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Multidisciplinary management of rare cancers: A case of recurrent neuroendocrine carcinoma of the appendix.

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A 74-year-old male was referred to a tertiary cancer centre with a large mesenteric mass. The patient had previously undergone three operations in an external centre for appendiceal carcinoma. In 2015, the patient was managed for acute appendicitis with a laparoscopic appendicectomy and was diagnosed with a perforated moderately differentiated appendiceal adenocarcinoma with involved margins. He went onto complete 6 months of adjuvant capecitabine and was recommended to undergo a right hemicolectomy. The patient declined operative intervention and was lost to follow up.

Four years later, recurrence was noted in the right iliac fossa, involving the caecum. An open right hemicolectomy was performed with histopathology from this procedure showing a T3N0M0 mixed neuroendocrine neoplasm of caecum, with components of mucinous adenocarcinoma and neuroendocrine carcinoma. Margins were clear at this procedure and CAPOX adjuvant chemotherapy was commenced. Serial PET imaging over the next four months showed persistent avidity in the right iliac fossa.

Due to persistent sepsis a drain was placed into an intrabdominal collection noted on CT. Drainage was unsuccessful and a laparotomy was performed. At this procedure, there was spillage of tumour and significant intra-abdominal sepsis noted. Adjuvant chemotherapy was commenced with carboplatin and etoposide. One month after laparotomy, and ten months after noting PET avid disease on imaging, the patient was referred to a specialist colorectal surgical oncology unit with a fistulating necrotic tumour involving the superior mesenteric artery. Repeat CT imaging showed a large multilobulated mesenteric lesion. On PET, this was intensely avid with avidity also noted along the drain tract and into the anterior abdominal wall (Figure 1). No evidence of distant disease could be found.

Following multidisciplinary discussion, the tumour was deemed appropriate for resection and the patient underwent laparotomy and en-bloc resection of the anterior abdominal wall, drain tract and mesenteric mass (figure 2a). No evidence of peritoneal carcinomatosis could be found. This required both small and large bowel resection due to invasion of these structures by the mass. The superior mesenteric artery and vein were involved and ligated distally,

preserving proximal jejunal branches. (figure 2b). The defect in the abdominal wall (figure 2c). was repaired with biologic mesh. Histopathology was that of a large cell neuroendocrine carcinoma arising from the ileocolic anastomosis with tumour present in the anterior abdominal wall drain site with clear margins. He was discharged home day 10 post op and has been commenced on adjuvant carboplatin and etoposide.

This case demonstrates an unusual progression of malignancy. Histopathology of the operative specimen was extensively reviewed. The initial specimen showed invasive appendiceal carcinoma. Subsequently, the recurrent caecal tumour was classified as a mixed neuroendocrine—non-neuroendocrine neoplasm with components of large cell neuroendocrine carcinoma and mucinous adenocarcinoma. The subsequent mesenteric mass showed features most in keeping with metastasis from the neuroendocrine component of the caecal tumour. Pathologist opinion is that the relationship between the appendiceal and caecal tumour is unclear however it likely represents evolution of mucinous adenocarcinoma to neuroendocrine carcinoma. This pattern of pathology has not been previously reported in the literature.

Appendiceal carcinoma is a rare primary malignancy. Appendiceal malignancies are reported at a frequency of 0.5-1% of all GI malignancies in the literature^{1,2}. Management options for appendiceal tumour depends on the underlying pathology. For mucinous adenocarcinoma and neuroendocrine tumours confined to the appendix, right hemicolectomy is recommended in the first instance^{1,2}. When margins are involved or when there is tumour perforation and peritoneal spread, referral to a peritoneal surface malignancy center is recommended³. Recently, the role of CRS and HIPEC in non- mucinous neoplasms – including mixed- adneoneuroendocrine carcinomas has been examined with findings showing that while mucinous and non- mucinous appendiceal tumours share a locoregional dissemination pattern, prognosis is worse following CRS and HIPEC for non-mucinous neoplasms⁴. In light of these recommendations the management of patients with rare tumours relies of expert opinion so that decisions made are patient appropriate.

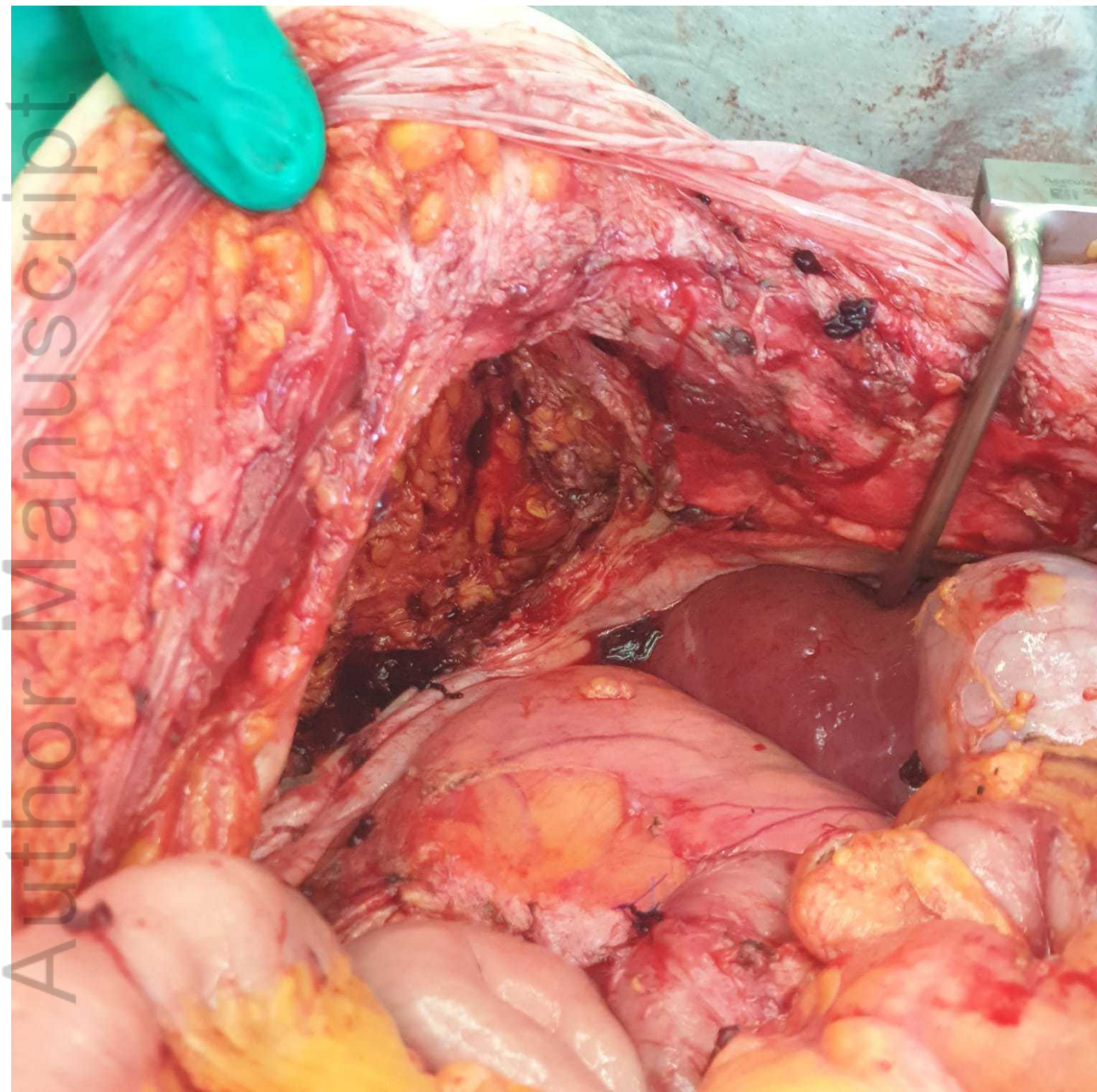
To facilitate expert opinion, quaternary facilities, including dedicated state- based cancer centres, have been shown to improve outcomes despite the perceived barriers of long waits and long travel times for patients⁵. This arrangement ensures patients have access to appropriate medical expertise, including accurate staging, technical skills – including access to technology, and access to clinical trials⁵. It should also be noted that in the case of rare solid malignancies 65% will require operative intervention and the initial surgical management of these patients often directly impacts on the long- term outcomes therefore early referral is preferred⁵.

Appendiceal carcinoma – especially metastatic neuroendocrine carcinomas, are exceedingly rare and as demonstrated by this case, early involvement of specialist services when difficult or uncommon oncological diagnoses are encountered is essential as there is demonstrated benefit from a multidisciplinary approach to care. The procedure performed was technically challenging and represents the challenges of decision making around complex cases where there is significant potential to cause harm through operative intervention.

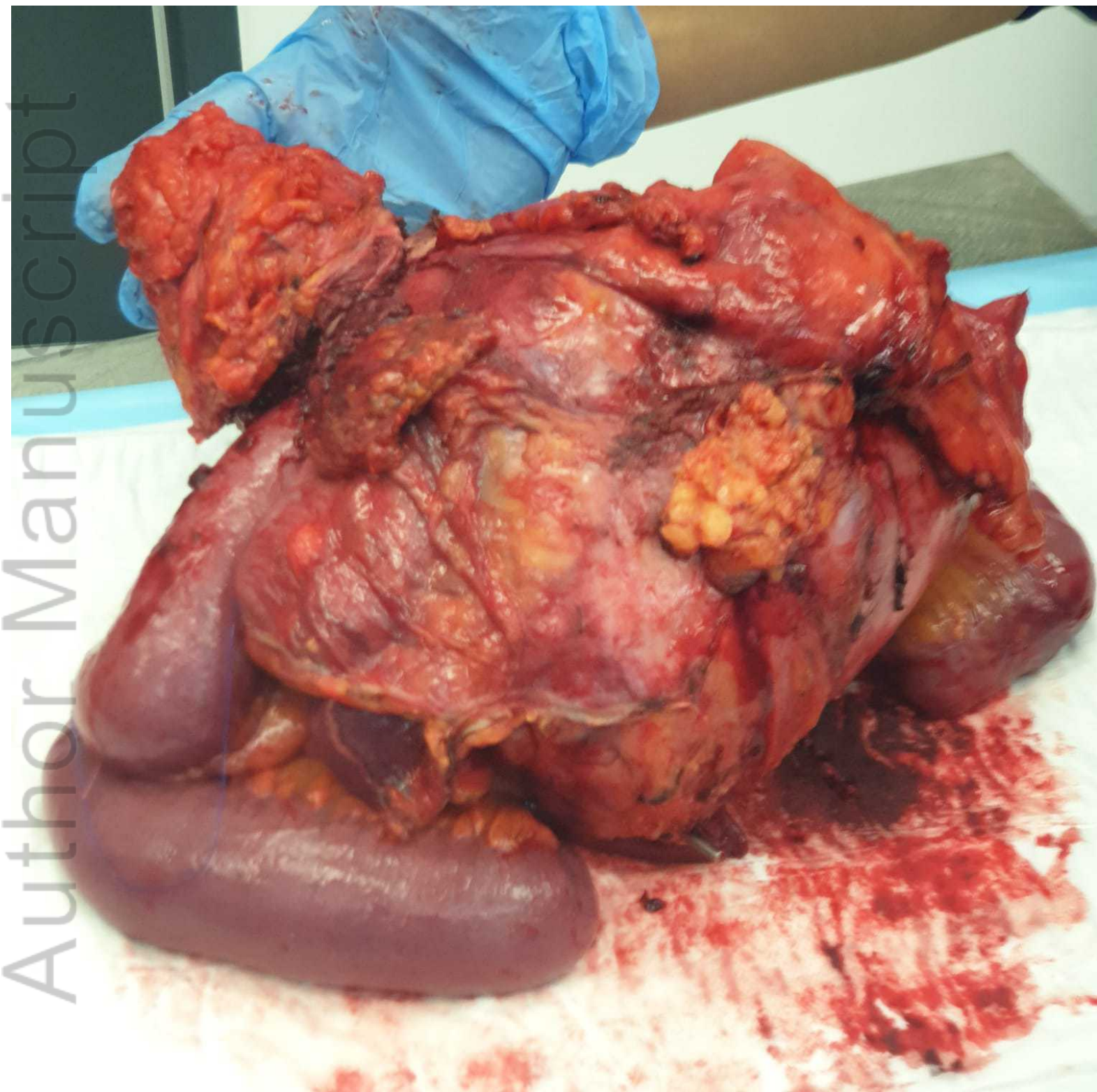
Figure 1 - Pre operative PET CT imaging

Figure 2 – A) enbloc resection of mesenteric tumour and drain tube site. B) central vascular ligation. C) abdominal wall defect

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