

Case report

Malignant peritoneal mesothelioma in a woman with bilateral ovarian serous borderline tumour: Potential interactions between the two diseases

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ABSTRACT

We report a case of a 59-year-old woman with peritoneal malignant mesothelioma and no previous exposure to asbestos with a diagnosis of bilateral ovarian serous borderline tumour with peritoneal implants one year before. We discuss the histopathological and immunohistochemical findings to explain possible and potential interactions between the two diseases. To our knowledge, the association of both serous borderline ovarian tumour and malignant peritoneal mesothelioma has never been described before in the same woman and in such a tight temporal connection. This finding raises numerous issues about the origin of the two tumours and further biomolecular studies are needed to fully understand the carcinogenetic process. From a clinical point of view, this case report can be useful to gynaecologists because it leads to recommend a careful examination of the peritoneal cavity during a surgical resection of borderline serous tumour. Moreover, it may suggest performing a close follow-up associated with a careful surveillance of the patient, especially in the case of micropapillary pattern, to oncologists. A complete clinical approach could help to detect sooner possible relapses or other metachronous malignancies.

1. Introduction

Malignant peritoneal mesothelioma is a fatal and aggressive disease and the clinical and morphological distinction from serous ovarian neoplasms can be difficult. Ovarian serous borderline tumour is usually confined to the ovary and has an indolent course; however, certain clinicopathological features, such as the presence of a micropapillary pattern, microinvasion and extraovarian implants have been linked to a more aggressive disease (Malpica and Wong, 2016).

In this manuscript, we describe a case of malignant peritoneal mesothelioma in a woman with bilateral ovarian serous borderline tumour. To our knowledge, the association of these two pathologies has not yet been reported in previous articles.

2. Clinical history

A 59-year-old woman with no family history of cancer, an unknown BRCA status and no previous exposure to asbestos was referred to our hospital for abdominal pain and large bowel obstruction. One year prior

to this referral, she underwent a previous surgery consisting in bilateral salpingo-oophorectomy with removal of a macroscopically unharmed omental flap measuring approximately 8 cm × 5 cm × 1 cm. The patient had a pre-surgical interview and refused to undergo a more radical treatment. For this reason the uterus was left in place. The diagnosis of bilateral serous borderline ovarian tumour (SBOT) with micropapillary pattern (Fig. 1), with an additional surface component was made. Non invasive implants located in the omentum flap were found on random biopsies and observed only at the microscopical examination. The stage of tumour was III2A according to the recent Prat et al. (2017). At the end of the surgery no macroscopical residual disease remained. No type of surveillance has been made to the patient. Post operative treatment was not given because the patient refused additional therapy.

The second surgery was performed under emergency conditions for abdominal pain and large bowel obstruction as reported above. For this reason, no preoperative diagnosis was made. No intraoperative frozen section was performed.

Intraoperative findings showed an abdominal mass 20 centimetre wide infiltrating the uterus and the intestinal wall in addition to

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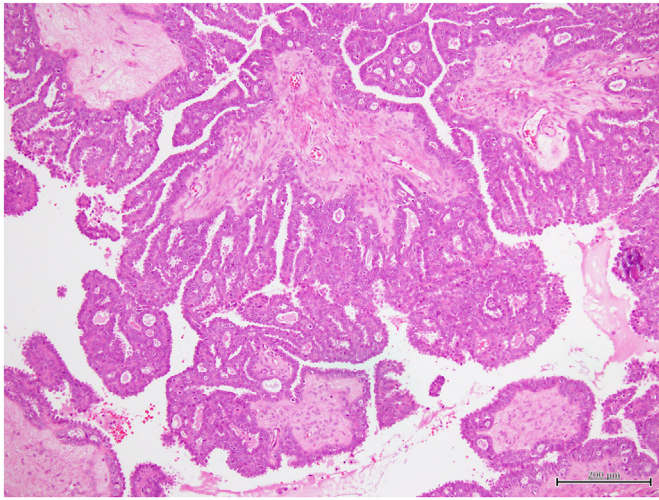


Fig. 1. The figure shows serous borderline tumour referred to the first surgery.

multiple omental masses and numerous peritoneal nodules. She underwent suboptimal debulking surgery, consisting of a total hysterectomy, omentectomy, left hemicolectomy and rectal resection. The surgery was sub-optimal due to the large extent of the disease which involved the abdomen wall and the left ileopsoas muscle. The occurrence of deep vein thrombosis and massive peritoneal relapse contributed to a general worsening of the patient's health and of a deterioration of clinical features. The woman deceased after three weeks.

3. Materials and methods

The surgical specimens were formalin-fixed and paraffin embedded. Immunohistochemistry was performed using primary monoclonal antibodies against Calretinin, Cytokeratin (CK) 5/6, CK7, CK8-18, CK19, D2-40, WT-1, BAP-1, Estrogen and Progesterone Receptors, PAX-8, Ki-67, p16, CEA with a Benchmark XT Automating Staining System (Ventana). Except for BAP-1 (Santa Cruz, 1:70) and Ki-67 (DAKO, 1:100), all the antibodies were provided by Roche company as pre-diluted.

4. Results

A histopathological examination of the resected specimens referring to the abdominal mass infiltrating the large bowel (second surgery) revealed the presence of polygonal or cuboidal tumour cells with well-demarcated borders, moderate atypia and variably prominent nucleoli. The mitoses are often present and the neoplasia revealed several foci of necrosis (Fig. 2A). These features led us to define an histological diagnosis of epithelioid malignant mesothelioma. This lesion, furtherly characterized by solid pattern, infiltrated all the specimens and the

intestinal resection margins. Interestingly, there was the presence in the mass of residual non invasive implants of the previous serous borderline tumour (Fig. 2B).

The immunohistochemistry revealed differences between the two tumours. Calretinin was strongly positive in mesothelioma cells while negative in SBOT and its implants (Fig. 3A and B). Cytokeratin (CK) 5-6 and D2-40 staining were negative in both the tumours. WT1 was focally and weakly positive only in SBOT cells while BAP-1 showed a greater positivity in mesothelioma than in SBOT (Fig. 4). Both mesothelioma and SBOT were positive for PAX-8, CK 7, 8, 18; CK19 showed a focal staining in very few mesothelioma cells. The proliferative activity was higher in mesothelioma (90%) than in SBOT (10%). The p53 staining was positive in the majority of mesothelioma cells but only in scattered few SBOT cells. The Estrogen and Progesterone receptors resulted to be positive in SBOT but not in mesothelioma (Fig. 3C). CEA was negative in both tumours and CA-125 was negative in mesothelioma but positive in SBOT. p16 was not expressed or a focal expression was seen in SBOT. Fig. 4 shows a representative staining of several markers. Only on mesothelioma, S-100 and melanoma cocktail to exclude a metastasis of melanoma were performed; to exclude GIST, c-kit and DOG-1, and to exclude a desmoplastic tumour round cells, Caldesmon, desmin and actin. All these markers revealed to be negative.

5. Discussion

To our knowledge, the presence of both bilateral serous borderline ovarian tumour (SBOT) and malignant peritoneal mesothelioma has never been described before in the same woman and in such a tight temporal connection. We believe that this new association raises numerous issues concerning the origin of the two tumours. Different hypotheses could be considered. We think that they may be classified as metachronous tumours or, a particular and less likely hypothesis could suggest a common, intended as shared, histogenetic pathway for these tumours. This can be related to the fact that the ovarian surface epithelium (OSE), the peritoneum, and subjacent connective tissue all originate from pleuripotential embryonic coelomic epithelium and subcoelomic mesenchyme (Auersperg et al., 2001). This epithelium, in the embryonic development, overlies the mesonephros, the mesodermally derived epithelium lining of the intraembryonic coelom. It overlies the presumptive gonadal area and, by proliferation and differentiation, gives rise to part of gonadal blastema. In addition, the coelomic epithelium originates, near the gonads for invagination, the Mullerian (paramesonephric) ducts, the primordia for the epithelia of the oviduct, endometrium, and endocervix (Sajjad, 2010). Thus, the coelomic epithelium in and near the gonadal area represents an embryonic field with the capability of differentiating along many different pathways. Several differences characterize the two parts of the pelvic mesothelium; the OSE is less differentiated and less committed to a mature mesothelial phenotype than the remainder of the pelvic peritoneum. CA125 is absent or rarely expressed in OSE while is expressed in extraovarian mesothelium (Jacobs and Bast Jr., 1989). These

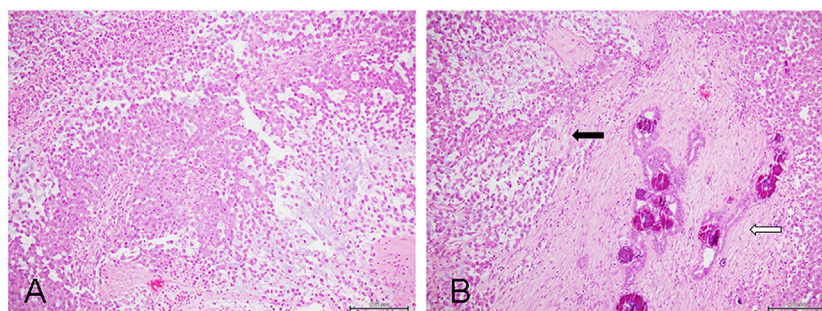


Fig. 2. Malignant mesothelioma (A) referred to the second surgery. Box B depicts the mesothelioma, highlighted by the black arrow, with residual microscopic non invasive implants of the previous serous borderline tumour with associated psammoma bodies, indicated by the white arrow.

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