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Editorial Open Access

Serum Tumor Markers Evaluation in Patients with Adnexal Masses – Current Value in Everydays Clinical Practice

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Editorial

According to the recent statistical data, ovarian cancer is responsible for the death of over 125,000 women worldwide each year and kills more women than all other gynecologic cancers combined. Also, it must be stressed that ovarian cancer is the second deadliest cancer for women and the fifth leading cause of cancer death in women. Symptomatology is usually complex, nonspecific and sometimes misleading, and the diagnosis of the disease in its' early stage is in approximately 20% of patients. 5-year survival rate is different, and ranges from 90% in early stage ovarian cancer patients up to 11% in the advanced stages of the disease.

In order to make a proper diagnosis in its' early stage and better patient care, numerous investigations were performed and several serum ovarian cancer biomarkers identified.

In spite of all these efforts, up to now there is no adequate screening test for ovarian cancer [1]. Therefore, the identification of oncology biomarkers for screening and monitoring of occult tumors has been highly prioritized.

In routine clinical practice assessment for early detection of ovarian cancer can be achieved using tumor markers such as CEA, Ca 19-9, Ca 15-3 combined with Ca-125 and HE4 levels [1-3]. Other tumor markers (such as CA72-4, OVX1, Inhibin, beta-hCG, AFP, M-CSF etc.) should be respected for early detection of ovarian cancer, but not used in everydays' approach [4,5].

Ca 125 is the most widely used and the most accurate tumor marker of ovarian cancer, until now. Screening with Ca-125 measurement and trans-vaginal ultrasonography every 6 months has been recommended for high-risk women [6,7]. However, serum Ca 125 has been investigated for ovarian cancer screening with conflicting results [8]. Ca 125 determination is useful for the detection of the persistence and recurrence and monitoring of the therapeutic effects in the patients with epithelial ovarian carcinomas. Ca 125 is the most reliable serum marker in use for serial measurements to calculate the risk of cancer, which appears to have greater utility than evaluation of a single value [8]. Levels of Ca 125 may indicate the disease extent and therefore, the likelihood of successful cyto-reductive surgery [9]. Still, elevated levels of Ca 125 can also be detected in many non-malignant gynecological diseases, especially in endometriosis, and even some physiological conditions. Numerous researchers have confirmed that Ca 125 has limitations when used to distinguish between benign and malignant ovarian masses, but have concluded that by using likelihood reference tables, clinicians will be able to better interpret preoperative serum Ca 125 results in patients with adnexal masses [10-12]. The diagnostic efficiency of Ca 125 in literature usually ranges between 70 and 90% [4,5].

Human epididymis protein 4 is a novel serum marker which is more sensitive in the prediction of risk of ovarian malignancy than CA125 alone in patients with a pelvic mass [13]. Researchers found elevated level of CA125 in 77 % and HE4 in 85 % of cases with ovarian cancer [14,15]. The median CA125 and HE4 levels are proven to be significantly higher in the patients with ovarian carcinoma than in those with benign disease. Moreover, serum HE4 testing is a more powerful tool than CA125 assay to discriminate ovarian cancer from ovarian endometriosis and pelvic inflammatory disease, to detect recurrence or monitor the response to therapy [16]. HE4 adds valuable information especially for premenopausal patients [17].

The positive rate of CA 125, CA 19-9, CA 15-3, and CEA in serous tumor can be 57.9, 7.9, 7.9 and 15.8%, respectively. These figures for mucinous tumor are 31.8, 40.9, 27.3 and 40.9%. The positive rate of CA 125 in the serous group are found to be statistically significantly higher than that in the mucinous group, while the positive rates for CA 19-9 and CEA in mucinous histology were significantly higher than those in serous tumors. Therefore it can be said that the elevation of serum CA 125 may suggest serous tumors, while the high level of serum CA 19-9 and CEA may indicate mucinous ovarian tumors [18]. CA19-9 is probably the most accurate tumor marker for mature cystic teratomas as it is the only tumor marker with a mean serum level above the cut-off value. As the tumor becomes bigger, this relationship becomes more distinct [19].

Literature data showed that combined multiple tumor markers can improve the overall diagnostic accuracy [2,13,15]. The sensitivity of a serum markers combination was significantly greater than the sensitivity of the CA 125 assay alone in patients with all stages of primary ovarian epithelial tumors of different histological types. When used as single markers, however, only the CA-125-II assay could distinguish invasive Stage I tumors from apparently healthy women [20]. A combination of serum and molecular markers such as serum CA125, CA19 and mRNA for Survivin gene could allow a better triage between endometriosis and malignant adnexal masses [21]. HE4 in combination with CA125 appears to be the most effective tool for the early diagnose of ovarian carcinoma [20]. Different risk models and screening algorithms that combine and evaluate tumor markers together, aimed at improving the specificity and sensitivity of diagnostic tests, allowing for an effective triage of women to appropriate institutions for their care, have been made so far. The most commonly used is Risk of Ovarian Malignancy Algorithm [ROMA] that utilizes the dual marker combination of HE4 and CA125 to stratify both postmenopausal and premenopausal women into high- and low-risk groups [19]. This model achieves the highest sensitivity and specificity. Furthermore, some researchers advise that in patients with an undiagnosed tumor in the pelvis, the CA-125/CEA ratio may be used to preoperatively identify a substantial fraction of patients with ovarian and non-ovarian malignancies [22], and confirm

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again that combination of serum tumor markers could improve ovarian cancer diagnosis [23].

In conclusion, blood levels of tumor markers can be good predictors of the adnexal masses nature. But still, for the most precise preoperative prognosis of adnexal tumors nature the combination of tumor markers should be used.

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