One biologic marker (carbohydrate antigen-CA 125), two different diseases (ovarian cancer and congestive heart failure): practical implications of monitoring CA 125 serum levels. A case report

Pompilio Faggiano, Antonio D'Aloia, Tommaso Bignotti, Livio Dei Cas

Division of Cardiology, University of Brescia, Brescia, Italy

Key words:
Atrial natriuretic factor; Congestive heart failure; Immunological system.

Carbohydrate antigen (CA) 125 is a glycoprotein produced by the serous epithelium, found to be increased in ovarian cancer and currently used in the follow-up of patients with this malignancy and to evaluate the response to therapy. However, an increase in the blood levels of this tumor marker has been recently reported even in patients with congestive heart failure. We report a case of a woman in whom previously high levels of CA 125 were related to the presence of an ovarian cancer; after bilateral oophorectomy and chemotherapy, the CA 125 levels remained within the normal range for several years, until a new increase was recently detected, raising the suspicion of a cancer recurrence. Clinical evaluation, together with comprehensive laboratory assessment, allowed us to exclude a malignancy and to identify the presence of congestive heart failure due to left ventricular systolic dysfunction as being responsible for the abnormal CA 125 levels. The patient's clinical improvement following medical therapy was associated with a reduction in the serum levels of CA 125 to normal values. The clinical relevance of this finding is discussed.

(Ital Heart J 2003; 4 (7): 497-499)

Received February 3, 2003; accepted April 17, 2003.

Address:

Dr. Pompilio Faggiano

Via S. Antonio, 6
25133 Brescia
E-mail:
faggiano@numerica.it

A 60-year-old woman was admitted to the Cardiology Unit with a clinical picture of severe heart failure. Her medical history included a hysterectomy with bilateral oophorectomy performed 16 years previously for ovarian cancer. On that occasion the patient had been submitted to chemotherapy with a subsequent complete remission of the disease persisting during follow-up. In particular, clinical and echographic evaluation performed 2 months before the current event excluded the presence of recurrent pelvic masses, and the serum levels of carbohydrate antigen (CA) 125, a tumor marker related to ovarian cancer[1], were within the normal range (< 35 U/ml). During the month preceding hospitalization for heart failure, the patient complained of vague symptoms such as progressive effort dyspnea and generalized asthenia; a recurrence of malignancy was suspected and partly supported by the finding of an increase above normal values of the serum levels of CA 125 (55 U/ml). Accordingly, an oncologic reevaluation was planned, but owing to clinical deterioration with the onset of rest dyspnea and orthopnea the patient was hospitalized before time.

At admission the clinical findings were suggestive of a NYHA functional class IV heart failure, with lung rales and systemic hypoperfusion. The electrocardiogram showed sinus tachycardia (120 b/min), left atrial enlargement, and incomplete left bundle branch block. Chest X-ray revealed the presence of cardiomegaly (cardiothoracic ratio 0.54), pulmonary venous congestion and interstitial-alveolar edema; there was no pleural effusion.

Two-dimensional echocardiography showed a mild left ventricular dilation with extensive and severe left ventricular wall hypokinesis (the left ventricular ejection fraction was approximately 15%). On color Doppler flow imaging, moderate mitral regurgitation with a restrictive pattern of left ventricular filling (deceleration time 80 ms) indicating a high left atrial pressure was recorded. Besides, tricuspid regurgitation was detected at color and continuous-wave Doppler, allowing a noninvasive diagnosis of pulmonary hypertension (the pulmonary artery systolic pressure was approximately 60 mmHg). There was no pericardial effusion.

A computed tomographic scan of the abdomen and pelvis did not reveal any ab-

normal masses or peritoneal effusion suggestive of cancer recurrence. A lung perfusion scan allowed us to exclude pulmonary embolism and coronary arteriography did not reveal significant coronary artery stenosis.

Among the laboratory values, the serum levels of CA 125 were found to have increased further (79 U/ml, normal value < 35 U/ml); on the other hand, the serum levels of other tumor markers such as carcinoembryonic antigen, alpha-fetoprotein, CA 15.3 and CA 19.9 were within the normal range. Finally, the serum levels of brain natriuretic peptide (BNP), as assessed by means of a bedside kit were extremely high (> 1300 pg/ml).

On the basis of the clinical and laboratory findings an aggressive therapeutic regimen for congestive heart failure was started with intravenous frusemide, vasodilators (sodium nitroprusside infusion), and an inotropic agent (dobutamine infusion at a rate of 5-7.5 γ/kg/min). The clinical picture improved quickly and the patient was placed on oral therapy with ACE-inhibitors, loop diuretics and spironolactone. After 10 days of therapy a two-dimensional echocardiographic reevaluation showed an improvement of the left ventricular systolic and diastolic functions (left ventricular ejection fraction 32%, early filling deceleration time 170 ms) and of pulmonary hypertension; furthermore, the serum levels of both BNP and CA 125 had returned to normal values (72 pg/ml and 22 U/ml respectively) (Fig. 1, Table I).

Table I. Clinical, hemodynamic, echocardiographic and hormonal data at the time of hospital admission for congestive heart failure and after 10 days of aggressive medical therapy.

	Admission	After therapy
NYHA class	IV	II
Weight (kg)	53	50
Third heart sound	Present	Absent
Pulmonary congestion	Present	Absent
Left ventricular ejection fraction (%)	15	32
Left ventricular end-diastolic diameter (mm)	57	56
Mitral regurgitation severity (grade 0-4)	3	1
Pulmonary artery systolic pressure (mmHg)	60	35
Deceleration time of early filling (ms)	80	170
CA 125 serum levels (U/ml)	79	22
BNP serum levels (pg/ml)	> 1300	72

BNP = brain natriuretic peptide; CA = carbohydrate antigen.

Discussion

An increase in the CA 125 serum levels has been initially described in women affected by ovarian cancer, especially in case of peritoneal involvement; accordingly, serial measurements of this tumor marker are currently used in the follow-up of these patients and to evaluate the response to therapy[1,2]. However, an increase in the serum levels of CA 125 has been recently reported even in patients with advanced heart failure[3,4].

In the patient here reported, on the basis of the presence of the initially non-specific symptoms and considering the previous history of ovarian cancer, the finding of a new increase in the serum levels of CA 125 was at first considered as being suggestive of the recurrence of

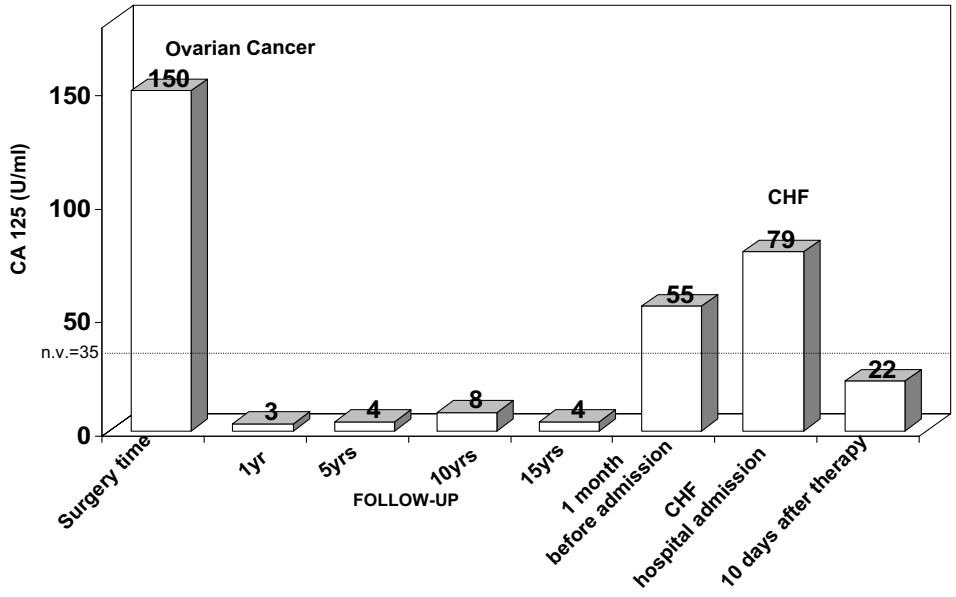

Figure 1. *Changes in the carbohydrate antigen (CA) 125 serum levels over time: at the time of surgery for ovarian cancer* (left)*, during the long-term follow-up* (middle)*, at the time of the appearance of the new symptoms, at the time of hospitalization for congestive heart failure (CHF) and following aggressive therapy* (right)*. The* dashed line *indicates the upper limit of normal for CA 125 serum levels.*

malignancy. Then, in the phase of overt heart failure, the CA 125 levels seemed to reflect the severity of the clinical picture and of the hemodynamic abnormalities as detected by means of Doppler echocardiographic evaluation and of the biohumoral (BNP) findings; finally, the changes in the CA 125 levels over time paralleled the clinical improvement and the response to medical therapy.

This finding seems to indicate a new potential application of the measurement of tumor marker CA 125 not related to the diagnosis and follow-up of cancer; furthermore, it emphasizes the need for caution in interpreting the serial changes of the tumor marker eventually observed in patients with a previous history of malignancy.

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