MOLECULAR CHARACTERISTICS AND GENETIC APPROCHES OF ENDOMETRIOSIS- RELATED OVARIAN CANCER

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- INTRODUCTION -

Endometriosis-related ovarian cancer (ERONs)

group of tumors including clear cell carcinoma, endometrioid carcinoma and seromucinous borderline tumors that supports the hypothesis that endometriosis is a cancer precursor.

Endometriosis - benign gynecological condition that affects 5-10% of premenopausal women.

Even it is a benign condition, endometriosis like cancer, is characterized by cell invasion and unrestrained growth.

There are also similarities such as the development of new blood vessels and a decrease in the number of cells undergoing apoptosis.

Even the pathogenesis of endometriosis is still unclear

the possibility that this pathology could, however, transform and become cancer, has been debated in the literature since 1925 by Sampson.

Advances in technology, primarily the ability for whole genome sequencing

->discovery of new mutations and a better understanding of the function of previously identified genes and pathways associated with endometriosis associated ovarian cancers (EAOCs) .

- OBJECTIVES -

The aim of this study is to review the mechanisms whereby genetic and molecular factors can be involved in the neoplastic progression of this pathology.

- MATERIAL AND METHOD -

A sistematic review of the literature was performed. The reasearch was conducted by searching in the PubMed database, by sistematically reviewing the original references from retrieved studies. Finally, we eliminated the duplicates and a number of 35 aticles were selected.

- RESULTS -

- ERONs has different prevalence: approximately 30%-60% are endometrioid carcinoma, 20% -35% clear cell carcinoma, 5%-10% serous carcinoma and 4%-10 % mucinous carcinoma and only 15% of cases are postmenopausal.
- Molecular analyses of the ERONs have identified a series of alterations that involves: the aberrant activation or inactivation of pathways such as *PTEN*, *KRAS*, *TP53*, *PIK3 CA*, *β-catenin* and rarely, *P53*.

- The loss of heterozygosity (LOH) at the *PTEN* locus is proved to be present in 10%- 20% of endometriosis cases and the patterns of LOH in ERONs are similar.
- The LOH rate for ERONs is higher than in cases of benign endometriosis and may reach values of 20-60%. LOH in the Xq region is about 38% in ERONs but it is infrequent in endometriosis. In atypical endometriosis (a high risk factor) LOH of 10q23 is found in 40% of cases, while in ERONs, LOH of 10q23 is higher than 45%.
- K-Ras* mutation is frequently found in endometriotic-associated carcinoma (10-20% of cases) and in more than 50% of cases of mucinous ovarian carcinoma. *B-catenin* is encoded by *CTNNB1* and the Wnt/ β -catenin signalling pathway dysregulation is occurring in 16-38% of ovarian endometrioid carcinoma, for which this mutation seems to be characteristic.
- The loss of *ARID1A*, a tumour suppressor gene that encodes BAF250a protein, is the most common molecular change in ERONs and seems also to be an early event. In ovarian cancers *ARID1A* mutations are found in 50% of endometrioid cancers and in 73% of clear-cell cancers, compared to approximately 10% of non-ERONs.

Author (year)	Study design	Sample size	Objective	Outcome
Mangili et al (2012)	Case Control	65 cases	Investigation of clinical and histologic features of EAOC subtype	Endometrioid subtypes of EAOC were associated with younger age, earlier stage and higher rates of concurrent endometrial cancer at diagnosis
Wiegand et al (2010)	Prospective study	665 cases	Identification of the genes involved in the pathogenesis of endometriosis to EAOC	ARID1A is a mutant gene in ovarian clear-cell and endometrioid carcinomas
Jimbo et al (1998)	Prospective study	172 cases	To examine the occurrence of ovarian endometriosis in epithelial ovarian cancer in Japan	Incidence of ovarian endometriosis in ovarian cancer was 14.5% (clear cell -40.6%, endometrioid- 23.1%, serous- 8.7%) mucinous 2.9%.

- CONCLUSIONS -

Understanding the molecular biology of endometriosis will be the key to better treatments for endometriosis and guide future early detection and prevention strategies to further reduce the incidence and mortality of EAOCs.

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