Small-cell Lung Cancer and Elevated CA 19.9 Tumor Marker Levels☆

Carcinoma microcítico de pulmón y elevación del marcador tumoral CA 19.9

Dear Editor,

The CA 19.9 antigen is a glycoprotein synthesized in several epithelia that is typically high in the serum of patients with pancreatic tumors. Thus, levels above 300 U/l have a positive predictive value of about 90%.[1] Other tumors (bile duct, gastric, colon, hepatic, ovarian, endometrial, pulmonary, or urothelial) or different benign processes (hepatitis, cirrhosis, cholangitis, cholecystitis, pancreatic pseudocyst, pancreatitis, pulmonary fibrosis, bronchial asthma, asbestosis, bronchiectasis, tuberculosis, renal failure, mucinous cysts, hydronephrosis, Sjögren's syndrome, rheumatoid arthritis, erythematous lupus, dermatopolymyositis, or giant cell arteritis[2–4]) may also run their course with high serum CA 19.9 levels (in the latter case, with more moderate values).

Increased serum levels of CA 19.9 in lung tumors, especially in adenocarcinomas, are a known fact, although uncommon.[5–7] Therefore, we consider it interesting to discuss 4 cases of pulmonary non-small-cell carcinoma treated in our unit within the last 2 years. The notably high CA 19.9, especially in 2 of the patients, made the initial suspected diagnosis lean toward digestive tumor processes.

In the time period, we treated 4 males, all with important smoking histories, non-small-cell lung cancer and CA 19.9 values higher than 300 U/l. Mean age was 64.5 (SD, 4.01), and general patient characteristics are shown in Table 1.

Except in one of the cases, the clinical presentation included severe deterioration of the patients' condition, with very striking cholestasis and hepatomegaly. This, together with high CA 19.9 levels (in all 4 patients above 500 U/l, and above 10 000 U/l in 2) meant that the initial suspected diagnosis did not coincide with the definitive diagnosis. In the 4 cases, abdominal computed tomography (CT) ruled out pancreatic masses. Meanwhile, neuron-specific enolase (determined in 3 patients) was clearly high, as was pro-gastrin-releasing peptide (Pro GRP), with values that were 200 times above normal. The poor survival in the 4 patients (just 16 weeks on average) reflected the advanced clinical state at presentation.

Tumor markers are substances that are produced or induced by either a tumor or by the surrounding tissues.[8] They have limited specificity and sensitivity, although they are of interest in tumor diagnosis. Their main application resides in follow-up, in the evaluation of treatment efficacy and in prognosis.

Neuron-specific enolase, Pro GRP, squamous cell carcinoma (SCC) antigen, or CYFRA 21.1 are markers that are usually used when given the suspicion for lung cancer (small-cell in the first 2

Table 1
Characteristics of Patients With High CA 19.9.

Case	Age/Sex	Symptoms	AST/ALT, UI/l[a]	GGT/FA, UI/l[b]	CA 19.9, U/l[c]	CEA, ng/ml[d]	CA-125[e]	Enolase[f]	CYFRA 21.1[g]	SCC[h]	Pro-GRP[i]	Diagnosis
1	68/M	Deterioration of general condition and weight loss; right hilar mass	92/73	568/392	524.2	9	3778	327	NO	NO	NO	Small-cell lung cancer with hepatic metastases
2	64/M	Deterioration of general condition, weight loss and general pain; right hilar mass	209/173	923/527	>60 000	35	57	275	14.4	1.1	13 400	Small-cell lung cancer with lung, mediastinal, bone, hepatic and suprarenal affectation
3	59/M	Affectation of the general condition and cough; left hilar mass	95/52	2698/324	10 599	896	91	NO	NO	NO	N	Small-cell undifferentiated carcinoma with hepatic and peritoneal metastases
4	67/M	Abdominal pain, affectation of the general condition and weight loss; right hilar mass	N/47	190/224	671	N	59	370	NO	NO	18 334	Small-cell lung carcinoma with pleural, hepatic and bone metastases

[a] AST: aspartate-aminotransferase, reference value (rv): 2-38U/l; ALT: alanine-aminotransferase, rv: 2–41 U/l.
[b] GGT: gamma-glutamyl transpeptidase, rv: 7–50 U/l; FA: alkaline phosphatase, rv: 40–129 U/l.
[c] CA 19.9, rv: 0–37 U/ml.
[d] CEA: carcinoembryonic antigen, rv: 0–5 ng/ml.
[e] CA-125, rv: 0–35 U/ml.
[f] Enolase, rv: 1–20 ng/ml.
[g] CYFRA 21.1, rv: 0.1–3.3 ng/ml.
[h] SCC: squamous cell carcinoma antigen, rv: 0–2 ng/ml.
[i] Pro GRP: pro-gastrin-releasing peptide, rv: 0–63 pg/ml.

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cases or epidermoid in the remainder). Nevertheless, publications in the medical literature about the management of this entity do not recommend the systematic use of tumor markers due to their very limited efficacy, and they hardly even mention CA 19.9, which is not considered useful in this context.[9,10]

CA 19.9 is present in the glands of bronchi and bronchioles. It is therefore plausible (although immunohistochemistry techniques are not done) that the origin of their increased level is the neoplastic bronchiolar epithelium,[7] regardless of the potential impact of the hepatic metastasis in all the reported cases.

It can thus be deduced that CA 19.9 may present higher levels in small-cell lung cancer, although its determination is not considered clinically useful. This consideration may be useful in order to properly interpret analytic and imaging results in this context.

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José María Prieto De Paula,[a,*] Eduardo Mayor Toranzo,[a] Laura Gallardo Borge,[a] Silvia Franco Hidalgo[b]

[a] *Servicio de Medicina Interna, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*
[b] *Servicio de Medicina Interna, Complejo Hospitalario de Palencia, Palencia, Spain*

* Corresponding author.
E-mail address: jmpripaula@yahoo.es (J.M. Prieto De Paula).

Superior Vena Cava Syndrome as the Initial Manifestation of Thymic Carcinoma☆

Síndrome de vena cava superior como primera manifestación de carcinoma tímico

Dear Editor,

Superior vena cava syndrome (SVCS) entails severe symptoms due to blood flow obstruction of the superior vena cava (SVC) towards the right auricle, caused by either extrinsic compression or invasion of the vena cava. Its diagnosis is symptoms-based, the most common symptom being dyspnea, along with findings on physical exploration, especially facial edema and venous distension of the neck and chest wall. Its origin is usually malignant in 90% of cases. Non-small-cell lung cancer (NSCLC) is the most frequent, followed by small-cell lung cancer (SCLC) and non-Hodgkin lymphoma (NHL). Other malignant tumors with rare presentation are thymomas, mediastinal germ-cell tumors, mesotheliomas and metastases. SVCS secondary to thymic carcinoma due to intraluminal invasion is rare, as in the patient that we present.

The patient is a 71-year-old male with hypertension, dyslipidemia, a history of atrial fibrillation, anti-coagulation therapy and stable ischemic heart disease. He came to our emergency department due to inflammation of the face, neck and shoulders that had been evolving over the previous 15 days without constitutional syndrome or previous respiratory symptoms. Upon physical examination, BP was 139/81 mmHg, 62 bpm and normal cardiopulmonary auscultation. Edema of the upper thorax, neck and face were observed. Chest radiology revealed an upper right mediastinal mass (Fig. 1). Therefore, computed tomography (CT) was ordered, which showed a mass in the upper right mediastinum that infiltrated and occluded the SVC (Fig. 1B) and small lower paratracheal and right hilar lymphadenopathies. Hemogram showed slight leukocytosis (10 400/μL). Biochemistry, coagulation and tumor markers (alpha-fetoprotein, PSA, CEA, Ca. 19.9 and β2 microglobulin) were strictly normal. Abdominal–pelvic CT ruled out any alterations in other territories. Treatment was initiated with dexamethasone, which resulted in improved symptoms in the patient, and CT-guided biopsy determined the mass to be thymic carcinoma. According to the Masaoka system, it was classified as stage III–IVb (microscopic invasion of neighboring organs [SVC in this case] and lower paratracheal and right hilar lymph metastasis). The patient was discharged from the hospital with corticosteroids and continued chemotherapy treatment with carboplatin and etoposide. The patient was later administered radiotherapy in order to reduce the size of the tumor mass and achieve surgical resectability, although this was unsuccessful.

SVCS is a pathology associated with malignancy that has a poor prognosis. Etiological possibilities include intrathoracic malignant tumor, which is responsible for 60%–85% of cases. Non-tumor causes represent 15%–40% of cases, depending on the series, and SVC thrombosis is on the rise due to the increasing use of intravascular devices (central venous catheters, pacemakers, etc.). The infectious etiology, which was the protagonist in the pre-antibiotic era, has diminished notably since the appearance of antibiotic therapy. Local vascular post-radiation fibrosis should also be considered. As for the origin of the tumor, the most frequent cause is usually a malignant lung tumor, and NSCLC is the most common (50% of cases), followed by SCLC (25% of cases). Both, together with NHL (10% of cases), constitute approximately 95% of malignant causes.[1] Other tumors that are less frequently associated with SVCS are malignant thymic tumors (4%), such as thymoma and thymic carcinoma; the latter represents less than 1% of these tumors. These

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