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A repertoire of biomarkers helps in detection and assessment of therapeutic response in epithelial ovarian cancer

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Abstract In epithelial ovarian cancer (EOC), the cancer antigen 125 (CA-125) has been conventionally used to help in diagnosis and assessment of response to treatment. Currently, YKL-40 (Tyrosine–Lysine–Leucine-40) and circulating cell-free DNA are being evaluated for possession of similar ability. In this study, we aimed to assess the ability of a repertoire of potential biomarkers in detecting and assessing therapeutic response, in advanced EOC. Blood levels of CA-125, YKL-40, total cell-free DNA (CFDNA), cell-free nuclear DNA (CFnDNA), and cell-free mitochondrial DNA (CFmDNA) levels were measured in 100 untreated patients of advanced EOC from November 2009 to June 2011, and again on treatment completion from the 20 patients who appeared for follow-up analysis. Significantly, higher proportion of untreated patients had serum CA-125 >3 times upper limit of normal (ULN) (90.0 %; $P < 0.0001$) and plasma YKL-40 >ULN (77.0 %; $P < 0.0001$), both of which significantly decreased, Posttherapy. posttherapy, CFDNA ($P < 0.0001$), and CFnDNA ($P < 0.0001$) levels significantly decreased as compared to pretreatment levels. Positive and significant correlations existed between pretherapy CFDNA and CFnDNA [Spearman rho (ρ) = 1.000; $P < 0.0001$], and also with CFmDNA ($\rho = 0.301$; $P = 0.002$), separately between CFnDNA and CFmDNA ($\rho = 0.303$; $P = 0.002$), as well as between plasma YKL-40 and patient age ($\rho = 0.353$; ($P < 0.0001$). On treatment completion, CFDNA and CFnDNA levels showed positive and significant correlation ($\rho = 1.000$; $P < 0.0001$). Therefore serum CA-125 and plasma YKL-40 aid detection and assessment of therapeutic response, in advanced EOC. CFDNA and CFnDNA help in estimating extent of therapeutic response in advanced EOC.

Keywords CA-125 · Cell-free DNA · ECOG · Epithelial ovarian cancer · YKL-40

Introduction

Epithelial ovarian cancer (EOC) contributes to a large proportion of mortality and morbidity among all cancers in women, with an annual worldwide incidence of 224,747 new cases and 140,163 deaths [1]. A typically late clinical presentation usually ensures a dismal prognosis when despite optimal treatment comprising cytoreductive surgery followed by platinum and taxane-based chemotherapy, very poor 5-year survival rates are usually observed [2, 3]. In developing countries, owning to lack of disease awareness, most patients usually seek treatment when malignancy is already well advanced. Additionally, many of these patients relapse. Hence it is vital to have reliable biomarkers which can effectively detect advanced lesions as well as predict disease course, posttreatment. Conventionally, in EOC, the cancer antigen 125 (CA-125) has been used for diagnosis and monitoring response to primary treatment [4]. Sustained attainment of serum values within the normal reference range (0–35 U/ml) is regarded

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