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Mixed Ovarian High-Grade Serous and Clear Cell Carcinoma with Unusual Squamous Differentiation: A Histopathological Rarity

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Dear Editor,

Mixed surface epithelial malignancies of the ovary most commonly involve endometrioid and clear cell components, likely due to their shared clonal origin from endometriotic precursors.[1] Also, squamous differentiation is more commonly observed in endometrioid adenocarcinomas of the ovary and is exceedingly rare in other surface epithelial subtypes.[2] A thorough literature review on PubMed revealed only four reported cases of ovarian serous carcinoma with squamous differentiation, all of which involved pure serous tumors.[3–5] Other reports have described primary ovarian squamous cell carcinomas arising from precursor lesions such as ovarian teratomas or endometriosis.[6] Hence, the biological behavior of high-grade serous carcinoma (HGSC) with squamous differentiation remains poorly defined. The present case features a highly unusual combination of HGSC and clear cell carcinoma with serous component exhibiting extensive squamous differentiation by morphology and later confirmed by immunohistochemistry (IHC).

A 60-year-old female patient presented with lower abdominal pain and discomfort. Magnetic resonance imaging of the pelvis performed at an external facility showed a large, fairly well-defined mass lesion with a predominant cystic component and multiple peripheral solid enhancing components in the pelvis, arising from the left adnexa, superior to the uterus and extending into the lower abdomen. Both the ovaries were not seen separately. Metastatic right common iliac and left para-aortic lymph nodes were also seen. Hence, a diagnosis of stage II ovarian carcinoma was given. Serum CA125 levels were high (157 U/mL).

She was then referred to our hospital for further management and underwent staging laparotomy. Intraoperatively, peritoneum was seen densely adherent to the anterior abdominal wall, uterus, and the pelvic mass. A controlled decompression of the mass was done to facilitate resection. The mass was removed in total and type A radical hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and bilateral pelvic and para-aortic lymph node dissection was done after identifying and preserving bilateral ureters and separating the rectum that was densely adherent to the posterior wall of the uterus and the mass.

Gross examination revealed tubo-ovarian masses measuring $6.0 \times 5.0 \times 4.0$ cm on one side and $5.5 \times 3.0 \times 3.0$ cm on the other. The external surfaces of both ovaries were adherent to the peritoneum and the laterality of the bilateral adnexa could not be made out. One side ovary displayed solid areas and a cyst filled with necrotic and friable material. The contralateral ovary appeared entirely solid, gray-yellow, and necrotic.

Microscopically, two distinct malignant epithelial components were identified: 60% of tumor showed serous carcinoma with cells arranged in papillae, solid nests, and sheets with extensive necrosis and neutrophilic abscess formation. Notably, portions of the HGSC component exhibited morphological features mimicking high-grade squamous cell carcinoma, characterized by polygonal to spindle-shaped cells with dense eosinophilic cytoplasm and hyperchromatic nuclei with prominent individual cell keratinization. Note that 40% showed clear cell component with a tubulocystic pattern. The cells were cuboidal and have clear to eosinophilic cytoplasm, vesicular nuclei, and prominent nucleoli; occasional hobnailing was also noted. Examination of the fallopian tube revealed tumor arising from the tubal epithelium with stromal invasion, excluding the possibility of metastatic origin. Tumor deposits were also noted on the ovarian capsule and pelvic peritoneum.

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IHC revealed diffuse PAX8 and p16 (block-type) positivity in the serous component with focal WT1 positivity, and a p53 mutant pattern with strong nuclear staining. The clear cell component showed patchy cytoplasmic granular positivity for Napsin A and diffuse PAX8 and p16 positivity. The squamous component demonstrated diffuse positivity for p63 and CK5/6, focal positivity for PAX8, and negative for estrogen receptor.

Based on histological and immunophenotypic features, a final diagnosis of bilateral mixed ovarian carcinoma comprising HGSC (60%) and clear cell carcinoma (40%) with extensive squamous differentiation was rendered. The patient underwent six cycles of adjuvant chemotherapy and was disease free at 1-year follow-up.

Patient Consent

Patients consent has been obtained.

Authors' Contributions

M.M. contributed to the design, literature search, and manuscript writing. S.R. contributed to the concept, manuscript editing, and review. S.K. contributed to design, manuscript editing, and review. The authors declare that the manuscript has been read and approved by all the authors, the requirements for authorship have been met and this manuscript represents honest work.

Conflict of Interest

None declared.

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