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IMAGE OF THE MONTH

Mixed adenoneuroendocrine carcinoma of the cecum

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KEYWORDS
Mixed adenoneuroendocrine tumor;
MANEC;
Cecum;
Diagnosis;
Cytoreductive surgery;
HIPEC

A 54-years-old man previously treated with appendectomy and ileostomy for mucinous adenocarcinoma (ADC) with peritoneal involvement was referred to our Department. Staging laparoscopy and ileostomy closure were performed first, delaying the definitive surgical procedure in order to decrease the infective risk. One month later, he underwent Cytoreductive Surgery (CS) including right hemicolectomy with greater omentectomy, cholecystectomy, lesser omentectomy, complete paracolic gutters and pelvic peritonectomy. At the end of the procedure, Hyperthermic Intraperitoneal Chemotherapy (HIPEC) at temperatures of 42—43 °C was given for 90 minutes with mytomicin at a dose of 12.5 mg/m^2. In postoperative day 10, relaparotomy was necessary for leakage of the ileocolic anastomosis. Macroscopic examination of the specimen revealed an ulcerated stenosing tumor in the cecum with serosal perforation and infiltration of the pericolic fat and peritoneum. Surgical resection margins and dissected regional lymphnodes were negative. Histology revealed two different components in a side-to-side pattern (Fig. 1). One part, representing about 40% was consistent with a mucinous moderately differentiated (ADC). The other part, representing about 60% was characterized by high-grade large cells neuroendocrine carcinoma. High mitotic count (> 20 × HPF) and Ki67 proliferative index (80%), as well as lymphatic and neural invasion were observed, but no vascular invasion was present. Immunohistochemical analysis staining was positive for CK20 (Fig. 2), AE1/AE3, CDX2, CD56 and synaptophysin (Fig. 3). Pathological diagnosis was high-grade mixed adenoneuroendocrine carcinoma (MANEC), T4N0M0 stage. No adjuvant chemotherapy was administered and one year after

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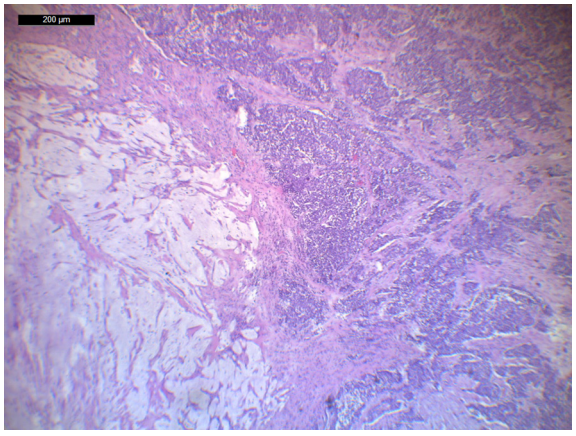

Fig. 1 Neoplasm composed of mucinous adenocarcinoma and large cell NEC (H&E, ×20).

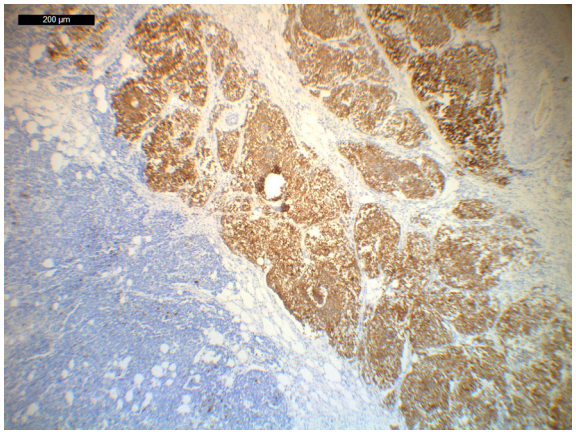

Fig. 2 Immunohistochemical analysis positive for CK20 (×20).

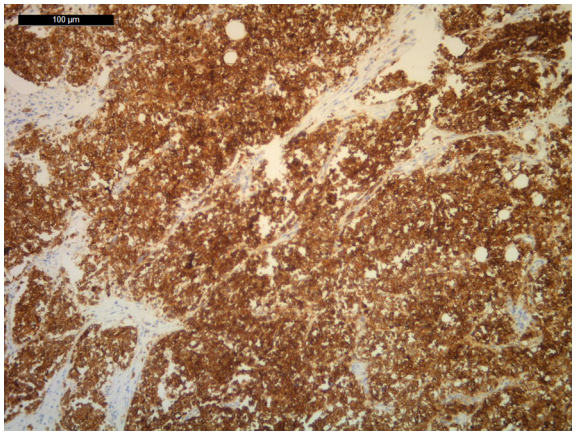

Fig. 3 Immunohistochemical analysis positive for synaptophysin (×20).

the patient developed abdominal recurrence. The patient received then Folinic acid, Fluorouracil and Oxaliplatin regimen but died 24 months after the initial surgical procedure.

Owing to the improved endoscopic screening and awareness of neuroendocrine histology, tumors with combinations of endocrine and exocrine components are increasingly observed. When at least 30% of either component is present, they can be defined MANEC and stratified in different prognostic categories according to the grade of malignancy of each component [1]. MANECs are classified into three different types. Composite tumor displays closely intermingled exocrine and neuroendocrine components, while collision tumor shows a side-to-side pattern. Amphicrine carcinomas, with exocrine and neuroendrocrine present in the same neoplastic cell, are exceedingly rare [1]. The neuroendocrine components of MANEC are classified into small or large cell carcinoma. The pathogenesis is poorly understood [2—4,5]. Colorectal location is extremely rare but the true incidence may be underestimate due to inadequate diagnosis [1—3]. Since the distinction with ADC on the basis of clinical symptoms and imaging features is challenging, the correct diagnosis depends on pathologic examination. At least two out of three commonly used immunohistochemical neuroendocrine markers (synaptophysin, chromogranin A or CD56) should be highly expressed to formulate the diagnosis of MANEC. High grade MANEC with large cell subtype usually shows also nuclear immunoreactivity for CDX2 [1,6]. Due to the rarity and lack of comprehensive molecular characterization of these tumors, optimal treatment is still unknown and left to subjective choice [2,3,7,8,9]. Radical surgical resection is the only potential curative treatment. Debulking is appropriate when > 90% of the tumors is reduced [7]. The effectiveness of adjuvant chemotherapy is not clear and prognosis of MANEC is significantly worse than ADC [2,3,6—9]. Due to the highly malignant behavior, aggressive multidisciplinary management including CS and HIPEC should be recommended.

Authors' contribution

FC and MV designed the report and critically revised the manuscript; FC and AR searched literature data; FC, MV and AR analysed and interpreted data; FC drafted the manuscript. All authors have approved the final article.

Disclosure of interest

The authors declare that they have no competing interest.

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