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IMMUNOHISTOCHEMICAL PROFILING OF ADVANCED-STAGE OVARIAN CANCER WITH PERITONEAL CARCINOMATOSIS

Esankulova B. S.
Nasullayeva M. M.
Samarkand State Medical University

Abstract:
Ovarian cancer remains a leading cause of gynecological cancer-related mortality, with advanced-stage disease (Stage III-IV) often presenting with peritoneal carcinomatosis. Immunohistochemistry (IHC) plays a critical role in characterizing tumor subtypes, guiding treatment decisions, and predicting patient outcomes. This article reviews the current understanding of IHC markers used in ovarian cancer, their prognostic significance, and implications for targeted therapies.

Keywords: Ovarian cancer, immunohistochemistry, peritoneal carcinomatosis, biomarkers, prognosis, targeted therapy.

Introduction:

Ovarian cancer is frequently diagnosed at an advanced stage, often accompanied by peritoneal carcinomatosis, which significantly worsens prognosis. Standard treatment involves cytoreductive surgery followed by chemotherapy; however, molecular profiling via immunohistochemistry has emerged as a pivotal tool for personalized therapeutic strategies.

Immunohistochemical Markers in Ovarian Cancer:

1. **Epithelial Markers:**

- Cytokeratins (CK7, CK20): Aid in distinguishing primary ovarian tumors from metastatic cancers.
- WT1 (Wilms' Tumor 1): Highly sensitive for serous ovarian carcinoma.
- PAX8: A nuclear transcription factor indicative of Müllerian origin, often positive in ovarian carcinoma.

2. **Proliferation and Apoptotic Markers:**
   - Ki-67: Indicates tumor proliferation rate; higher levels correlate with aggressive disease.
   - p53: Frequently mutated in high-grade serous ovarian carcinoma, guiding therapeutic options.
3. **Hormonal Receptors:**
   - Estrogen (ER) and Progesterone Receptors (PR): Expression suggests potential for hormonal therapy.
4. **Angiogenesis and Hypoxia Markers:**
   - VEGF (Vascular Endothelial Growth Factor): Associated with tumor angiogenesis and poorer prognosis.
   - HIF-1α (Hypoxia-Inducible Factor-1α): Overexpressed in hypoxic tumor environments.
5. **Mesenchymal and Adhesion Markers:**
   - N-cadherin and E-cadherin: Indicators of epithelial-mesenchymal transition (EMT) in metastatic spread.
   - Vimentin: Suggests a mesenchymal phenotype and aggressive behavior.
6. **BRCA1/2 and DNA Damage Response Markers:**
   - Loss of BRCA expression can indicate responsiveness to PARP inhibitors.
   - RAD51 foci formation: Predicts response to DNA-damaging agents.

Clinical Implications of Immunohistochemistry in Advanced Ovarian Cancer:

- **Diagnosis and Differential Diagnosis:** IHC helps differentiate ovarian carcinoma from peritoneal metastases of non-gynecologic origin.
- **Prognostic Value:** Certain markers, such as high Ki-67 and p53 mutations, are associated with poor survival.
- **Therapeutic Targeting:** Expression of specific markers allows for targeted therapies, such as PARP inhibitors for BRCA-mutated tumors and anti-angiogenic therapies for VEGF-expressing cancers.

Challenges and Future Directions: Despite the utility of IHC in ovarian cancer, challenges include intratumoral heterogeneity and the need for standardization of scoring systems. Future advancements in molecular pathology may integrate IHC with genomic and proteomic profiling for improved precision medicine.

Conclusion:

Immunohistochemical analysis is indispensable in the management of advanced-stage ovarian cancer with peritoneal carcinomatosis. It provides crucial insights into tumor biology, prognostication, and therapeutic decision-making, ultimately contributing to personalized patient care.