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Ovarian Clear Cell Adenofibroma of Low Malignant Potential developing into Clear Cell Adenocarcinoma.

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Figures 2

Our institution does not require IRB review or consent for case reports. The case has been deidentified.

Precise: A rare case of borderline clear cell adenofibroma giving rise to clear cell adenocarcinoma is presented

Keywords: clear cell adenocarcinoma, adenofibroma, pathology, ovarian neoplasms

Abstract:

Ovarian clear cell adenofibroma is uncommon, and borderline clear cell adenofibroma (low malignant potential) is extremely rare. Borderline clear cell adenofibromas may represent the precursor lesion of clear cell adenocarcinoma of the ovary, but this has not been established.

We present a case of a woman in her mid-fifties with a clear cell adenofibroma ranging from benign to borderline to frankly invasive. While some clear cell adenocarcinomas are thought to arise from endometriosis, this range of findings supports the theory that some ovarian clear cell adenocarcinomas originate from borderline tumors.

Introduction:

Clear cell adenocarcinoma (CCA) is a high grade ovarian carcinoma, accounting for approximately 5% of all ovarian malignancies ⁽¹⁾. As with other types of ovarian carcinoma, their signs and symptoms are nonspecific; about one third of CCA present with extrapelvic metastasis at diagnosis ⁽²⁾. CCA is frequently associated with endometriosis, suggesting at least some CCA develop from endometriosis ⁽³⁾. Some CCAs are associated with clear cell adenofibroma and borderline clear cell adenofibroma ⁽⁴⁾. Benign clear cell adenofibroma is uncommon and borderline ovarian clear cell adenofibromas are very rare. Some authors have speculated that they might be precursors of CCA ⁽⁵⁾. Here, we report a case of CCA with benign and borderline clear cell adenofibromatous components, which supports the theory of malignant transformation.

Case Report:

A woman in her mid-fifties presented with GI bleeding and was found to have a moderately differentiated adenocarcinoma of the sigmoid colon. CT of the abdomen and pelvis also incidentally demonstrated a 6.6 cm mass in the right ovary. Hysterectomy and bilateral salpingectomy-oophorectomy were performed at the same time as the colonic resection.

Pathology

On gross examination, a 6.5 cm cyst was identified in the right ovary, containing yellow/brown serous fluid. The internal lining of the cyst was smooth except for a papillary area measuring 2.5 x 1.5 cm. Adjacent to the cyst was a firm solid mass measured 3 x 2.5 x 2.3 cm.

Histology of the solid area showed glands and microcystic spaces of various sizes distributed in dense fibrous stroma. The lining epithelium of these glands was flat or cuboidal without atypia. Basophilic and eosinophilic secretions were present in the lumen of these glands and stroma around the glands was condensed (Figure 1 A). This was consistent with benign clear cell adenofibroma. Some adjacent glands next to the cyst were lined by hobnail cells with mild to moderate atypia showing enlarged hyperchromatic nuclei and prominent nucleoli (Figure 1 B). This finding was consistent with a borderline adenofibroma. The papillary area which projected into the cyst was lined by one to two layers of atypical hobnail epithelial cells with scant to moderate eosinophilic cytoplasm (Figure 2 A). There were also several foci of solid areas identified and cells in these areas showed clear cytoplasm and pleomorphic high grade features consistent with clear cell adenocarcinoma (Figure 2 B). These solid foci of CCA were adjacent to its benign and borderline adenofibromatous counterparts (Figure 2 C). The neoplastic cells were

positive for Napsin-A (Figure 2 D,E) and negative for WT1 and ER immunostains, which mitigated against papillary serous cystadenocarcinoma (not shown). The diagnosis of clear cell adenocarcinoma arising in a borderline clear cell adenofibroma was rendered. The patient made an uneventful recovery.

Discussion:

Ovarian clear cell tumors are subclassified into benign, borderline, and malignant based on the degree of cytological and architectural atypia and/or the presence or absence of stromal invasion. Benign clear cell adenofibroma consists of small round tubular glands lined by flat or low cuboidal cells lacking nuclear atypia in a background of fibrous stroma. Borderline clear cell adenofibroma shows a similar appearance except that it contains microinvasion (< 5mm) or mild to moderate atypical glandular epithelium. Borderline clear cell tumor is distinguished from CCA by lacking papillary projections into cysts or destructive stromal invasion ⁽²⁾. At times, the lack of cytologic atypia in invasive clear cell adenocarcinoma makes the distinction between benign and malignant difficult, and stromal invasion must be sought.

Another diagnostic challenge is to differentiate CCA with a predominantly papillary pattern from low grade serous papillary adenocarcinoma. The shared papillary architecture, low mitotic index, bland cytology, and occasional eosinophilic cytoplasm are potentially overlapping features. However, usually other growth patterns of CCA can also be recognized in the same tumor including solid and tubulocystic patterns. The papillae of CCA are lined by one to two layers of cells; in contrast, the surface of papillary serous cystadenocarcinoma is lined by pseudostratified cells. The presence of classic hobnail cells or clear cells is another helpful diagnostic feature of CCA. The unilaterality of disease and any coexisting endometriosis are also helpful clues in favor of CCA. Presence of Napsin-A and HNF1B and absence of WT1 and ER expression favor CCA over papillary serous cystadenocarcinoma ^(1, 2).

Clear cell adenofibroma is uncommon, and borderline clear cell adenofibroma is extremely rare. In the present case, a clear cell adenocarcinoma arose from adjacent benign and borderline clear cell adenofibromatous components. This combination of three patterns in one tumor supports the idea that some clear cell adenocarcinomas develop from their benign and borderline counterparts. It has also been speculated that endometriosis induces a fibromatous reaction resulting in the formation of clear cell adenofibromas, which then develop into borderline adenofibromas and eventually CCAs ⁽⁶⁾. There was no endometriosis identified in the current case. In comparison with CCA without a clear cell adenofibroma component, CCA with clear cell adenofibroma showed a higher frequency of low-grade tumor, a lower proliferating index, and better patient prognosis ⁽³⁾.

Declaration of Conflicting Interests:

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Figure 1 Legend: Benign and borderline components in the tumor: Benign clear cell adenofibroma component was identified (A 10 X). Some glandular lining epithelium showed hobnail features with moderate atypia, consistent with borderline adenofibroma (B 40 X).

Figure 2 Legend: Clear cell adenocarcinoma component: The papillae were lined by one to two layers of hobnail atypical epithelial cells with scant to moderate eosinophilic cytoplasm (A 40 X). Cells in multiple foci of solid area showed clear cytoplasm and pleomorphic high grade features (B) 40 X). A focus of CCA (star) is adjacent to borderline (arrowhead) and benign (arrow) clear cell adenofibromatous components (C 10X). The neoplastic cells are positive for Napsin-A stain in the carcinoma and adenofibromatous areas(D40x,E 10X) .

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