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LETTER TO THE EDITOR

Is the Determination of CA-125 Serum Levels Useful for the Diagnosis of Pulmonary Tuberculosis?

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Dear Editor,

In their article, Fortún *et al.* [1] found higher CA-125 serum levels in patients with pulmonary tuberculosis than in other lung infections and concluded that this tumor marker is useful for the diagnosis of tuberculosis. There are, however, some points of concern in that study.

A major point is the effect of pleural involvement. In diseases with pleural, pericardial or peritoneal involvement increases in CA-125 are almost constant, because this antigen is present in mesothelial cells of these structures, especially in areas of inflammation [2]. Benign serous effusions, particularly ascites, are associated with increased serum concentrations of CA-125, reaching very high values of up to 100 times the normal limit [3-7]. In fact, CA-125 has proved to be an excellent marker for ascites in patients with benign liver diseases (sensitivity 98%, specificity 96%, positive predictive value 94%, negative predictive value 99%, efficiency 97%) [3]. Therefore, whenever serous effusion of any etiology is present, CA-125 is expected to be substantially elevated, losing its diagnostic value.

Although the proportion of patients with pleural effusion was similar in the control and tuberculosis groups in the authors' study (14.8% and 11.4%, respectively), no information is provided about the estimated amount of pleural fluid. This aspect is important because CA-125 is very sensitive to minimal amounts of ascites and correlates very well with the amount of ascitic fluid, decreasing rapidly following therapy and even predicting the recurrence of ascites [3, 8].

The authors do not provide information about the individual CA-125 values, but the means, SD and medians clearly indicate that the distribution was markedly non-Gaussian, particularly in the tuberculosis group. In fact, the range of CA-125 values in this group multiplied by 50. Therefore, considering the sensitivity of this marker and its strong relationship with the amount of fluid, the results could have been biased towards the patients with greater pleural effusions.

Moreover, the authors state that the Mantel-Haenszel test was used to compare continuous variables. However, this test contrasts categorical variables. Therefore, it is not clear which test was actually used, but given the marked non-Gaussian distribution of CA-125, if parametric tests had been used to assess the differences in CA-125 levels, their results would not have been reliable.

Also, the alleged conclusion about the usefulness of CA-125 in tuberculosis patients with negative sputum smears did not derive from the study, because all but one of the patients had positive sputum smears, which represented a quicker and much more reliable procedure than CA-125 for the diagnosis of tuberculosis in this series. Moreover, the limited yield of sputum smears in tuberculosis, and the association of positive smears with extensive disease, suggest that these patients had advanced disease, biasing additionally the results.

Finally, the decrease in CA-125 levels following therapy reported by the authors is not unexpected, as the pleural fluid and inflammation disappeared. Decreases in other markers have also been described in patients receiving successful treatment for tuberculosis [9, 10].

Therefore, the impact of pleural effusion on the results was presumably substantial. In addition, the control group was hardly comparable, because tuberculosis patients have usually more extensive disease than other lung infections, particularly in HIV-infected patients, who were also misbalanced between the two groups, and conditions such as exacerbated COPD should not be compared with tuberculosis for this purpose (even in 12 control patients there were no infiltrates). To evaluate the real value of CA-125 in tuberculosis diagnosis, only patients without pleural effusion, even in minimal amounts, and with comparable conditions (i.e. extensive pneumonia) should have been considered, because this marker losses its value in patients with serous effusions, as it reflects the existence and amount of effusion and pleural involvement rather than the underlying disease.

REFERENCES

[1] Fortún J, Martín-Dávila P, Méndez R, *et al.* Ca-125: a useful marker to distinguish pulmonary tuberculosis from other pulmonary infections. Open Respir Med J 2009; 3: 123-7.

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[2] Kabawat SE, Bast RC Jr, Bhan AK, Welch WR, Knapp RC, Colvin RB. Tissue distribution of a coelomic-epithelium-related antigen recognized by the monoclonal antibody OC125. Int J Gynecol Pathol 1983; 2: 275-85.

[3] Collazos J, Genolla J, Ruibal A. CA 125 serum levels in patients with non-neoplastic liver diseases. A clinical and laboratory study. Scand J Clin Lab Invest 1992; 52: 201-6.

[4] Touitou Y, Bogdan A. Tumor markers in nonmalignant diseases. Eur J Cancer Clin Oncol 1988; 24: 1083-91.

[5] Bergmann JF, Bidart JM, George M, Beaugrand M, Levy VG, Bohuon C. Elevation of CA 125 in patients with benign and malignant ascites. Cancer 1987; 59: 213-7.

[6] Bergmann JF, Beaugrand M, Labadie H, Bidart JM, Bohuon C. CA 125 (ovarian tumour-associated antigen) in ascitic liver diseases. Clin Chim Acta 1986; 155: 163-6.

[7] Mezger J. Elevated serum CA 125 levels in patients with benign ascites or pleural effusions. Tumor Biol 1988; 9: 47-52.

[8] Aguilar RJ, Rey RC, Ortega VM, Hernández PA, Sayago MM. Cancer antigen 125 levels in serum can predict the recurrence of ascites in patients with cirrhosis of the liver. Hepatogastroenterology 1990; 37 (Suppl 2): 163-5.

[9] Collazos J, España P, Mayo J, Martínez E, Izquierdo F. Sequential evaluation of serum adenosine deaminase in patients treated for tuberculosis. Chest 1998; 114: 432-5.

[10] Collazos J, Martínez E, Mayo J. Evolution of serum β2-microglobulin concentrations during treatment of tuberculosis patients. Scand J Infect Dis 1999; 31: 265-7.

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