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Elevated Serum CA-125 Levels in Patients with Ovarian Fibrothecomas

J. Schneider, M. Avila, G. Barrenetxea, F. Montoya and F.J. Rodriguez-Escudero

TO DATE, CA-125 is the best tumour marker for ovarian adenocarcinoma [1]. It has been found to be especially useful for monitoring the response to treatment of ovarian carcinoma patients with initially elevated CA-125 levels. Of them, 90–100% will have persistent ovarian cancer at second-look laparotomy if their serum CA-125 fails to decline during treatment [2]. However, up to 50% will still have residual disease despite normal CA-125 levels, although in these cases the residual tumour is usually minimal [2].

Unfortunately, ovarian cancer is not the sole condition associated with elevated serum CA-125 levels. Other gynaecological cancers arising from the celomic epithelium (fallopian tube, endometrium, endocervix), non-gynaecological cancers (pancreatic, hepatic, breast, colon and lung), as well as pancreatitis, peritonitis, renal failure and liver cirrhosis, together with some benign gynaecological diseases (pelvic inflammatory disease, endometriosis) have all been associated with abnormal elevation of CA-125 [3]. This limits its usefulness as a screening tool for ovarian cancer in asymptomatic patients. Even in the presence of clinical signs suggestive of ovarian carcinoma, a high serum CA-125 is still not necessarily indicative of the disease. We have performed serial determinations of serum CA-125 levels in 6 consecutive patients with benign ovarian fibrothecomas diagnosed and treated at our hospital during the last 2 years. Initial serum CA-125 was invariably elevated in all patients before surgical treatment, in some of them extremely so (above 500 U/ml, which is the top limit at our laboratory). Serum levels had returned to normal in all patients after a maximum of 6 months following surgical excision (Fig. 1). The elevation of CA-125 in these patients seems to be associated with the proliferation of the rather inert fibrous stromal component of their tumours, since 1 patient with a pure ovarian thecoma diagnosed during the same period showed normal pretherapeutic CA-125 levels. The hypothesis is further supported by the findings of Walker *et al.* [4], who reported about 2 cases of ovarian cellular fibromas associated with an elevated CA-125. To corroborate it, we determined CA-125 serially in 5 patients subject to controlled ovarian hyperstimulation as part of an *in vitro* fertilisation program. Gonadotrophin hyperstimulation, as practised on these patients, often produces massively enlarged ovaries by acting mainly on the granulosa-cell population of them, and only secondarily affecting the inert stromal component. All 5 patients (data not shown) showed normal (below 30 U/ml) prestimulation and serial CA-125 levels throughout their stimulation cycles, also at the point of maximal stimulation, as determined by means of oestradiol plasma levels and ultrasound examination of follicle growth.

Correspondence to J. Schneider.

The authors are at the Universidad del Pais Vasco, Hospital de Cruces, Department of Gynecology, E-48903 Baracaldo (Vizcaya), Spain.
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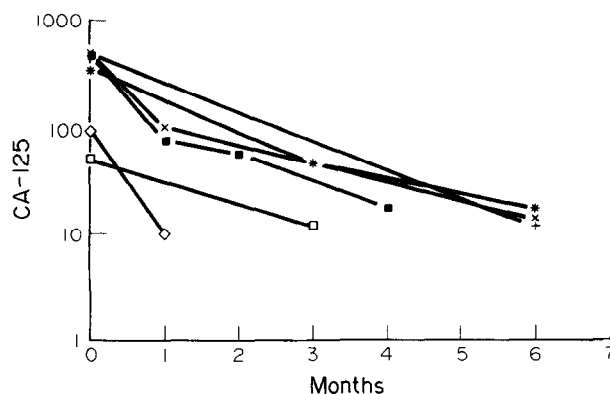


Fig. 1. Decline of CA-125 levels, expressed in U/ml on the y-axis, after surgical excision of the tumour. All values below 20 U/ml after a maximum of 6 months.

Ovarian fibrothecoma, thus, which is one of the most benign and well-differentiated tumours arising in this organ, consistently elevates serum CA-125. In view of this fact, it is remarkable that CA-125 expression has been found to be inversely correlated with the degree of differentiation of cultured ovarian carcinoma cells, as reported by Brooks *et al.* [5]. One explanation for this may be that mesothelial tumour cells behave quite differently from fibrous stromal cells regarding the expression of CA-125, even if belonging to the same organ.

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Fotemustine–Dacarbazine Combinations in the Treatment of Metastatic Melanoma

Ofer Merimsky and Samario Chaitchik

AAMDAL *ET AL.* [1] have recently reported encouraging results with dacarbazine and fotemustine used sequentially for meta-

Correspondence to O. Merimsky.

The authors are at the Department of Oncology, Ichilov Hospital, The Tel-Aviv Sourasky Medical Center and Sackler Faculty of Medicine, 6 Weizman str., Tel-Aviv University, Tel-Aviv 64239, Israel.
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