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Liquid biopsy in ovarian cancer

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ABSTRACT

Ovarian cancer is typically diagnosed at an advanced stage and poses a significant challenge to treatment and recovery. Relapsed ovarian cancer and chemoresistance of ovarian tumor cells are other clinical challenges. Liquid biopsy is an essential non-invasive diagnostic test that evaluates circulating tumor cells and tumor DNA, as well as other blood markers that may be useful in guiding precision medicine. Although liquid biopsy is not a routinely used diagnostic test, the potential applications in the diagnosis and prognosis in ovarian cancer are rapidly growing. This review explores recent studies examining the clinical potential of circulating tumor cells, cell-free microRNA, exosomes, tumor DNA, and other analytes as a source of liquid biopsy biomarkers in ovarian cancer diagnosis, prognosis and response to treatment.

1. Introduction

1.1. Ovarian cancer

Among the gynecological malignancies, mortality rates due to ovarian cancer are very high. Because of the lack of screening strategies, the diagnosis is possible only at advanced stages (stage III or stage IV) for 75% of the patients [1]. Due to the late diagnosis, patients have a less than 30% 5-year survival rate [2]. Ovarian cancer is generally described as a silent killer. As per the National Cancer Institute USA, there is an estimate of 21, 750 new cases and 13, 940 ovarian cancer deaths in 2020. The 5-year relative survival between 2010 and 2016 is 48.6%. Among the group of ovarian cancers, epithelial ovarian cancer (EOC) is the most common one. The traditional classification of EOC includes serous, mucinous, sero-mucinous, clear cell, and endometrioid types [3]. Histopathology, immunohistochemistry, and molecular genetic analysis, further assist in the accurate classification of ovarian tumors. Although the patients respond initially well, relapse and chemoresistance are significant issues in the treatment. Thus it is essential to find novel ways to screen, diagnose, and treat this deadly disease. In the past few years, a growing body of researches illustrated the applicability of liquid biopsy in the screening and diagnosis of ovarian cancer.

1.2. Liquid biopsy

Through needle biopsy, computed tomography-guided biopsy, surgical biopsy, etc., solid tissues for pathological examination are removed. Although these procedures give us valuable information about the nature of tissues, there are inherent risks to the patients and limitations in collecting the right portion of the sample with the majority of diseased and or altered cells. Infection to the patients, insufficient sample, and collection of proper representative tumor tissue, especially considering the tumor heterogeneity background, are some of the critical limitations in traditional biopsy procedures. Liquid biopsy is the collection of blood samples mostly and examining it for cancerous cells, cancerous DNA, circulating microRNAs (miRNAs), and exosomes that substantially decrease the risk to the patients during their pathological examination. Liquid biopsy is an alternative and emerging multimodal diagnostic tool in clinical oncology. It is less invasive and depending upon the sensitivity of detecting various analytes in different cancers; it offers quick identification of the clonal evolution of cancer cells and also monitors the development of any changes leading to drug resistance in the future. Detection of circulating tumor cells and cell-free DNA in human blood and correlation with the disease by investigators in the 1900s opened the door for further explorations into the field of liquid biopsy technology. Primary cancer cells undergo various lytic changes, such as apoptosis, necrosis, and phagocytosis. During this process, they release different cellular analytes, including DNA into the blood circulation, which is described as cell-free tumor-derived DNA or

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