1130-0108/2015/107/6/396-397
Revista Española de Enfermedades Digestivas

Rev Esp Enferm Dig (Madrid
Vol. 107, N.º 6, pp. 396-397, 2015

Letters to the Editor

Well differentiated neuroendocrine tumor of the appendix and low-grade appendiceal mucinous neoplasm presenting as a collision tumor

Key words: Appendiceal neoplasms. Neuroendocrine tumors. Pseudomyxoma peritonei. Adjuvant chemotherapy.

Dear Editor,

Primary tumors of the appendix represent approximately 0.4% of all gastrointestinal tract tumors (1) and are usually incidentally found in about 1% of appendectomies (2) with collision tumors being extremely unusual in this location (3-5). In this report, we present two cases of collision tumors with low-grade mucinous neoplasm of the appendix and well differentiated neuroendocrine tumors.

Case report

Case 1. A 49-year-old female presented with an epigastric hernia that was taken to surgery. Pathologic diagnosis of the hernial sac revealed acellular mucin which prompted other diagnostic studies. Computed tomography (CT) scan of the abdomen revealed a cystic mass in the right lower quadrant with free fluid in the paracolic gutter that measured 7 cm in greatest dimension with a calcified rim (Fig. 1). She was taken to radical cytoreduction and hyperthermic intraperitoneal chemotherapy. An enlarged perforated mass of the appendix was found intraoperatively (Fig. 1). The patient's peritoneal carcinomatosis index was 27 and complete cytoreduction was achieved. Her postoperative course was uneventful and she was discharged from the hospital on day 11 without complications.

Case 2. A 45-year-old male complained of 3 years of progressive abdominal distension who finally presented in 2011 with an epigastric hernia, Preoperative imaging studies revealed free fluid in abdominal cavity. He was taken to diagnostic laparoscopy that confirmed an epigastric hernia, multiple abdominal mucinous tumor implants and a tumor-like lesion on the tip of the appendix. An appendectomy and omentectomy were performed at the moment at another institution. In 2012, this patient was taken to radical and hyperthermic intraperitoneal chemotherapy cytoreduction, finding extensive involvement by an appendiceal mucinous neoplasm. In 2013 presented with perihepatic and pleural recurrences and extensive progression of the abdominal disease was documented. Due to inability to achieve complete cytoreduction, it was recommended to treat with chemotherapy alone.

Microscopic findings in both cases showed collision of two different neoplastic proliferations: The first neoplasia was a well differentiated neuroendocrine tumor and the second one was a cystic lesion lined by well-differentiated mucinous epithelium with a villous architecture (Fig. 1). The appendiceal mucin dissected focally the wall and had numerous acellular mucinous implants in the abdominal cavity. No transition of the two epithelial components was seen and no regional lymph nodes were compromised.

Immunohistochemistry in both patients showed positivity of the neuroendocrine tumors with chromogranin (Fig. 1E) and synaptophysin (Fig. 1F). The Ki67 was 1% in both cases. These findings were consistent with a well differentiated neuroendocrine tumor, grade 1 (carcinoid tumor) according to the current WHO classification (6). The mucinous neoplasms were positive for cytokeratin 20 and CDX-2 and negative for cytokeratin 7, the findings were consistent with low-grade mucinous neoplasias of the appendix according to Misdraji et al. (7).

Discussion

A collision tumor is defined by two histologically different neoplasias that grow at the same anatomic location without tran-

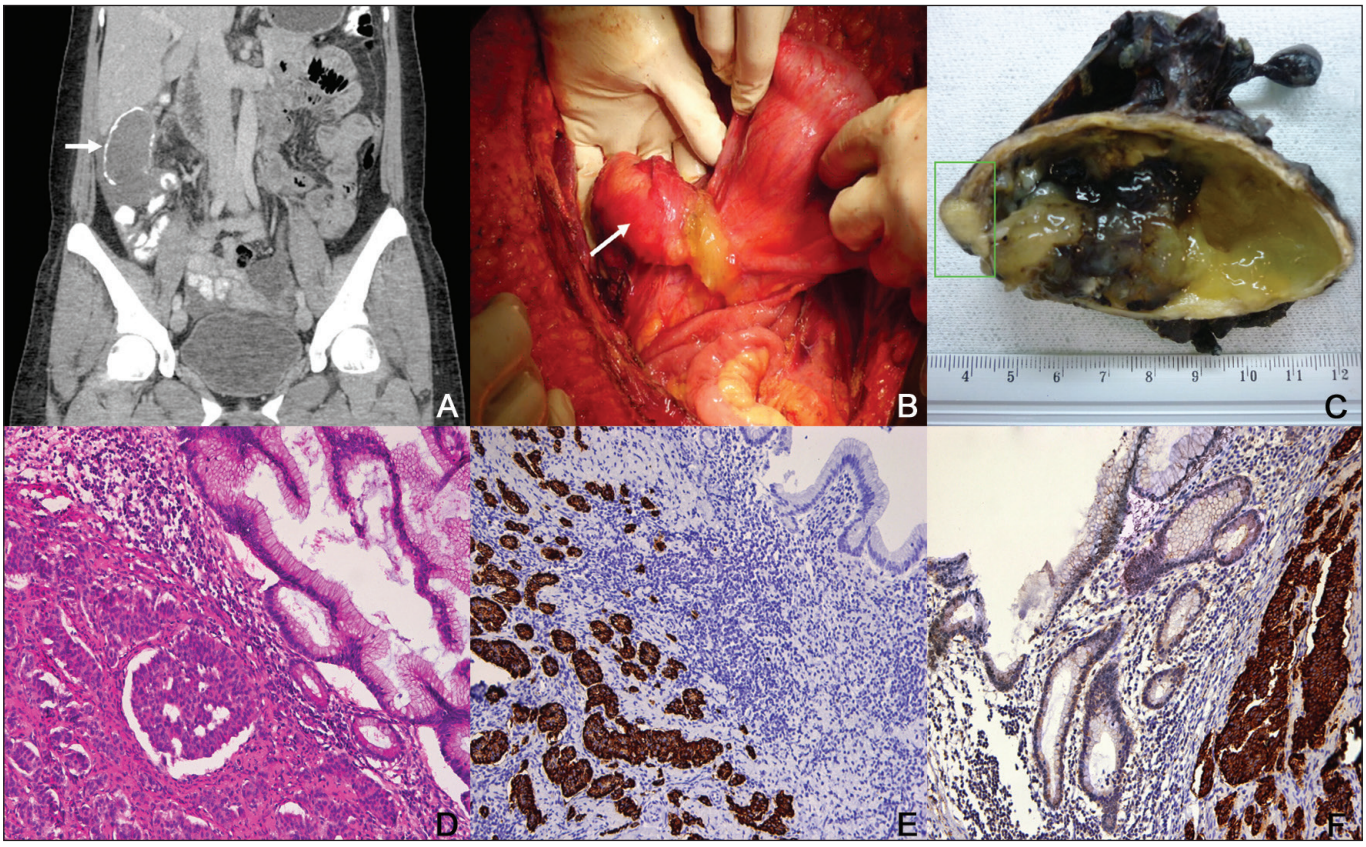

Fig. 1. Preoperative computerized tomography scan of the abdomen with contrast. A 7 cm appendiceal mass with peripheral calcification (bold arrow) (A). Intraoperative findings. The appendiceal mass in situ with extravasation of mucin (bold arrow) (B). Gross findings in case 1 showed a (green box) yellow obliterating 2 cm area consistent with neuroendocrine tumor, localized in the middle of the appendix with a distal cystic dilatation with mucoid content, corresponding to a low-grade mucinous neoplasm (C). Case 2. Collision of mucinous neoplasia with a well differentiated neuroendocrine tumor, H&E, 200X (D). Immunohistochemistry was positive for chromogranin, 200X (E) and synaptophysin, 200X (F) in both cases.

sition and with a different clonal origin. These are different than mixed tumors, which share the same carcinogenic pathway but later on differentiate in two different histological phenotypes (3).

Although mixed tumors are rare in the gastrointestinal tract, the appendix is one of the most common sites for its development (3,8). Most of the cases reported in the literature are adenocarcinoid tumors and Goblet cell carcinoids (8), these tumors are different entities where the morphology resembles Goblet cells but the immunophenotype is neuroendocrine (9).

Collision tumors of the appendix are even rarer, to our knowledge these is the fourth report of cases after Singh et al. (3), Rossi et al. (5) and Chetty et al. (10) and is also the only collision tumor formed by a well differentiated neuroendocrine tumor and a low grade mucinous neoplasia. The histologic findings are relevant for the prognosis and treatment of the patient because usually is the most aggressive component the one that metastasize and determines the evolution of the disease (3).

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