Slide Seminar "Difficult cases in Gynecological Pathology"- Case 2

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Clinical history

A 27-year old woman, 4 months long history of dry cough and dyspnea on exertion. Hospitalized (March 2009) with right-sided pleural effusion, ascites, clinical suspicion of malignancy in the omentum and peritoneum, and enlarged lymph nodes in the retroperitoneum and mediastinum.

Pathological findings

Pleural effusion tapped at another hospital prior to admission to our hospital was reported as reactive at that hospital, as well by a consultant at the Norwegian Radium Hospital. The patient was tapped again for pleural effusion, as well as for ascites, and underwent bone marrow and peritoneal biopsy. All specimens showed proliferation of small cells with irregular cell and nuclear form, high n/c ratio, even chromatin and prominent nucleoli. Mitoses were few. Biopsy from the peritoneum showed diffuse infiltration by tumor cells which grew without any specific formation, with variable amount of intervening stroma.

By immunohistochemistry (IHC), tumor cells in the bone marrow expressed Estrogen and Progesterone receptors and pan-cytokeratin (punctate), and were negative for hematological markers. Cells in the peritoneal tumor diffusely expressed hormone receptors and were positive for both vimentin and pan-cytokeratin. Tumor cells in the pleural effusion were immunohistochemically positive for hormone receptors and CD99, and expressed Fli-1 and c-Kit focally. Tumor cells in the pleural effusion were further positive for CD56 and CD99 by flow cytometry.
Molecular analysis of fresh viable cells from a subsequent pleural effusion was negative for EWSR1-FLI1, EWSR1-ERG, PAX3/7-FOXO1, SS18-SSX1/2/4 translocation, excluding Ewing sarcoma, alveolar rhabdomyosarcoma and synovial sarcoma. Cytogenetic analysis showed abnormal karyotype suggestive of malignancy, not informative of a specific diagnosis.

Based on the combined results from analysis of all specimens, the following diagnosis was reached:

PERITONEAL BIOPSY WITH A MALIGNANT SMALL CELL TUMOR, SUGGESTIVE OF SMALL CELL CARCINOMA

Follow-up

The patient was treated by chemotherapy (6 courses of BEP and EP), blood transfusions and effusion tapping. She additionally received anti-hormonal therapy with good response, but treatment was discontinued due to side-effects. She developed two recurrences in the peritoneum and one probable recurrence in the endometrium. The tumor in the peritoneum developed a new morphological feature, i.e. the presence of larger cells with more prominent atypia and mitotic activity, which were interpreted of having rhabdoid features. The tumor was again immunostained with a broad panel of markers in order to exclude hematological malignancy, sarcoma, melanoma, mesothelioma and germ cell tumor, but the immunophenotype was essentially unaltered. The patient was treated by Taxol, but died of disease October 2010.

Discussion

Small cell carcinomas of the genital tract are rare aggressive tumors that often affect young women. They are most often localized to the cervix, but may be found in the vulva, endometrium, fallopian tube and ovary [1]. In the latter organ, they may be of the hypercalcemic type or pulmonary (neuroendocrine) type [2-3]. A PubMed search undertaken by the presenter of this case generated only 3 previous reports of primary peritoneal small cell carcinoma, of which one was of the large cell hypercalcemic type, thereby different from the presented case [4-6]. Notably, the tumor reported by Ordóñez et al. [4] co-expressed cytokeratin and vimentin, as the presented tumor did, though the former was additionally desmin-positive.

The differential diagnosis of tumors that morphologically resemble the current case, when in the ovary, is broad and consists primarily of small blue round cell tumors, including intra-abdominal desmoplastic small round cell tumor, PNET, Ewing sarcoma, rhabdomyosarcoma and hematological cancers. Neuroblastoma, melanoma, synovial sarcoma, angiosarcoma, germ cell and sex cord tumors and mesothelioma additionally need to be considered. All these

entities have been effectively excluded in the present case by repeated IHC analyses and by the flow cytometry and molecular analyses performed on fresh material. Another entity, endometrial stromal sarcoma, has been the main differential diagnosis in this case, especially in view of the pronounced and consistent expression of hormone receptors by tumor cells. However, the absence of CD10 expression and the expression of Ber-EP4 and CD56 in flow cytometry analysis essentially rule out this diagnosis. While the absence of chromogranin and synaptophysin expression is not characteristic of small cell carcinomas, the morphology of the tumor and CD56 expression, combined with the absence of other markers, suggest a poorly differentiated small cell carcinoma in our opinion.

References

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