Abstract:
Ovarian metastasis is common in patients with advanced breast cancer. Metastatic breast carcinoma can mimic a primary ovarian carcinoma with similar features making it difficult to differentiate between primary and secondary ovarian carcinomas. PAX8 and Gross Cystic Disease Fluid Protein-15 (GCDFP-15) can be used to differentiate primary ovarian tumor from metastatic breast carcinoma to ovary.

Keyword: PAX8, GCDFP-15, Metastatic breast carcinoma, primary ovarian carcinoma

INTRODUCTION: Ovarian metastasis are seen in 22% to 40% of prophylactic oophorectomy patients with advanced breast cancer\(^1,2\). It is one of the most common tumors metastasizing to ovary next to colon and appendix\(^3\). Women with BRCA1 and BRCA2 mutation are at increased risk for primary breast and ovarian carcinomas, with breast cancer usually occurring first and ovarian cancer diagnosed later in life\(^4\). Since primary and metastatic deposits of breast carcinoma to ovary have similar histomorphological features\(^5\), immunohistochemical markers like PAX8 and GCDFP-15 helps in distinguishing between primary and metastatic breast carcinoma of ovary.

CASE REPORT: Patient was a known case of breast carcinoma, who had underwent mastectomy 5 months ago, completed 6 cycles of chemotherapy and 25 cycles of radiotherapy, presented with abdominal pain and distension of 3 months duration. Imaging with computed tomography revealed a mass lesion in right ovary with ascites and focal lesion in liver. Patient underwent oophorectomy.

GROSS FINDINGS: Ovarian mass measured 13 x 10 x 5.5 cm, fallopian tube could not be made out grossly. External surface appeared nodular. Cut surface revealed predominantly a solid gray white firm tumor composed of discrete nodules with focal yellow and grey brown hemorrhagic areas. Few cystic spaces filled with gelatinous material were seen.
Normal ovarian parenchyma was not made out grossly. (Fig-1)

Fig-1. Cut surface revealed grey white nodules and few cystic spaces

**MICROSCOPIC FINDINGS:**
Histopathological examination revealed a malignant tumor composed of cells arranged in cribriform and glandular pattern, showing areas of comedonecrosis. Individual cells were round and of moderate size with moderate amount of eosinophilic cytoplasm and vesicular nucleus exhibiting pleomorphism and atypia. (Fig-2). Normal ovarian parenchyma was made out in the periphery.

Fig-2.Cribriform and glandular pattern showing comedonecrosis (10x)

**IMMUNOHISTOCHEMISTRY:**
Immunohistochemical staining with Gross Cystic disease fluid protein-15 showed diffuse strong cytoplasmic positivity (Fig-3, 4) and negative for Pax8. (Fig-5)

Fig-3. Diffuse immunoreactivity for GCDFP-15(10x)  Fig-4.Cytoplasmic positivity for GCDFP-15(40x)

Fig-5.Negative reaction for PAX8 (10x)
**DISCUSSION:**

About 7% of lesions presenting clinically as primary ovarian tumors are of metastatic origin. Breast carcinoma metastasizing to ovary is common and constitutes about 8.5% of all metastatic tumors. Patients with BRCA1 & BRCA2 mutation are at increased risk of developing both breast and ovarian carcinomas. Both carcinomas have similar histomorphological features and it may be difficult to distinguish metastatic breast carcinoma from primary ovarian carcinoma. In this scenario, Pax8 and GCDFP-15 are useful. GCDFP-15 is found in breast cystic fluid in abundance. In addition, it is also present in salivary glands, apocrine glands, Paget's disease of skin, vulva and prostate. The positive predictive value and specificity of GCDFP-15 are both reported to be 99%. About 40 to 70% of breast carcinomas, metastatic to ovary, have been reported to be positive for GCDFP-15; whereas primary ovarian carcinomas are almost always negative. GCDFP-15 show strong and focal positivity in metastatic carcinoma of breast to ovary. PAX-8 is a nuclear transcription factor and a useful marker for tumors derived from mullerian system, thyroid glands and metanephros. It is positive in most of the ovarian non-mucinous surface epithelial tumors (serous, endometrioid and clear cell types), renal tumours and thyroid tumours. Gene expression analysis using DNA microarrays showed that PAX8 is more highly expressed in ovarian carcinomas than in breast carcinomas. Breast carcinoma is consistently negative for PAX8.

**CONCLUSION:**

Pathological diagnosis is of utmost importance in differentiating primary and secondary ovarian carcinomas in the management of patients, as chemotherapy agents will differ for each diagnosis. Immunohistochemistry using PAX-8 and GCDFP-15 plays an important role in distinguishing primary ovarian carcinoma from metastatic breast carcinoma to ovary.

**BIBLIOGRAPHY:**


