The OVA1: a breakthrough in evaluating adnexal mass

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... imagine now lost in that deep labyrinth where you don't find Ariadne's thread that can guide you out of the dark roads and will allow you to return to the paradise in which you previously lived in.

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Tumor markers have been one of the great promises in Oncology. A test that is sensitive, specific, with easy application and interpretation and low cost has always been its ideal characteristic. The concept that with a serum marker an undergoing early tumor, susceptible of prompt treatment, can be diagnosed is truly attractive. However the widespread belief, since the mid-1980s, that with a simple and unique lab test it could be solved, it has not yet reached. That absolutist vision has been re-accommodating gradually and currently appears as one efficient instrument. Today we can say that tumor markers are used in the following situations:

a) Screening in the population healthy at risk for a particular disease,

b) As a factor of diagnostic confirmation

c) To measure the response to a specific treatment

d) And monitoring.

The evolution of markers in neoplastic diseases in Gynecology is perhaps one of greatest development. The use of markers such as LDH, alpha fetoprotein and HCG in the germinal ovarian tumors or inhibin in granulosa tumors is part of routine diagnosis and follow-up in these pathologies.

In 1983, a team of researchers at the MD Anderson Cancer Center in Houston, headed by Robert C Bast, published in New England Journal of Medicine report of its work on a marker in epithelial ovarian cancer. Originally formed by monoclonal antibody of murine origin OC 125 was achieved, by an immunoradiometric assay, determine their values in serum. In its early years, the CA 125 only included a specific antibody for the immune locus Hayvancilik 433, very sensitive for the detection of serous tumors but, leaving aside other histological subtypes as the Mucinous. From
1996, CA 125 of second generation (CA 125 II) is optimized with the use of monoclonal antibody M 11 that allowed greater sensitivity, especially in detection as well as not serous tumors. Through this amendment, when evaluating patients with epithelial ovarian cancer (EOC), more than half of the patients in stage I and 90%, 92% and 94% of the patients with disease stage II, III and IV, respectively, had a significant elevation of the marker. (1)

Still, with this progress, sensitivity of the CA 125 II was still looking to improve. It is well known that this glycoprotein is present in a large number of healthy tissues, especially those derived from the epithelium coelomic as fallopian tubes, endocervix, endometrium, pancreas, colon, kidney and lung and in those of mesothelial origin as the peritoneum, pleura and pericardium. This is why the presence of this marker below 35 IU/ml is considered normal. Besides, the CA 125 level in healthy women varies significantly with age, smoking, race, the menstrual cycle and pregnancy. Benign conditions such as uterine myomatosis, endometriosis, pelvic inflammatory disease, cirrhosis, and inflammatory bowel disease also elevate this marker. This is one of the reasons why the determination of CA 125, still in its second version, has been disappointing in the research of ovarian cancer. Its utility, is mainly limited to the follow-up of patients with EOC that have registered a significant increase of the marker in the pretreatment phase and, in conjunction with the pelvic physical exam and transvaginal ultrasound, in the diagnosis of a relapse with a sensitivity of 90%. (2)

Recent efforts have been focusing on the design of a multiple trial, through the determination of other markers to join the CA 125 II, in order to raise the profile of sensitivity. In 2009 the Food and Drugs Administration approves use of the OVA1 ® (Vermillon, Austin, Texas, USA) as a test to predict the risk of malignancy in patients with diagnosis of adnexal mass. This test that includes the measurement of CA 125 II, transthyretin, apolipoprotein A1, beta - microglobulin and transferritin is expressed in the form of an index that stratify the risk that the observed adnexal mass is a malignant lesion. On a scale ranging from 0 to 10 points, it has been determined that the cut-off for menopausal patients point is greater than or equal to 4.4 and in Premenopausal is greater than or equal to 5. The main utility of this tool is not only the ability to predict whether an adnexal mass is malignant, but something just as important, is a reliable way to differentiate patients who must be referred for care by specialists in Gynaecologic Oncology in a specialized center.

With a sensitivity of 93% and a specificity of 43%, a negative predictive value (NPV) of 93% and positive (PPV) of 42%, is today a real breakthrough. The OVA1, in the study of Ueland et al which included 516 patients, elevated the diagnostic sensitivity in those specialists who were not gynecologist’s oncologists from 72% to 92% and 78% to 99% in onco-Gynecology specialists. The VPN is raised in gynecologists from 89% to 93%, while for onco-Gynecology specialists raised from 86% to 98%. The sensitivity in the premenopausal patient went from 60% with CA 125 II only to 89%, with the use of the OVA1; while the VPN improved from 90% to 94%. For menopausal patients the sensitivity and the VPN went from 81% and 85% to 98% and 96%, respectively. The sensitivity in the detection of tumors by histology was 99%, 78%, 75% and 94% for malignant
epithelial tumors, non-epithelial malignant tumors, low potential for malignancy tumors and metastatic tumors, respectively. (3, 4)

The use of the OVA1 allows raising the profile of care of the patient with an adnexal mass. The decision to refer the patient, with an OVA1 above the values of cutting to a specialized center will allow to decrease the incidence of incomplete surgical protocols which entail, most of the time, the lack of the necessary information to indicate adjuvant chemotherapy and an eventual relaparotomy, not exempt of morbidity, delaying the start of adjuvant therapy. According to a presentation by Robert Bristow, in the Congress of the Society of Gynecologic Oncology in 2013 in the United States, only 37.4% of patients with EOC receive an appropriate surgical and adjunctive treatment, a truly alarming figure. (5) In our continent this data remains unknown. One of the most common challenges faced in the service of Gynecology Oncology of the Luis Razetti Institute is decision making in the patient with EOC referred to us with incomplete surgery. In these cases, the clinical evaluation by a multidisciplinary team, new paraclinical studies until the final recommendation may take between 2 and 4 weeks, generates a great anxiety in the patient and their family members. In addition, the possibility a new intervention and/or the delay in referral to medical oncology service constitute an obstacle that will inevitably affect the prognosis of the patient and care costs.

It is worrying that a good proportion of those cases is the result of the diagnosis in the final biopsy in patients without a frozen cut of the adnexal mass or managed as an "emergency patients”. An adnexal mass, in almost all cases is not an emergency. The occurrence of a phenomenon of torsion, rupture or hemorrhage is possible but rare. This scenario is perfectly avoidable with an approach rational diagnosis based on efficient diagnostic tools available as the OVA1, which should be available in the attention centers. The clinical and imaging evaluation at the same time with the OVA1 will allow a more accurate diagnosis and thus offer the best therapeutic option in each case and decreasing the insufficient treatment in epithelial ovarian cancer.

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References:

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