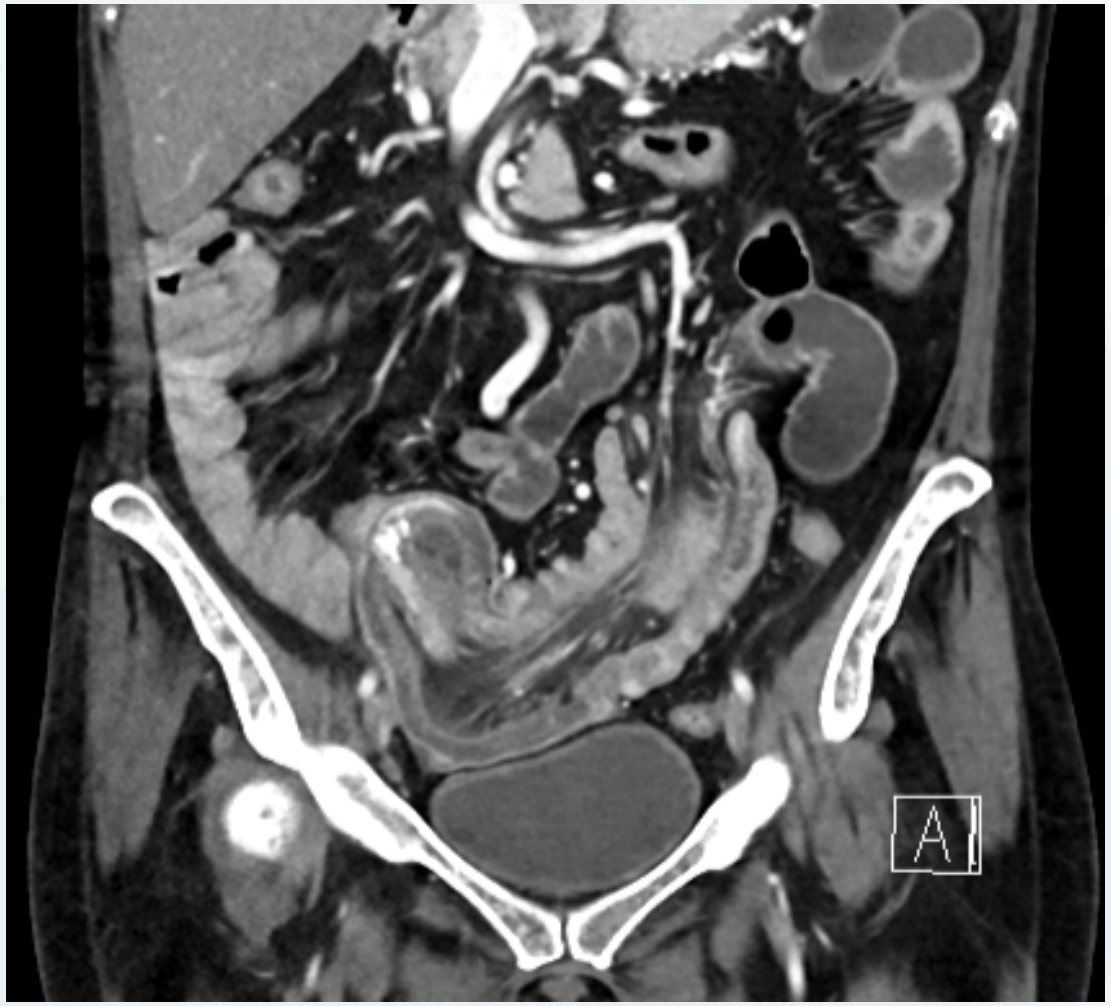
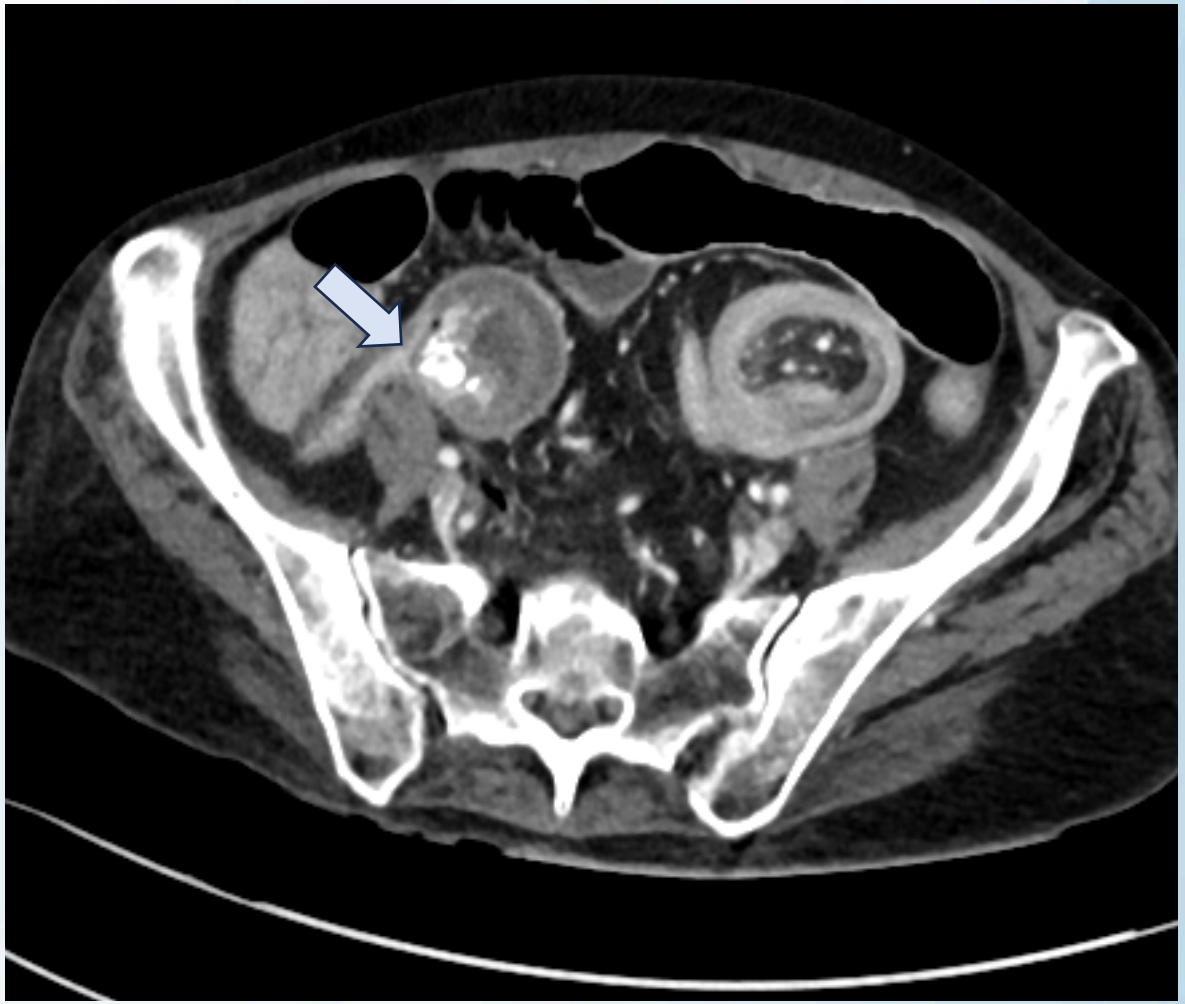
Case Presentation

- A 56 year old lady presented to A&E with severe generalised abdominal pain, nausea, vomiting and bleeding per rectum. She had a background of oesophagitis, duodenitis, and Factor V Leiden heterozygote with previous pulmonary emboli and DVT, but was not currently anticoagulated. She also reported a background of daily abdominal pain for 8 months, and weight loss.
- Observations and blood tests performed in ED demonstrated mild tachycardia, hyponatraemia, CRP 29mg/l , normal haemoglobin and white blood cell count. She was apyrexial.
- On examination, her abdomen was mildly distended, with marked generalised tenderness on palpation. She was focally peritonitic in the lower abdomen.

CT Findings

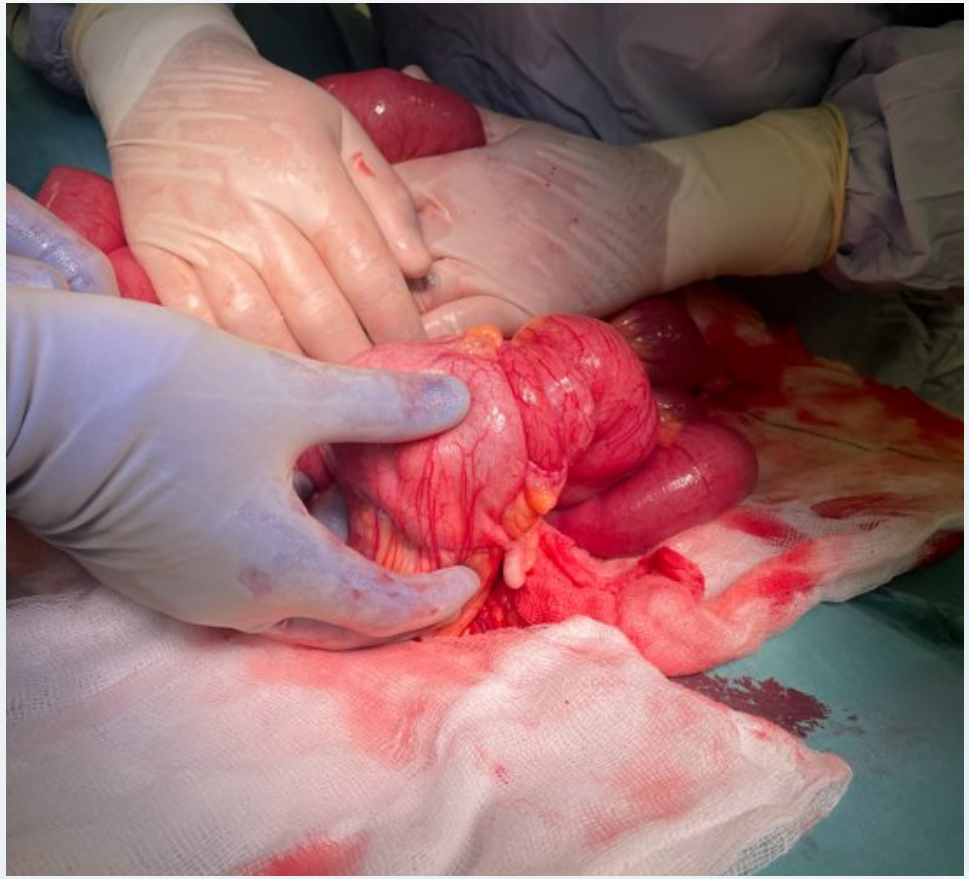
- A CT of the abdomen and pelvis with contrast was performed which showed a large ileocolic intussusception over at least 20cm in the lower abdomen, causing upstream small bowel obstruction.
- There was marked mural oedema throughout the affected bowel with small volume surrounding fluid, however no large perforation, collection or features of established bowel ischaemia.
- A lead point was identified, consisting of a calcified mass in the ileum measuring 17mm.
- The following slide demonstrates these CT findings





Above: Coronal (left) and axial (right) contrast-enhanced CT images showing an extremely long ileocolic intussusception with resultant small bowel obstruction . The lead point is a 17mm calcified mass in the ileum (arrow).

Intra-operative findings & procedure

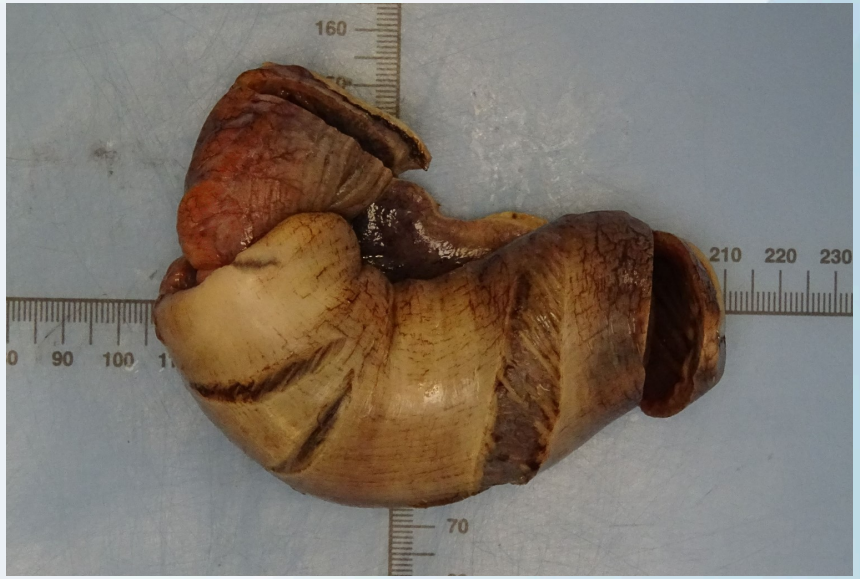


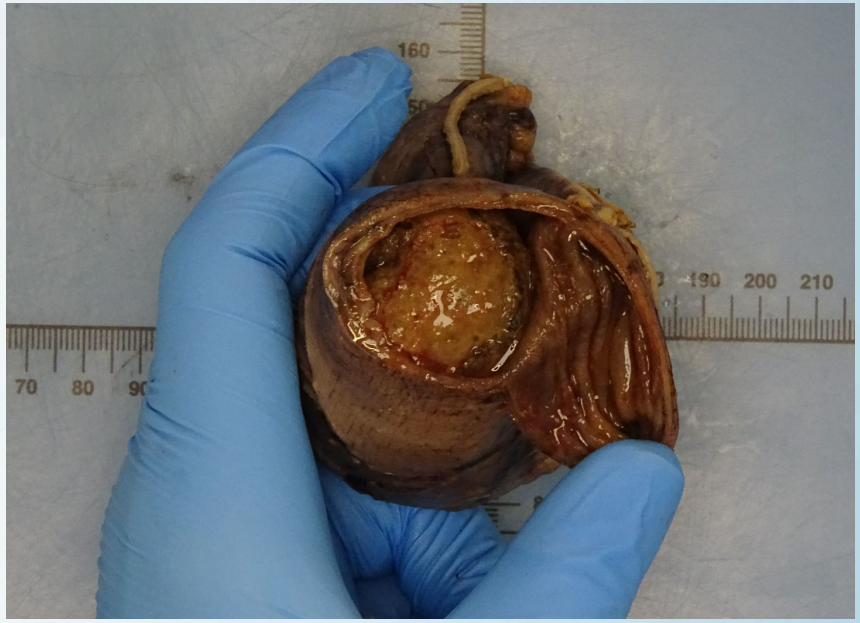
Above: Intra-operative photograph of the small bowel intussuscepting into the caecum.

- A midline laparotomy was performed and the bowel exposed. The small bowel and colon were meticulously inspected and a lead point for a segment of intussuscepted small bowel identified.
- Clear reactive fluid was found in the abdominal cavity; there was no evidence of pus or enteric contents.
- The small bowel had intussuscepted and tracked distally all the way into the caecum. The intussusception lead point was identified around a hard palpable mass 30-45 cm from the ileo-caecal junction. The terminal ileum was grossly oedematous, but the bowel was deemed viable
- The intussusception was reduced as much as possible, freeing up a 30cm length of small bowel. Due to the bowel's gross oedema, serosal tears were noted over the lead point after reduction.
- A small bowel wedge resection was performed around the lead point and a small mesenteric lymph node dissected; these specimens were sent to histopathology for analysis. A side-to-side small bowel anastomosis was performed.

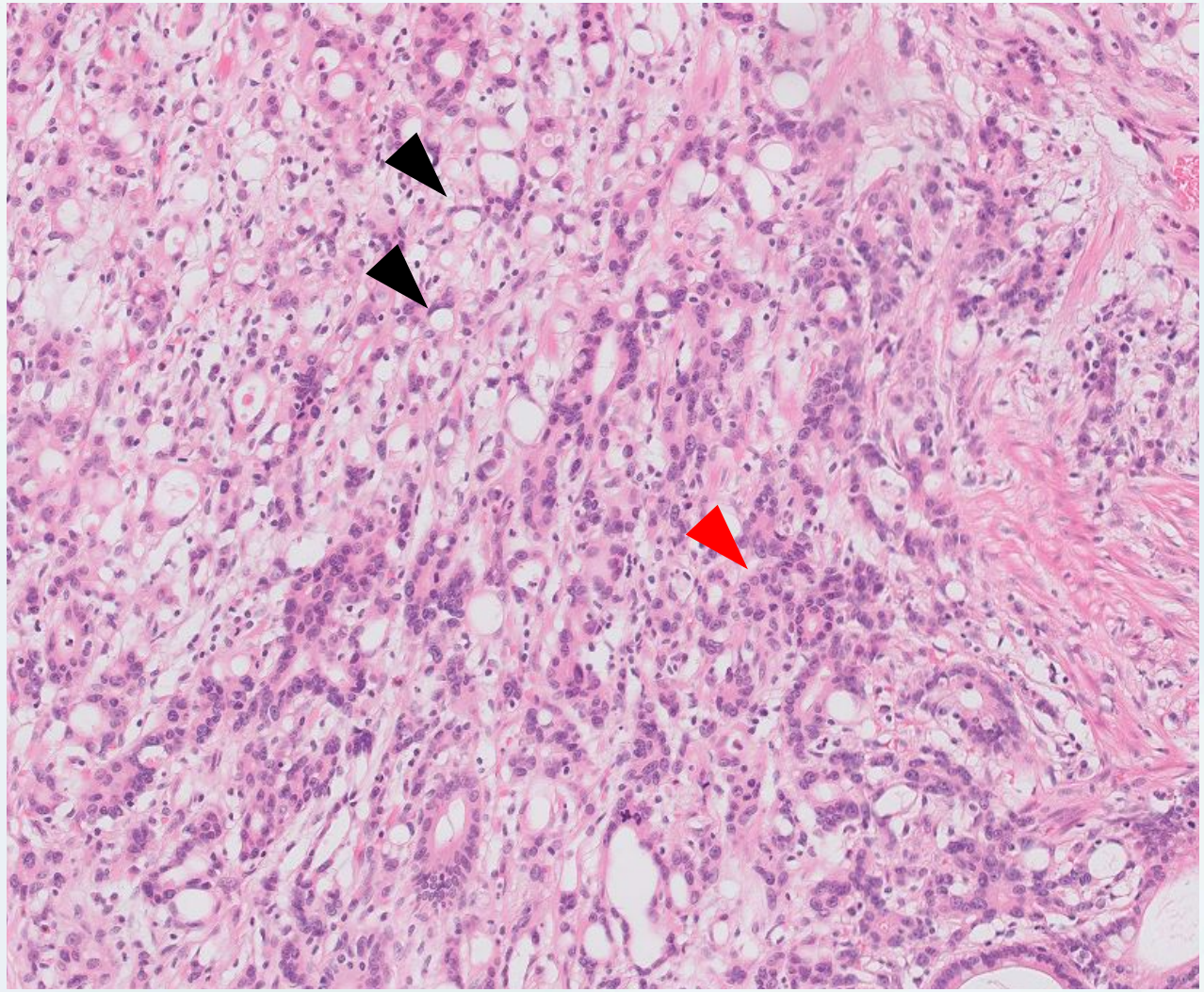
Gross pathology

- The specimen (right) comprised a segment of small bowel with noticeable intussusception measuring 100mm in length with a maximum diameter of 40mm.
- There is evidence of partial serosal defect (tearing).
- Slicing through the specimen revealed a speckled calcified nodule within the lead point of the intussusception measuring 15mm in maximum diameter
- It was 80mm from the nearest margin.





Histopathology



- Histological examination showed the tumour was comprised predominantly of poorly differentiated sheets of tumour cells with focal atypical glands, signet rings (black arrows) and focal areas with a rosette pattern (red arrow).
- There was a central focus of extracellular mucin. Immunohistochemistry showed the lesion was positive for BerEP4 (carcinoma marker).
- There was patchy positive staining for neuroendocrine markers chromogranin and synaptophysin. There was weak positive staining for CDX2 (marker for intestinal adenocarcinoma).

Final diagnosis:

- Grade 3 adenocarcinoma with focal signet rings and focal neuroendocrine differentiation (30 mm, pT3 pN0 pMx)

Learning Points

Small bowel cancer

- Small bowel cancer is rare, accounting for approximately 3% of digestive cancers, however the incidence is rising.[1]
- The four main histological subtypes are adenocarcinoma, neuroendocrine tumours, stromal tumours and lymphoma.
- The most common site for small bowel malignancies is the duodenum (36%), followed by the ileum (30%). <1% are in Meckel's diverticulum.[2]

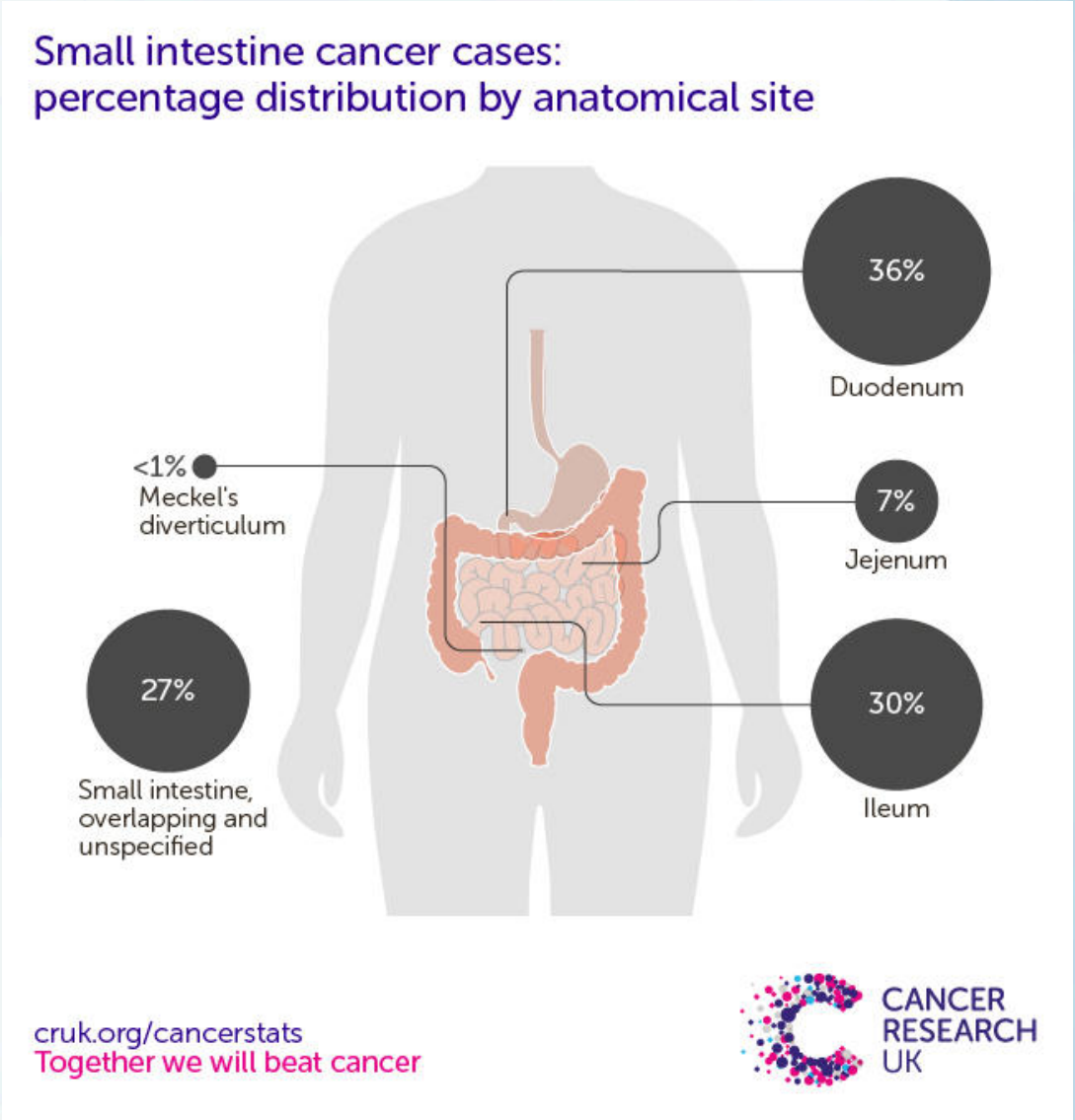
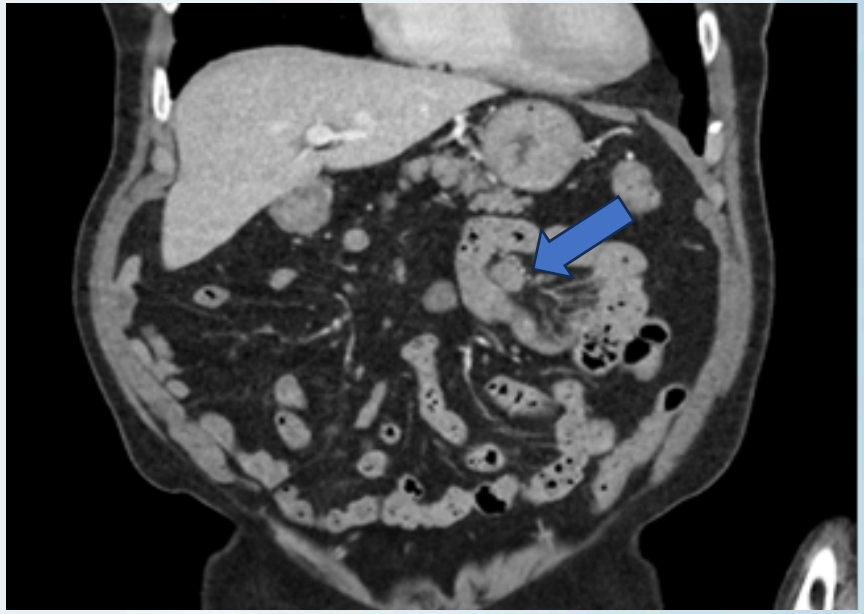
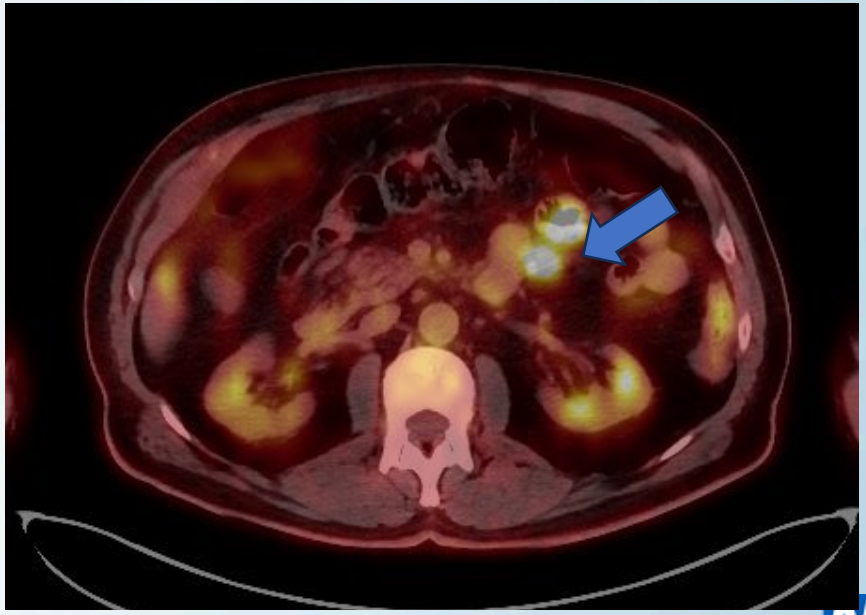


Image courtesy of Cancer Research UK [2]

Small bowel adenocarcinoma

- The duodenum is most frequently affected segment, accounting for 55–82% of cases, followed by the jejunum (11–25%) and ileum (7–17%)[1].
- Risk factors include Lynch syndrome, familial adenomatous polyposis (FAP), Peutz-Jeghers syndrome and Crohn's disease.

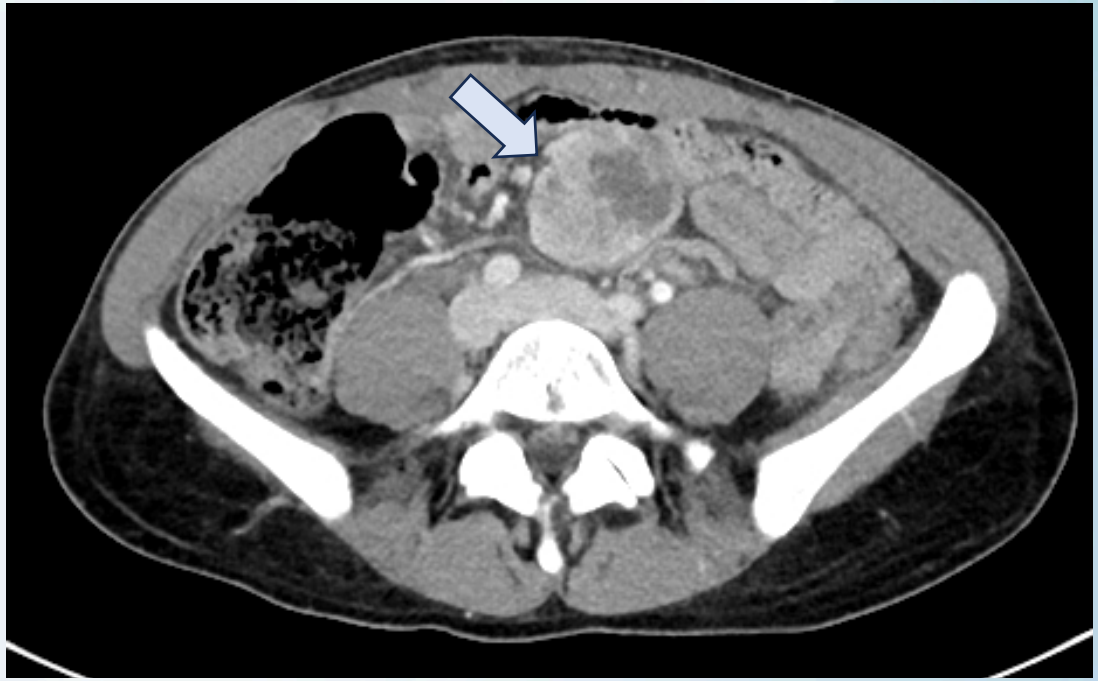




- Right: Above: Coronal image from contrast enhanced CT on a 75 year old patient with Lynch syndrome, demonstrating a 15mm nodal mass adjacent to the jejunum.
- Below: It was FDG avid on PET-CT, and there was also focal avidity of the adjacent jejunum.
- Laparoscopic biopsy demonstrated poorly differentiated adenocarcinoma.

Neuroendocrine tumours

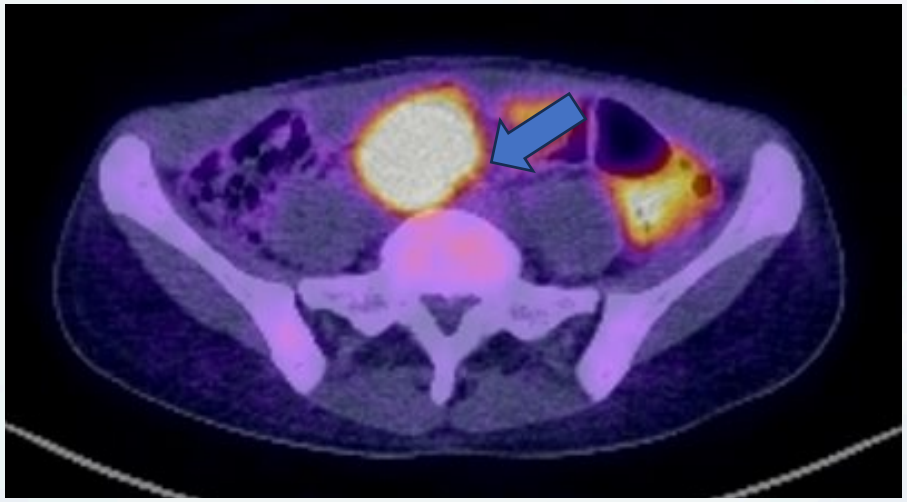
- Neuroendocrine tumours arise from the hormone-secreting cells in the skin, lungs, reproductive organs, pancreas, GI tract, pituitary and adrenal glands.[3]
- Small bowel is second most common site (after lung).
- Risk factors include smoking and family history.
- They can be small and difficult to identify on CT imaging until they metastasise.
- The metastasis may appear as a spiculated mass in the mesentery due to surrounding desmoplastic reaction and can calcify.

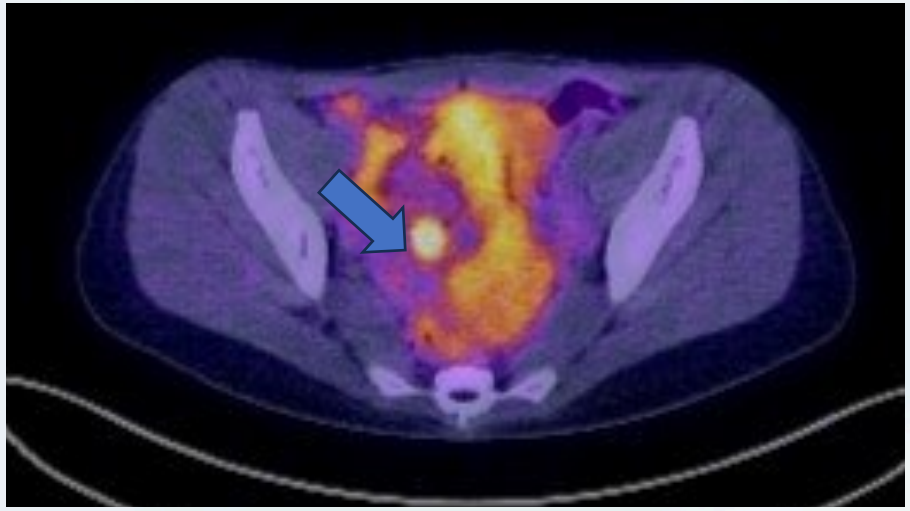


Above: Contrast enhanced CT of a 37 year-old lady with a 3 week history of lower abdominal pain. There is a 5cm heterogenous mass in the mesentery. This example does not have the typical calcification or surrounding desmoplastic reaction.

A primary was not identified on initial CT.

Dotatate PET-CT

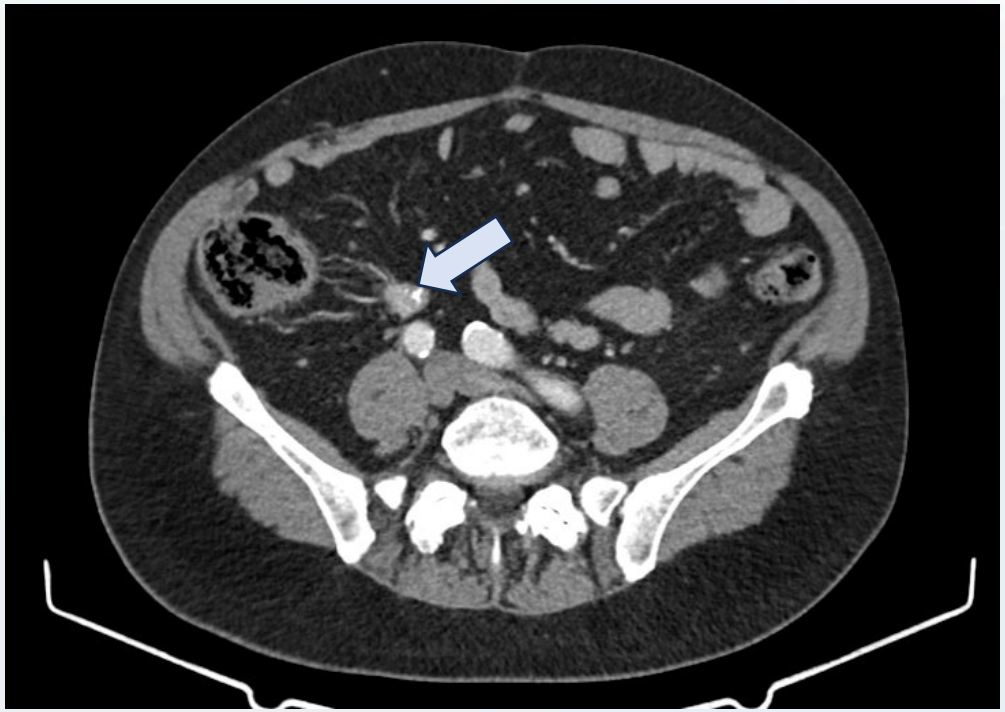




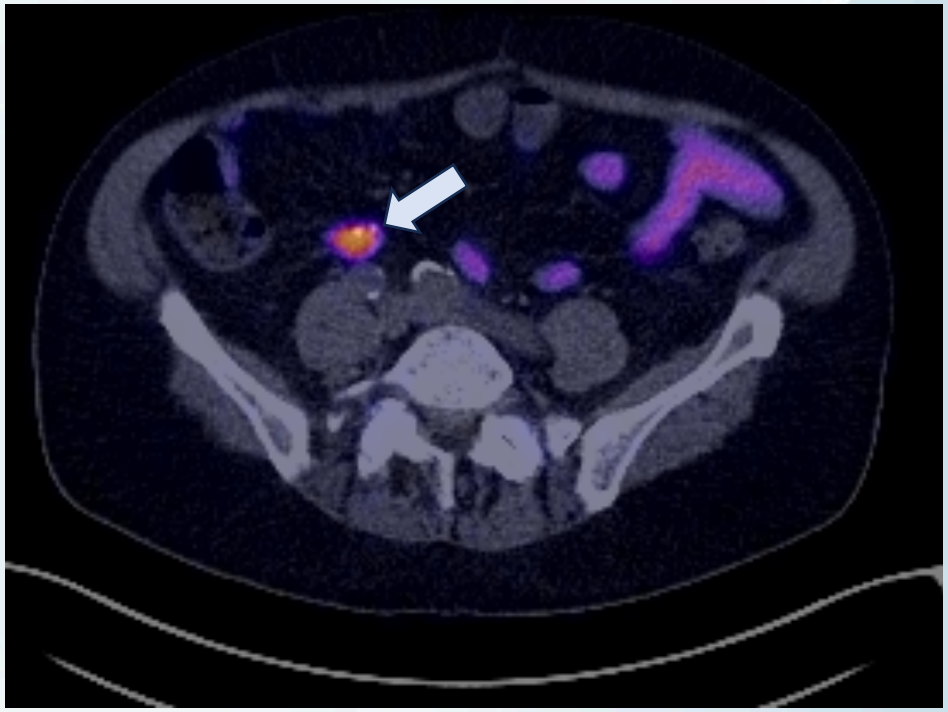
- Top: The patient underwent Dotatate PET CT which demonstrated avidity of the large mesenteric mass.
- Bottom: A small focus of avidity in the right hemipelvis, inseparable from the adjacent ileal loops is favoured to be the primary tumour.

- Laparascopic biopsy of the mesenteric mass showed a grade 1 well-differentiated neuroendocrine tumour and the patient is undergoing workup for surgery.
- Dotatate PET-CT can aid diagnosis and identify the otherwise occult primary tumour in well-differentiated cases.
- Poorly differentiated tumours may be avid on FDG PET-CT but not Dotatate PET-CT, and this can be an indicator for worse prognosis. [4,5]

Here we have another example of a small bowel neuroendocrine tumour:

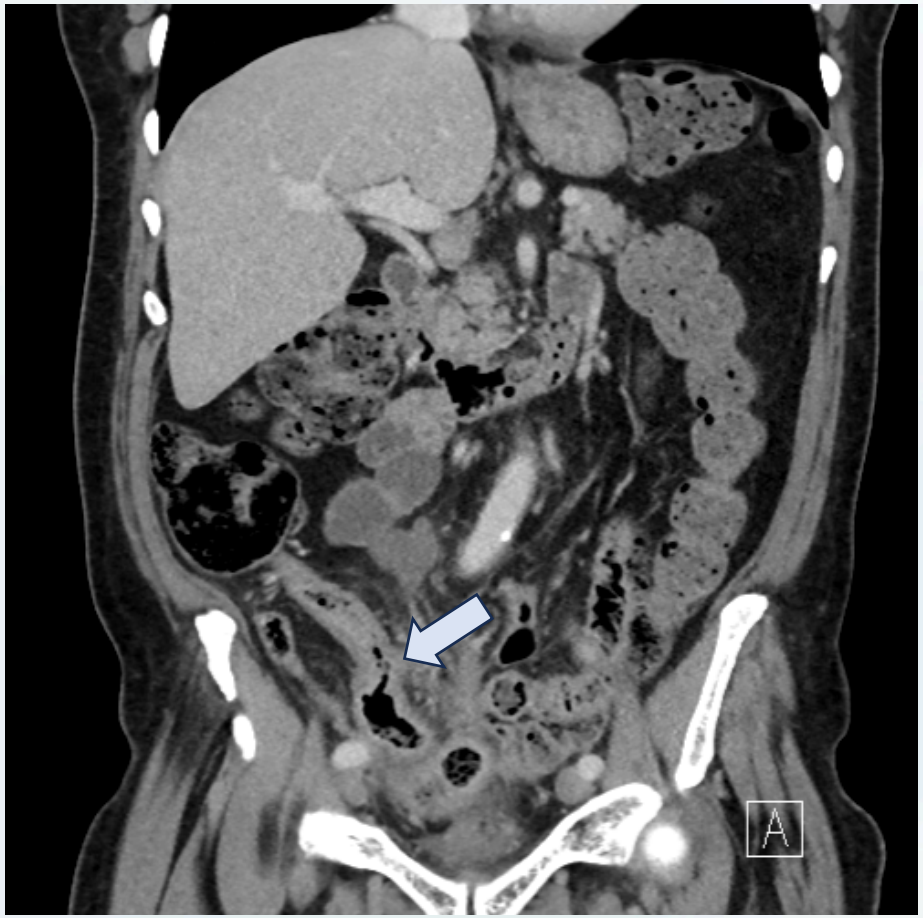


Contrast-enhanced CT showing characteristic features of a small bowel neuroendocrine tumour metastasis in the mesentery, with internal calcification and spiculated surrounding desmoplastic reaction.



Dotatate PET-CT confirmed avidity in this mesenteric mass. The primary tumour was seen as a focal area of avidity in the distal ileum more inferiorly, occult on contrast-enhanced CT.

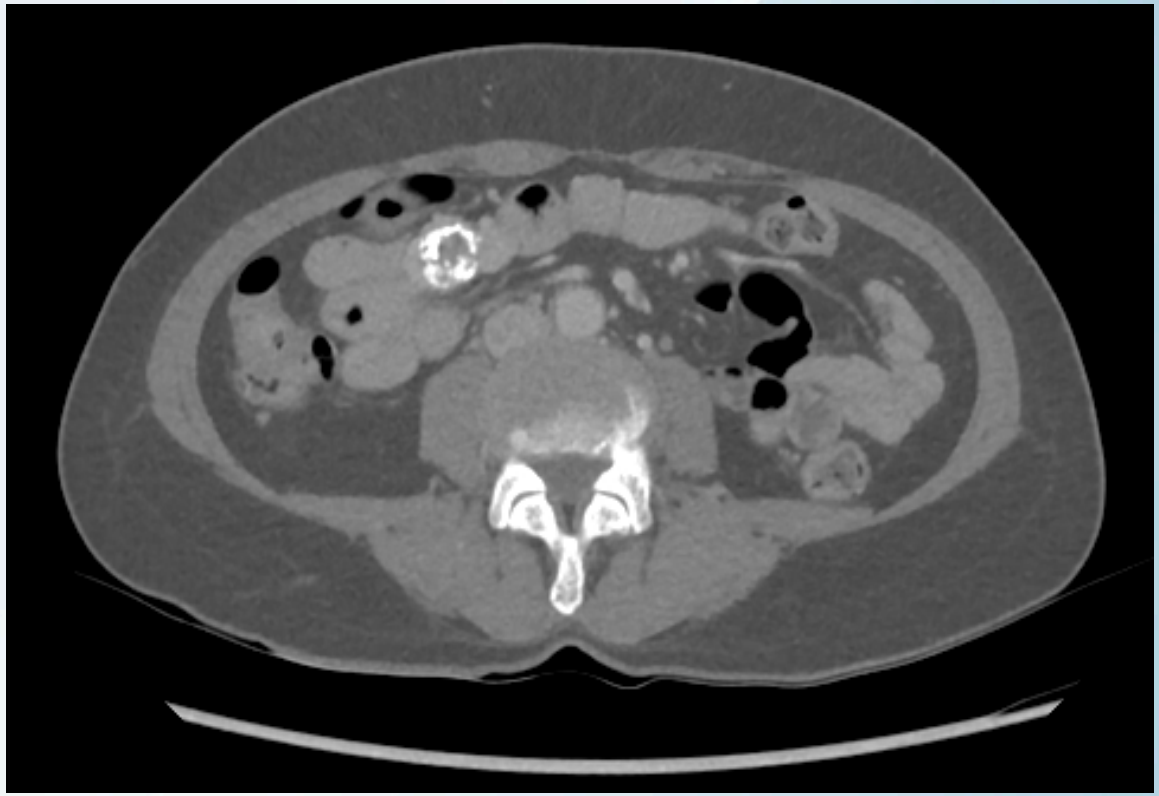
Small bowel lymphoma



- GI tract is the most common extra-nodal site for lymphoma, however primary gastrointestinal lymphoma is rare – 1-4% of all gastrointestinal malignancies.[6]
- The most common site is stomach, followed by the small bowel and ileo-caecal region.
- Almost 90% are of B-cell lineage, with few T-cell lymphomas and Hodgkin lymphoma.
- CT enterography can aid with diagnosis by providing luminal distension for easier identification of thickened bowel wall.
- Typically circumferential thickening with homogenous enhancement. May have adjacent involved nodes. [7]
- Left: Coronal CT image showing diffuse thickening of the distal small bowel in a 76 year old man with symptoms of constipation. It was histologically confirmed as B-cell lymphoma.

GIST – Gastro-intestinal stromal tumour

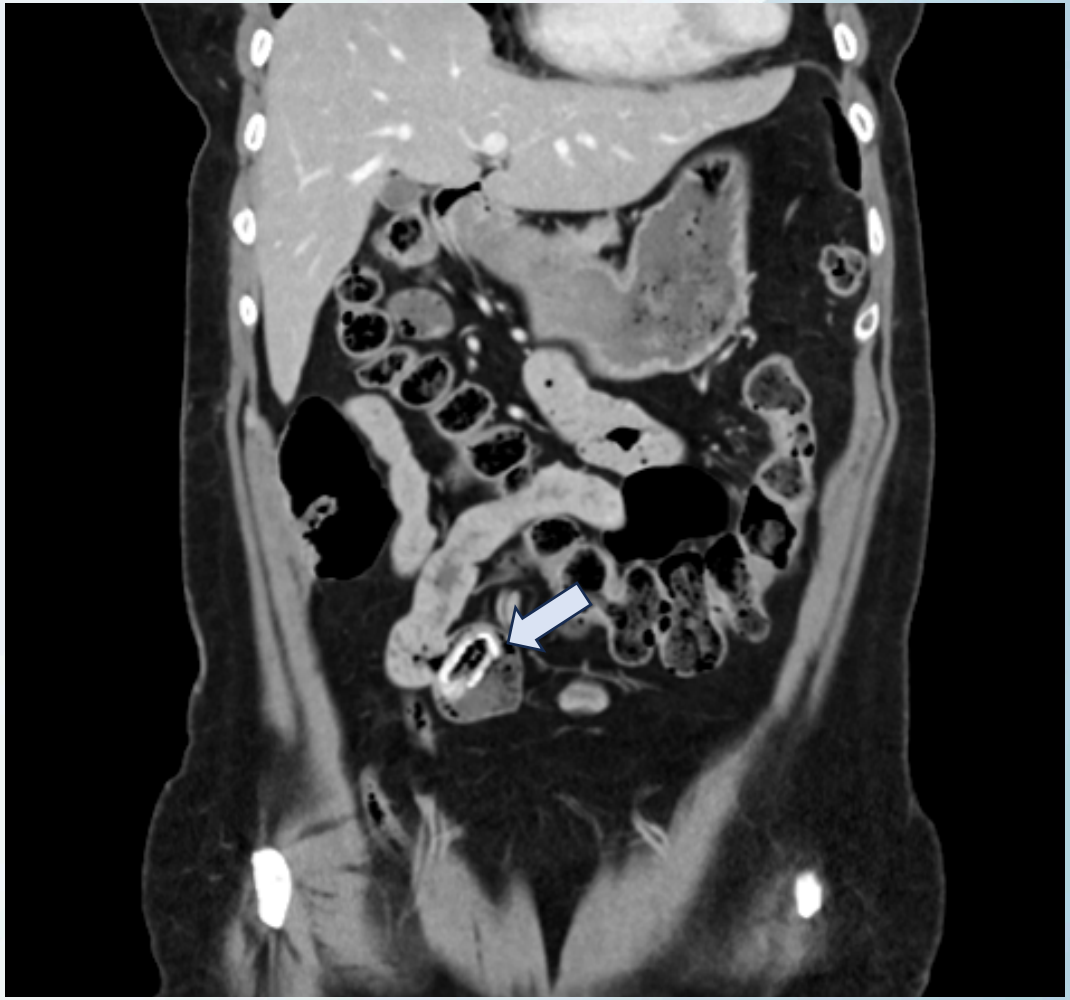
- Typically benign (70%)[8]
- Comprise 0.1-3% of all GI malignancies
- Arise from the same cell lineage as the interstitial cells of Cajal.
- Resection is preferred treatment, or treatment with tyrosine kinase inhibitors if metastatic/not a suitable candidate for surgery.[8,9]
- Calcification may be seen but is variable. [10]



This calcified tumour in the jejunum was histologically confirmed as a GIST

Meckel's diverticulum based masses

- It is a true congenital diverticulum, containing all 3 bowel wall layers (mucosa, submucosa, muscularis propria, and serosa)[9].
- It follows the "*rule of 2s i.e. it affects 2% of the population, 2% of patients are symptomatic, it is mostly found 2 feet from the ileo-cecal valve, symptoms normally become evident before the age of 2 years, ectopic tissue can be found in 1 out of 2 cases, most are about 2 inches long and the ratio of male-to-female incidence is 2 to 1*"
- Malignancies within this is rare, at around 0.5%–3.2% of Meckel's diverticula. Most common subtype is neuro-endocrine/carcinoid (33-44%), followed by leiomyosarcoma (18-25%), adenocarcinoma (12-16%) and GIST (12%).
- Right: Coronal contrast-enhanced on a 67 year old CT for follow up of melanoma demonstrating a calcified mass in a Meckel's diverticulum. This mass contains gas and has been present for two years and this case is felt to be a bezoar rather than a soft tissue tumour.



Discussion

- Our case of mixed adenocarcinoma with focal neuroendocrine differentiation is rare.
- This tumour type has been described in the literature in the oesophagus, stomach, duodenum, jejenum, colon and rectum. [11-15]
- The only other case described in the literature is in an ileal conduit in a patient with a renal transplant (and resultant immunosuppression). [16]
- Due to its rarity, there is limited evidence on the ideal treatment pathway for these patients.
- Histologically, this tumour subtype is separate from mixed neuroendocrine and non-neuroendocrine neoplasm (MiNEN) (also known as MANEC - mixed adeno-neuroendocrine carcinomas), where the neuroendocrine component must histologically make up at least 30% of the cells (which is also rare). [17,18,19]

Summary

- Our case is a striking example of extensive intussusception involving 30-40cm of small bowel.
- Prompt imaging and surgical reduction negated the need for extensive bowel resection.
- A lead point was identified, consisting of a calcified mass.
- The final histological subtype of small bowel adenocarcinoma with neuroendocrine differentiation is rare, with only a handful of cases in the literature, which is distinct from MiNEN.
- Differentials for small bowel masses include adenocarcinoma, neuroendocrine tumour, lymphoma, GIST and any subtype within a Meckel's diverticulum.
- Imaging features can help inform suitable differential diagnosis and the next step in investigation, diagnosis and management.

References

1. Aparicio T, Pachev A, Laurent-Puig P, Svrcek M. Epidemiology, Risk Factors and Diagnosis of Small Bowel Adenocarcinoma. Cancers (Basel) [Internet]. 2022 May 1 [cited 2024 Jan 22];14(9). Available from: /pmc/articles/PMC9103761/
2. Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/small-intestine-cancer/incidence#heading-Three, Accessed January 2024.
3. Gonzáles-Yovera JG, Roseboom PJ, Concepción-Zavaleta M, Gutiérrez-Córdova I, Plasencia-Dueñas E, Quispe-Flores M, et al. Diagnosis and management of small bowel neuroendocrine tumors: A state-of-the-art. World J Methodol. 2022 Sep 20;12(5):381–91.
4. Raj N, Reidy-Lagunes D. The Role of 68Ga-DOTATATE Positron Emission Tomography/Computed Tomography in Well-Differentiated Neuroendocrine Tumors: A Case-Based Approach Illustrates Potential Benefits and Challenges. Pancreas. 2018 Jan;47(1):1–5.
5. Alevroudis E, Spei ME, Chatziioannou SN, Tsoli M, Wallin G, Kaltsas G, et al. Clinical Utility of 18F-FDG PET in Neuroendocrine Tumors Prior to Peptide Receptor Radionuclide Therapy: A Systematic Review and Meta-Analysis. Cancers (Basel). 2021 Apr 10;13(8).
6. Ghimire P, Wu GY, Zhu L. Primary gastrointestinal lymphoma. World J Gastroenterol. 2011 Feb 14;17(6):697–707.
7. Lo Re G, Federica V, Midiri F, Picone D, La Tona G, Galia M, et al. Radiological Features of Gastrointestinal Lymphoma. Gastroenterol Res Pract. 2016;2016:2498143.
8. Burch J, Ahmad I. Gastrointestinal Stromal Cancer. StatPearls [Internet]. 2022 Sep 26 [cited 2024 Jan 22]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK554541/
9. Kabir SA, Raza SA, Kabir SI. Malignant neoplasms of Meckel's diverticulum; an evidence based review. Annals of Medicine and Surgery [Internet]. 2019 Jul 1 [cited 2024 Jan 23];43:75. Available from: /pmc/articles/PMC6582065/
10. Levy AD, Remotti HE, Thompson WM, Sobin LH, Miettinen M. Gastrointestinal stromal tumors: radiologic features with pathologic correlation. Radiographics [Internet]. 2003 [cited 2024 Jan 23];23(2):283–304. Available from: https://pubmed.ncbi.nlm.nih.gov/12640147/
11. Wang KL, Yang Q, Cleary KR, Swisher SG, Correa AM, Komaki R, et al. The significance of neuroendocrine differentiation in adenocarcinoma of the esophagus and esophagogastric junction after preoperative chemoradiation. Cancer [Internet]. 2006 Oct 1 [cited 2024 Jan 23];107(7):1467–74. Available from: https://pubmed.ncbi.nlm.nih.gov/16955509/
12. Kim JJ, Kim JY, Hur H, Cho YK, Han SU. Clinicopathologic Significance of Gastric Adenocarcinoma with Neuroendocrine Features. J Gastric Cancer [Internet]. 2011 [cited 2024 Jan 22];11(4):195. Available from: /pmc/articles/PMC3273688/
13. Suzuki S, Tanaka S, Hayashi T, Harada N, Suzuki M, Hanyu F, et al. Small-cell neuroendocrine carcinoma of the ampulla of Vater. J Hepatobiliary Pancreat Surg. 2006 Sep;13(5):450–3.
14. Cimpeanu E, Zafar W, Circiumaru I, Prozumenshikov A, Salman S. Rare presentation of small bowel adenocarcinoma with neuroendocrine differentiation in the jejunum: A case report and summary of diagnostic and management options. Mol Clin Oncol. 2019 Nov;11(5):461–4.
15. Zeng YJ, Lai W, Liu L, Wu H, Luo XX, Wang J, et al. Prognostic significance of neuroendocrine differentiation in colorectal adenocarcinoma after radical operation: a meta-analysis. J Gastrointest Surg [Internet]. 2014 [cited 2024 Jan 23];18(5):968–76. Available from: https://pubmed.ncbi.nlm.nih.gov/24549474/
16. Matulewicz RS, Fryer JP, Yang XJ, Goyal R, Hairston JC. Renal Transplantation in the Setting of Prior Urinary Diversion: A Case of Poorly Differentiated Adenocarcinoma in an Ileal Conduit. Urol Case Rep [Internet]. 2015 May 1 [cited 2024 Jan 22];3(3):53. Available from: /pmc/articles/PMC4714278/
17. Paspala A, Machairas N, Prodromidou A, Spartalis E, Ioannidis A, Kostakis ID, et al. Management of MANEC of the colon and rectum: A comprehensive review of the literature. Mol Clin Oncol [Internet]. 2018 Jun 11 [cited 2024 Jan 22];9(2):219. Available from: /pmc/articles/PMC6083408/
18. Jacob A, Raj R, Allison DB, Soares HP, Chauhan A. An Update on the Management of Mixed Neuroendocrine-Non-neuroendocrine Neoplasms (MiNEN). Curr Treat Options Oncol [Internet]. 2022 May 1 [cited 2024 Jan 22];23(5):721–35. Available from: https://pubmed.ncbi.nlm.nih.gov/35347561/
19. Volante M, Rindi G, Papotti M. The grey zone between pure (neuro)endocrine and non-(neuro)endocrine tumours: a comment on concepts and classification of mixed exocrine-endocrine neoplasms. Virchows Arch [Internet]. 2006 Nov [cited 2024 Jan 22];449(5):499–506. Available from: https://pubmed.ncbi.nlm.nih.gov/17033797/