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Case report

COLLISION TUMOR OF A PRIMARY COLONIC ADENOCARCINOMA AND A PANCREATIC DUCTAL ADENOCARCINOMA

FEDERICO RAZUMNY[1], DANIELA SPEISKY[2], MARIANA RIZZOLO[2], MARÍA FLORENCIA SÁNCHEZ[2], GUSTAVO GARAVAGLIA[2], MIRTA KUJARUK[2].

[1]Servicio de Anatomía Patológica, Hospital General de Agudos Dr. Juan A. Fernández, [2]Unidad de Anatomía Patológica, Hospital de Gastroenterología Dr. Carlos Bonorino Udaondo, Buenos Aires, Argentina

Postal address: Daniela Speisky, Hospital de Gastroenterología Dr. Carlos Bonorino Udaondo, Av. Caseros 2061, 1264 Buenos Aires, Argentina
E-mail: danispeisky@gmail.com
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Abstract

Collison tumors are rare entities characterized by the juxtaposition of two histological distinct neoplastic populations in the same organ without intermixture of the different malignant components. Due to their infrequency, especially in the digestive tract, limited prior cases have been reported and the pathogenesis, biological behavior and treatment remain controversial. We present the case of a 79-year-old woman with a solid pancreatic mass and a rectosigmoid wall thickening, accompanied by multiple hepatic lesions. These findings suggested a pancreatic neoplasm with liver metastasis and a probable synchronous colonic tumor. Surprisingly, the histological study of surgical rectosigmoid resection showed a collision tumor comprised of two independent components: a primary colonic adenocarcinoma and a pancreatic ductal adenocarcinoma with one lymph node metastasis of the intestinal component. Immunohistochemical and molecular studies, confirmed the histomorphological findings. This case outlines the effectiveness of an exhaustive pathological sampling and the importance of the histological, immunohistochemical and molecular studies to increase diagnostic accuracy. To the best of our knowledge, this is the first reported case of collision between these two types of adenocarcinomas in the rectosigmoid region. We highlight the importance of reporting this entity, in order to contribute to the available literature.

Key words: collision tumor, gastrointestinal tract, colorectal adenocarcinoma, pancreatic ductal adenocarcinoma

Resumen

Tumor de colisión entre un adenocarcinoma colónico primario y un adenocarcinoma ductal pancreático

Los tumores de colisión son entidades raras caracterizadas por la yuxtaposición histológica de dos neoplasias en el mismo órgano que no se entremezclan entre sí. Debido a su baja frecuencia, especialmente en el tracto digestivo, pocos casos han sido reportados y su patogénesis, comportamiento biológico y tratamiento siguen siendo controversiales. Presentamos el caso de una mujer de 79 años con una masa sólida pancreática y engrosamiento rectosigmoideo, acompañados de múltiples lesiones hepáticas. Estos hallazgos sugerían un tumor pancreático con metástasis hepáticas y un probable tumor sincrónico colónico. Sorprendentemente, el estudio histológico de la pieza quirúrgica rectocolónica, evidenció un tumor de colisión constituido por dos com-

ponentes independientes: un adenocarcinoma primario colónico y un adenocarcinoma ductal pancreático, con metástasis de tipo intestinal en un ganglio linfático. Los estudios por inmunohistoquímica y moleculares confirmaron estos hallazgos histomorfológicos. El presente caso remarca la eficacia de un muestreo patológico exhaustivo y la importancia de los estudios histológicos, inmunohistoquímicos y moleculares para incrementar la precisión diagnóstica. Según nuestro conocimiento, este es el primer caso reportado de un tumor de colisión entre estos dos tipos de adenocarcinoma en la región rectosigmoidea. Destacamos la importancia de reportar este tipo de tumores con el objetivo de contribuir a la literatura actual.

Palabras clave: tumor de colisión, tracto gastrointestinal, adenocarcinoma colorrectal, adenocarcinoma ductal pancreático

Collison tumors (CTs) are rare entities characterized by the presence of two histologically distinct neoplastic populations in the same organ[1]. The understanding of these tumors is not simple, reason why different criteria were described to attempt a common definition. Despite subtle differences, most of the authors agree that CTs belong to a large family of mixed neoplasms with no histological mixing of the different malignant components colliding in the same mass[2-4]. The pathogenesis of CTs also remains as a controversial issue, suggesting as possible mechanisms: the proliferation of two different cell lines at the same time, a common pluripotent stem cell that differentiate into two lineages or the juxtaposition of two distinct tumors. Given that no specific radiological or clinical features for CTs were described, the diagnosis is often incidental during pathological evaluation of surgical specimens[3,4].

In the gastrointestinal tract, the stomach is the organ most frequently affected by CTs followed by the esophagus. The colon is much less often involved, but nevertheless there are some case reports of CTs composed of an intestinal adenocarcinoma and other malignant components, most of them of neuroendocrine lineage or lymphomas[3-7]. It is even rarer to find a collision tumor (CT) of this location constituted by two histomorphological and immunohistochemical distinct types of adenocarcinomas. Even though, a few cases of colorectal and gastric adenocarcinomas were reported in the current literature[1,2]. Here, we present a CT consisting of two-independent components: a primary colonic adenocarcinoma and a pancreatic ductal adenocarcinoma. To the best of our knowledge, this is the first reported case of collision between these two types of adenocarcinomas in the rectosigmoid region.

Case report

A 79-year-old female was admitted to our hospital with dull abdominal pain and a weight loss of 8 kg in the last month. She had a family history of different neoplasms: her father and a brother were diagnosed with pancreatic carcinoma and a second brother was followed by a colonic carcinoma. However, no specific familial cancer syndrome was detected. Blood work and laboratory values showed low hemoglobin levels and altered kidney function. An abdominal and pelvic ultrasound and computed tomography scan revealed a heterogeneous mass in the pancreatic neck measuring 35 x 30 mm, multiple nodular lesions in the liver and a colonic wall thickening in the sigmoid colon, accompanied by multiple enlarged retroperitoneal lymph nodes. A biopsy of the pancreatic mass was performed, and histopathological study was consistent with a moderately differentiated ductal adenocarcinoma. All these findings were interpreted as a pancreatic adenocarcinoma with multiple liver metastasis and a probable synchronous colonic tumor.

Before a colonoscopy and a biopsy of the liver masses could be performed, the patient presented with acute abdominal pain, bloating, peritonitis, oliguria and impaired sensory perception. This was interpreted as a colonic perforation; therefore, an emergency rectosigmoid resection with end colostomy was carried out.

Macroscopic examination of the specimen showed an exophytic and ulcerated mass of 2.5 x 2 cm with transmural colonic involvement (Fig. 1A). The solid and endophytic component of the lesion was whitish and homogeneous, without macroscopic differences throughout the mass. Surgical margins were tumor-free. Exhaustive sampling of the tumor was performed. The histological sections of the material embedded in paraffin colored with hematoxylin and eosin, showed a neoplastic proliferation of duct-like structures with an intestinal pattern which involved colonic mucosa and muscularis propria. Areas of conventional adenomatous high-grade dysplasia were seen on the edge. Interestingly, a second component of adenocarcinoma was identified in muscle layers and subserosa. However, these groups of neoplastic cells

were columnar to cuboidal with less mucin production and clearer cytoplasm (Fig. 1B-D). Lymph node metastases of intestinal adenocarcinoma was found in one of 14 resected nodes. Immunohistochemistry was performed on histological sections of 3 microns using an automated system according to the manufacturer's guidelines (BOND-MAX-Leica Biosystems). The colonic tumor expressed CK20 (cytokeratin 20), CDX2 (caudal type homeobox 2) and SATB2 (special AT-rich sequence-binding protein 2) with negativity for CK7 (cytokeratin 7), whereas the second component of the tumor was only positive for CK7 and completely negative for the other markers (Fig. 2). The immunohistochemical profile in accordance with the morphological findings, confirmed the diagnosis of a collision tumor composed of two histologically distinct cell lineages including a colorectal adenocarcinoma and pancreatic ductal adenocarcinoma.

Molecular studies were carried out in the original pancreatic biopsy and in resection specimen, both of which revealed the same specific KRAS mutation in the pancreatic component of the tumor. As expected, this mutation was not found in the colonic adenocarcinoma.

After surgery, the multidisciplinary oncology committee decided to follow up closely without adjuvant treatment due to her low performance status. Four months later the patient presented with abdominal pain and jaundice related to the pancreatic mass which had grown and currently blocked the common bile duct. Even though an emergency biliary drainage was performed, the patient died a few weeks later in palliative care.

Written consent was obtained from the patient´s son.

Discussion

Collison tumors are rare entities in which at least two distinct tumor types involve the same organ site without histological mixing of the two neoplastic components[1]. The interest of reporting CTs focuses on different aspects. First, their rare localization in the large and small intestine make them an attractive field of research.

Figura 1 | Collision tumor of rectosigmoid region. Macroscopic and microscopic examination. A: Resected specimen with an exophytic mass of 2.5 cm involving colonic wall with extension into the subserosa. Independent tumoral components were indistinguishable at macroscopic examination. B and C: Histological sections (H&E) showed two different phenotypes of adenocarcinomas with intestinal (right) and pancreatic patterns (left). D: Areas of adenomatous high-grade dysplasia of intestinal type were seen on the edge of the ulcer. Original magnification: 40x (B and D); 100x (C)

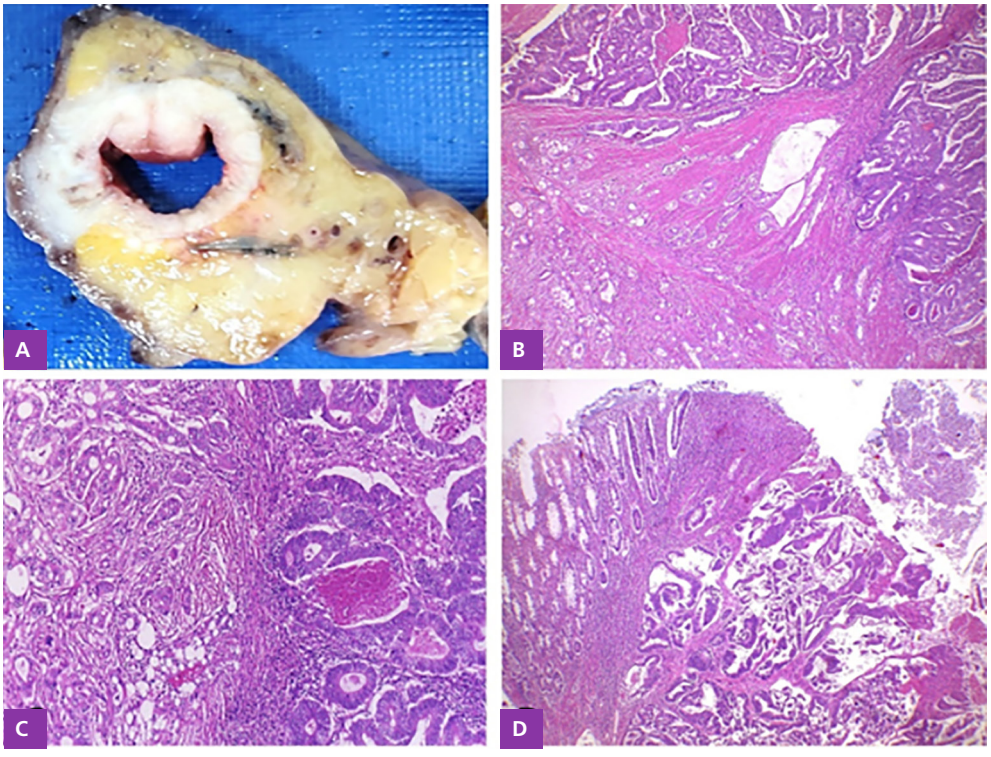
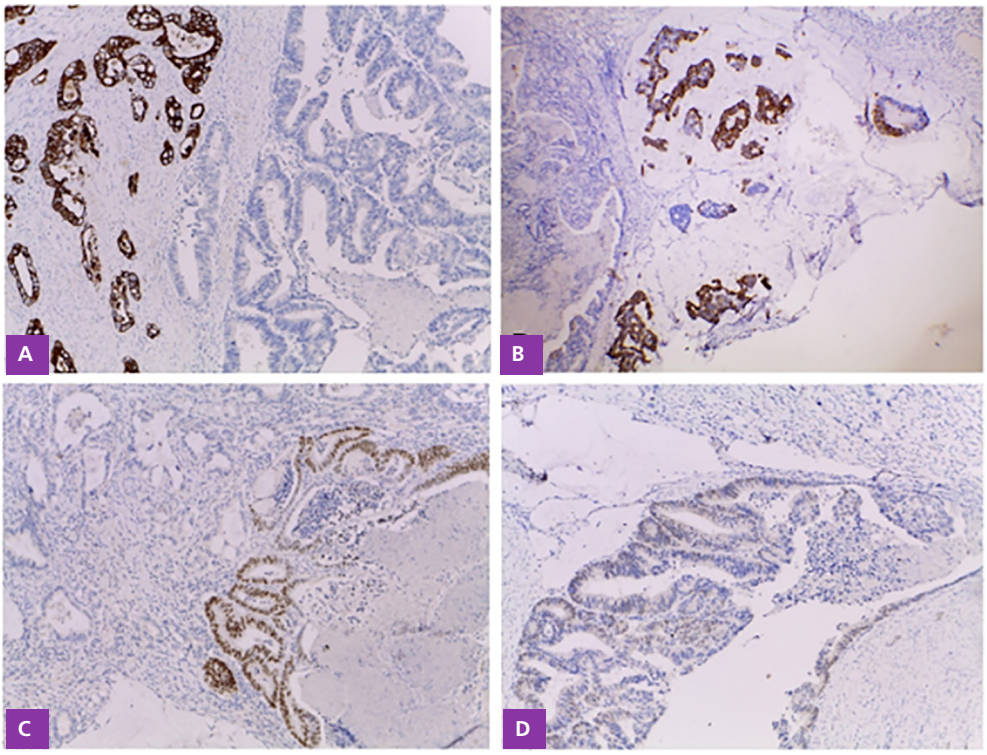


Figura 2 | Immunohistochemical techniques. Colorectal immunoprofile (positivity with CK20, SATB2 and CDX2, and negativity with CK7) and pancreatic immunoprofile (negativity with CK20, SATB2 and CDX2, and positivity with CK7) were confirmed in the same tumor mass, without intermixture of the different malignant components. A: CK7 (cytokeratin 7). B: CK20 (cytokeratin 20). C: SATB2 (special AT-rich sequence-binding protein 2). D: CDX2 (caudal type homeobox 2). Original magnification: 100x



Several studies have reported colorectal CTs including associations between adenocarcinomas and other neoplastic cell lineages most of them lymphomas or neuroendocrine tumors. However, more infrequent associations between adenocarcinomas and other neoplastic types such as transitional cell carcinomas or leiomyosarcomas were also described[3-10]. It is even rarer to find a colorectal CT composed of two adenocarcinomas with different phenotype. Even though, occasional neoplasms consisting of intestinal and gastric adenocarcinomas in this unusual location were published in the literature[1,2]. Interestingly, here we reported a case of a rectosigmoid lesion comprised of two morphological types of atypical glandular proliferations with immunohistochemical and molecular profiles consistent with colorectal and pancreatic ductal adenocarcinomas, which is an extremely rare presentation.

The second point of interest is related to the difficulty in the diagnosis of CTs before surgery. Given that no specific radiological or clinical features for CTs were described, the diagnosis is often incidental during pathological evaluation of surgical specimens[1,4]. These results highlight the importance of an exhaustive sampling and histological examination of these lesions for an accurate diagnosis. Immunohistochemical study is a useful tool for neoplastic lesions where different tumor lineages are not so clear by morphology. Interestingly, in our case, the two neoplastic components were indistinguishable on macroscopic examination, but a clear boundary between them could be identified by histology. Due to the unexpectedness of this finding, immunohistochemical and molecular techniques were carried out and confirmed the diagnosis.

Finally, it has been reported that the presence of different histological components significantly increases the complexity of the therapeutic approach[4]. Nonetheless, the only available data in relation to treatment strategies for CTs comes from rare case reports or small series. Although

no standard therapeutic guidelines exist for the management of these patients, some studies suggest that treatment should target the most aggressive component[2]. However, it is very difficult to predict if long-term outcome will depend on the predominant element or the more histologically aggressive lineage. In a case reported by Miyamoto et al, the peritoneal dissemination of the gastric adenocarcinoma was assumed as the most aggressive element in comparison to colonic one[1]. In our case, we may assume that pancreatic ductal adenocarcinoma was the most aggressive component, based on the known poor prognosis of these neoplasms[11]. However, the only metastatic lymph node was of colonic adenocarcinoma. Even though the patient was in advance stage of cancer because of the liver metastasis, the emergency rectosigmoid resection was imperative and the liver masses could not be biopsied to determine their tumor lineage. This controversial finding emphasizes the uncertainty in predicting which component has predominant behavioral features.

In conclusion, we present a rare case of a rectosigmoid CT with immunohistochemical and molecular profiles consistent with colorectal and pancreatic ductal adenocarcinomas. This case outlines the effectiveness of an exhaustive sampling and the importance of histomorphological, immunohistochemical and molecular studies to increase diagnostic accuracy. We underline the importance of a multidisciplinary teamwork to deal with these complex patients and encourage the report of CTs to expand the knowledge of this interesting entity.

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Conflicts of interest: None to declare

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