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Paraneoplastic antigens as biomarkers for early detection and prediction of recurrence of ovarian cancer

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Routine disease monitoring of ovarian cancer patients is generally recommended by gynecologic oncologists for women from high-risk families and for ovarian cancer patients during after the completion of primary surgery and first-line chemotherapeutic treatments. The recurrence is determined by measuring the level of serum CA125, one of the most extensively used tumor biomarkers in standard clinical practice for disease surveillance. Numerous studies have shown the role of tumor autoantibodies as biomarkers for ovarian cancer diagnosis and its recurrence. These autoantibodies to tumor associated antigens (TAAs) arise due to the generation of humoral immune response before evidence of clinical symptoms in cancer patients. Previously, we showed that 3 biomarker panel predicted ovarian cancer recurrence at a median lead time of 9.07 months with 94.7% sensitivity, 86.7% specificity and 93.3% accuracy, in a cohort of ovarian cancer patients where normalization of CA125 had occurred after the surgery and completion of chemotherapy. One of those biomarkers was a peptide epitope from a known paraneoplastic antigen, HARS. Paraneoplastic antigens can elicit a humoral immune response in cancer patients as these antigens are expressed in the cells of nervous system and tumor. The appearance of these onconeural antibodies in ovarian cancer patients leads to the development of various neurological disorders called paraneoplastic syndromes, particularly dermatomyositis or polymyositis but can precede the occurrence of dermatomyositis or polymyositis. Although the clinical implication of these onconeural antibodies as biomarkers for early diagnosis of ovarian cancer has been reported in many case studies, the usefulness of these antibodies has yet to be evaluated in monitoring disease status in ovarian cancer patients after cytoreductive surgery and chemotherapy treatments. In the present study we evaluated the role of a panel of 3 recombinant paraneoplastic antigens, HARS, CDR2 and Ro52 in combination with 3 of our previous biomarkers in predicting recurrence in new and independent cohort of ovarian cancer patient population in which most of the patients had no elevation in CA125 level months before their clinical recurrence. Our results indicate that autoantibodies to HARS, Ro52 and CDR2 and 5H6 antigens predicted ovarian cancer recurrence 5.03 months before the clinical or symptomatic relapse in 21 ovarian cancer patients with a sensitivity of 90.5% when CA125 levels were below the standard cutoff (35 U/ml). We have expanded the biomarker panel and test a larger sample size for the early detection of ovarian cancer using a newly developed ELISA protocol employing a large number of sera from patients and women with benign gynecological diseases.

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