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Müllerian Tumor Originating from the Pleura in a 47-Years Old Woman: A Case Report

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Abstract

Introduction: Malignant müllerian tumors usually originate from the female genital tract as müllerian ducts develop during embryogenesis to form fallopian tubes, uterus and the upper third of the vagina. An extragenital origination occurs infrequently, but it has been mainly described in the peritoneum or retroperitoneum.

Case Presentation: We report the case of a 47-years old woman presented with thoracic pain progressively worsening and cough. A chest CT revealed right pleural effusion and a paramediastinic nodule. She underwent a video-assisted-toracoscopy with pleural biopsies. The immunohistochemical profile observed, particularly the positivity for WT-1 and PAX-8, together with the negativity of other lineage-specific markers allowed us to lead to the diagnosis of Primary Müllerian tumor of the pleura.

Discussion: PAX8 is a very useful marker for diagnosing carcinomas of müllerian origin. Besides, our patient received chemotherapy with carboplatin-paclitaxel and bevacizumab followed by bevacizumab maintenance, achieving a long lasting stable disease. To our knowledge, this is the second case of primary pleural müllerian tumor up to now report in the literature.

Keywords: Extra-genital müllerian tumors; PAX-8; Pleura; WT-1

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Introduction

Malignant müllerian tumors usually originate from the female genital tract as müllerian ducts develop during embryogenesis to form fallopian tubes, uterus and the upper third of the vagina. An extragenital origination occurs infrequently, but it has been mainly described in the peritoneum or retroperitoneum [1]. Here, we report the case of a primary müllerian tumor originating from the pleural surface. To our knowledge, this seems to be the second case of primary pleural müllerian tumor up to now reported in the literature [2].

Case Presentation

A 47-years old woman started to complain thoracic pain progressively worsening and cough. Chest X ray revealed pleural effusion and subsequently a CT scan of abdomen and chest (Figure 1A) confirmed right pleural effusion and showed a paramediastinic nodule (16 x 18 mm) in absence of ascites or abdominal mass, and the uterus and the ovaries were described as normal. A PET/CT (Figure 1B,C and D) showed slight increased uptake in the paramediastinal lesion and in the right parietal pleura, without other area of pathological accumulation in the remaining part of the body. She underwent a video-assisted-thoracoscopy with pleural biopsies. The biopsy material consisted of fragments of parietal pleura with chronic fibrosing pleuritis and foci of poorly differentiated adenocarcinoma both infiltrating the connective tissue (Figure 2) and superficially spreading between the reactive mesothelium (Figure 3). Neoplastic cells were focally aggregated in papillary structures containing occasional psammoma bodies (Figure 2A). No benign tubal epithelium was described in the pleura. A similar histopathological picture imposes a differential diagnosis between a metastatic carcinoma, conceivably from ovary or lung and a mesothelioma. The immunohistochemical profile observed (Table 1), particularly the positivity for WT-1 and PAX-8 (Figure 2E and F) together with the negativity of other lineage-specific markers, particularly calretinin (Figure 2B,C and D), allowed us to exclude all these possibilities being the picture very consistent with a müllerian origin [3-

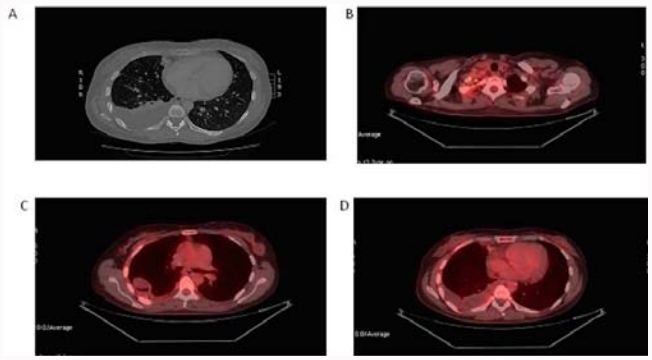

Figure 1: CT scan revealed right pleural effusion with paramediastinic mass (**A**) and PET/CT showed slight increased uptake in the paramediastinic lesion and in the right parietal pleura (**B-D**), in particular in the apical portion (**B**).

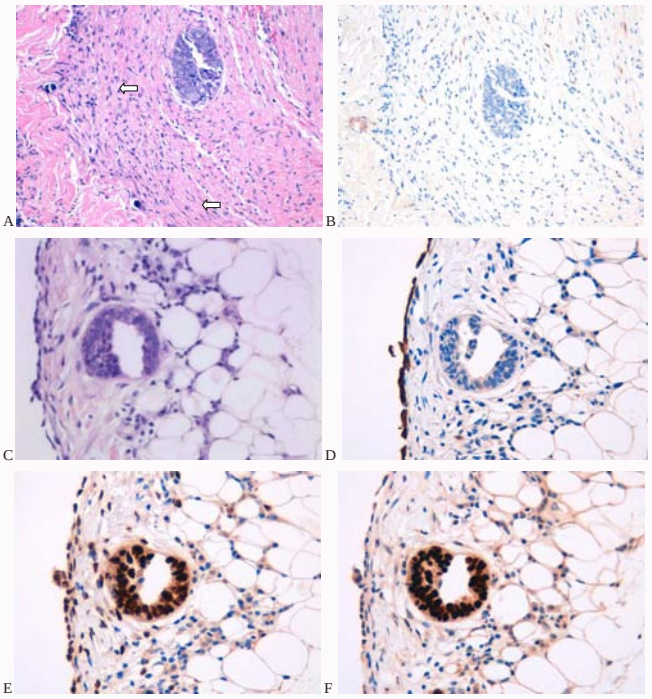

Figure 2: Primary Mullerian tumor of the pleura. A. Poorly differentiated carcinoma infiltrating the connettive tissue of the parietal pleura with adiacent psammoma bodies (arrows). B. Negative calretinin expression of the same malignant proliferation as in figure 2A. C. H&E of malignant glandular structure infiltrating the adipose tissue of the parietal pleura. D. Superficial mesothelium show calretinin positive stain whereas malignant infiltrating proliferation is negative. E. WT-1 immunoreactivity in neoplastic gland. F. The same neoplastic structure shows PAX-8 positive immunostain. Original Magnification x20 (A, B), x40 (C, D, E, F).

6]. Therefore the final diagnosis was Primary Müllerian tumor of the pleura.

Six courses of chemotherapy were administered with carboplatin-paclitaxel, and bevacizumab. A CT scan after 6 cycles revealed reduction of pleural effusion. Currently she is well and she continues receiving bevacizumab as maintenance therapy. A longitudinal observation of the patient, with a follow up of 12 months after diagnosis, confirms the stable pleural disease, without pelvic or peritoneal lesions on CT scan or other areas of pathological accumulation on PET.

Discussion

Peritoneum and its adjacent mesenchyme have a müllerian

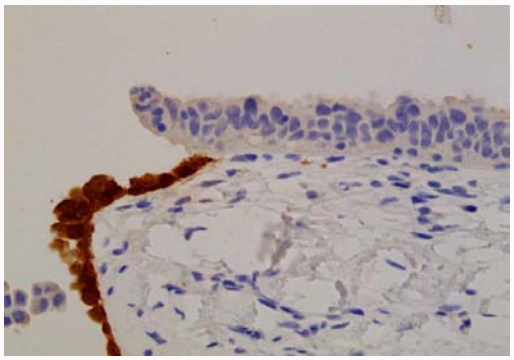

Figure 3: Primary Müllerian tumor of the pleura. Poorly differentiated adenocarcinoma both infiltrating the connective tissue and superficially spreading between the reactive mesothelium. Superficial area of the tumor showing negativity for calretinin, the adjacent mesothelium (left) is positive.

Table 1: Immunohistochemical profile of the case described.

ANTIBODY	CLONE	RESULT
CYTOKERATIN 7	OV-TL12/30	positive
TTF-1	8G7G3/1	negative
NAPSIN	IP64	negative
CALRETININ	5°5	negative
CA125	OV185:1	negative
WT-1	WT49	positive
BER-EP4	BER-EP4	positive
MOC-31	MOC-31	positive
ER	6F11	focally positive
D2-40	D2-40	negative
HBME-1	HBME-1	negative
CYTOKERATIN 5/6	D5/16B4	negative
CALDESMON	h-CD	negative
CYTOKERATIN 20	KS20.8	negative
CD141	15C8	negative
PAX8	PAX8 Rabbit Polyclonal Antibody	positive

potential because they share mesodermal ancestry with the primary müllerian system, which derives from invaginated coelomic epithelium. Lauchlan [7] extensively described these lesions in 1972, hypothesizing the existence of the "secondary müllerian system". Extregenital müllerian neoplasms have been reported not only in women, but also in men [8]. In literature there is only another case of a müllerian tumor originating from the pleura, and not from ovaries or peritoneum. This could be explained in that also pleura share the same embryological origin of the peritoneum.

In our case, pleural biopsies revealed a neoplastic epithelial component forming papillary structures and containing psammoma bodies. Immunohistochemistry showed positivity for WT-1, BerEp4, MOC-31, PAX-8, ER; negativity for: calretinin, TTF-1, HBME-1, D2-40, cytokeratin 5/6, caldesmon, cytokeratin 20, CD 141. Overall, the staining for epithelial glycoproteins (Ber-EP4 and MOC-31) and the lack of calretinin and CK5/6 staining was felt not to support a mesothelial differentiation. Immunohistochemistry contrasted also with a pulmonary origin (TTF1-). Positivity of ER, WT-1 and PAX-8 was highly suggestive for pleural malignant müllerian neoplasm. Few specific immunohistochemical markers are available for

carcinomas of müllerian origin. ER, PR and WT1 have been used in combination with other immunohistochemical markers to suggest possible müllerian origin, however, their relatively low specificity is well known. ER and PR are present in breast carcinomas in addition to other gynecologic tumors. WT1, a nuclear transcription factor important for the development of the müllerian duct system, has been used as a surrogate marker for ovarian carcinoma. WT1 is also detected in benign and malignant mesothelial cells. PAX8 is a member of the PAX gene family encoding for nine well-characterized transcription factors. PAX8 is detected in the specialized precursor cells of the müllerian ducts in the coelomic epithelium in the early embryonic stage [9]. The müllerian ducts subsequently separated from the coelomic epithelium, grow caudally and in female fetus eventually become fused at the midline to form the uterine corpus and cervix and the upper third of vagina. The non-fused portions form the fallopian tubes and fimbrial ends. Remnants of the most proximal müllerian ducts that do not participate in organogenesis constitute the secondary müllerian system which is hypothesized to be the source of ovarian and paraovarian disorders including the so called müllerianosis (endometriosis, endocervicosis and endosalpingiosis), epithelial ovary carcinomas and peritoneal serous carcinomas [10]. All these tissues, both normal, ectopic and neoplastic, consistently express PAX8 [3,6].

Therefore PAX8 is a very useful marker for diagnosing carcinomas of Mullerian origin in serous effusions, which can help us to distinguish between müllerian from non-müllerian origin of metastatic carcinoma (including breast, lung, pancreas, gastrointestinal tract and malignant mesothelioma) [3-5]. Conceivably the case described herein and the other reported so far [2] might be derived from embryonic remnants of the cranial portion of the primitive coelomic epithelium. In our patient it was decided to administer chemotherapy with carboplatin-paclitaxel and bevacizumab, as müllerian tumors of ovarian or peritoneal origin typically are responsive to this regimen. A CT scan after 6 cycles showed reduction of pleural effusion. She continues receiving bevacizumab as maintenance therapy with substantial stable disease at 12 months from diagnosis.

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