Controversial origin of \textit{Pseudomyxoma peritonei}

Alejandro Rojo Sebastián, Francisco José Fernández Morejón, Pedro Bretcha Boix, José Farré Alegre, Jerónimo Forteza Vila and Antonio Brugarolas Masllorens

Plataforma Oncológica. USP Hospital San Jaime. Torrevieja, Alicante. Spain.

\textit{Pseudomyxoma peritonei} describes the accumulation of mucinous material in the abdominal cavity. The main diagnostic problem appears when the primary site of origin could be appendix or ovary. In this paper describe clinicopathological features and biological markers that support appendiceal origin.

\textbf{Key words: pseudomyxoma peritonei, peritoneal implants, mucinous adenocarcinoma.}

INTRODUCTION

\textit{Pseudomyxoma peritonei} is a clinical concept which describes the presence of mucinous material within the abdominal cavity. The etiology includes both benign and malignant neoplasms, thus it could be difficult to determine the origin and grade of malignancy. We report a case of a 75 years-old woman with \textit{pseudomyxoma peritonei} of supposed clinical ovarian origin.

CLINICAL CASE

75 years-old woman without any familiar or personal history that presents urinary incontinence. The abdomen was distended without feeling masses. TAC and RMN reveal a great multicystic mass in the left ovary, suggestive of primary ovarian carcinoma. The value of tumor markers were CA 125: 14.6 U/ml (N < 55 U/ml), CA 19.9: 55.9 U/ml (N < 25 U/ml) and CEA: 58.5 ng/ml (N < 5 ng/ml). Two weeks later the patient underwent surgery; the Pathology Department receives left anexectomy and a great amount of mucinous material (5 kg). Grossly, the tumour (580 g, 15 x 14 x 8 cm) was multicystic and had thin walls (< 5 mm of thickness) with mucous content (fig. 1). The intraoperative study reveals atypical cells in the mucinous deposits (fig. 2) and no infiltrative mucinous ovarian tumour in frozen section; the intraoperative

Correspondence: A. Rojo Sebastián.
Departamento de Anatomía Patológica.
Plataforma Oncológica, USP Hospital San Jaime.
C/ Partida de la Loma, s/n.
03180 Torrevieja, Alicante, Spain.
E-mail: arojo@hotmail.com

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Fig. 3. Mucinous epithelium with calcified perforated wall in appendix.

diagnosis was "mucinous carcinoma," making suggestion of appendiceal review. Short time later is received the appendix with mucinous external implant (fig. 1), and calcified perforated walls. Frozen section reveals a primary mucinous appendiceal tumour with papillary architecture (fig. 3).

Definitive study shows atypical cells in peritoneal implants (carcinomatosis) and non-invasive tumoral nests in ovary with well differentiated epithelial cells. Appendix shows papillary lining with mild atypical cells without stromal invasion, although calcified tumoral tissue was connected between serosal and luminal surface.

Immunohistotypic pattern was cytokeratin 20 positive and cytokeratin 7 negative. Analysis of clonal nature was done to study of K-ras mutations, showing the same point mutation G12S in heterocigosis in the ovarian, appendiceal and peritoneal tumours.

In summary, the patient had a mucinous adenocarcinoma of appendiceal origin with ovarian and peritoneal extension. The therapy was cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (Sugarbaker procedure).

DISCUSSION

The definition of pseudomyxoma peritonei is controversial. Some authors use this term to describe the finding of mucoid material in the abdominal cavity, apart from having epithelial cells; others advise to use only when the mucous contain epithelial cells, whereas another groups need the presence of fibrous stisual response to differentiate it from spillage of mucous or tumour rupture during surgery. This problem explains the differences in prognosis between reported series depending on used criteria.

To avoid this problem, Scully et al. advise to specify the term "acellular" or "cellular" in all cases of pseudomyxoma peritonei; when are acellular (mucinous ascitis) the prognosis is good, whereas the cases of cellular ascitis the source can be a low grade (adenomuciosis) or high grade (carcinomatosis) tumour. The primary site can arise from gastrointestinal tract, having gastric, pancreatic and biliar origin special features which help their distinction.

The measurement of tumour markers serves like diagnostic and prognostic tool. Carcinoembryonic antigen (CEA) is a glycoprotein used like colorectal carcinoma marker, and has been shown to correlate with stage of the disease, degree of differentiation and tumour burden. CA 19.9 shows more association with hepatopancreatoiliary disease, although elevated CA 19.9 has been reported also in nearly 50% of patients with gastric or colorectal malignancies in advanced cases.

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The main problem arises when it is necessary to make a distinction between supposed ovarian or appendiceal origin, as long as they have similar features. The possibility of coexistence of ovarian and appendiceal tumour is broadly known, without certainty whether they have metastasis or have an independent origin. There are a lot of suggested features trying to clarify the origin of primary tumour. Features that favour an appendiceal origin are ovarian bilaterality, presence of loose and/or signet ring cells, tumoral necrosis (and others). On the other hand features that favour ovarian origin are unilaterality (especially left side), large size (> 10 cm) and presence of benign epithelial cells. Immunohistochemistry has been a great aid because appendiceal carcinoma is usually cytokeratin 7 negative, cytokeratin 20 positive and CEA positive, whereas ovarian carcinoma is cytokeratin 7 positive, cytokeratin 20 positive and CEA negative. Although there is not unanimity yet, a majority of investigators believe that the primary tumour origin is the appendix.

A clinicopathologic study with comparative analysis of K-ras mutations in six cases of synchronous ovarian-appendiceal tumours showed identical mutational patterns in all them. Because K-ras mutations are considered to represent an early event in tumorigenesis, this result supports a clonal nature of studied tumours.

The malignancy criteria in appendiceal tumours are presence of destructive invasion of the wall, high-grade cytologic atypia and complex epithelial proliferation. When the tumour lacks this features, the division between benign and malignant neoplasm can be very difficult. Misdraji, with a follow-up study in 107 cases of appendiceal mucinous neoplasms, conclude that tumours who can be placed in the low-grade group with peritoneal spread have worse prognosis (10 years survival rate of 45%) than low-grade