Eur J Cancer Clin Oncol, Vol. 24, No. 8, pp. 1381–1382, 1988.
Printed in Great Britain

0277-5379/88$3.00+0.00

Letter to the Editor

Cancer Antigen CA125 in Epithelial Ovarian Cancer: Immunohistochemical Expression Before and After Chemotherapy

CHARLES REDMAN,* MARK G. BRADGATE,† TERENCE P. ROLLASON,† CHRIS J. HILTON* and ANN WILLIAMS†

**West Midlands CRC Clinical Trials Unit, Queen Elizabeth Medical Centre, Birmingham, U.K. and †Departments of Pathology and Gynaecology, Birmingham and Midland Hospital for Women, Birmingham, U.K.*

CA125 is a glycoprotein found on the surface of most ovarian epithelial carcinomas [1], which can be detected using a murine monoclonal antibody OC125. Within CA125 positive tumours, positive and negative cells are found to be intimately intermixed demonstrating tumour cell heterogeneity [1, 2]. This heterogeneity has important implications in tumour response to therapy [3].

Serum CA125 levels are elevated in 80–90% of ovarian cancer cases compared to 1–3% of healthy controls [4] and correlate well with disease burden [5], although there is a wide range of values in patients with bulky disease indicating that the proportion of antigen-releasing cells varies from tumour to tumour. The effect of chemotherapy on the proportion of cells expressing CA125 within a tumour has not been studied.

We performed a retrospective analysis of CA125 expression in chemosensitive ovarian carcinomas, assessing tumour CA125 positivity before and after chemotherapy and assessed the prognostic significance of these changes.

Specimens were obtained from 19 patients who had histologically confirmed FIGO stage III–IV epithelial ovarian cancer. All patients had residual disease following primary operation after which they had received either single agent or combination platinum chemotherapy before undergoing a second operation. All patients had responded to chemotherapy but had macroscopic disease at the second operation.

Histological type was assessed from haematoxylin-and-eosin stained sections by one author using WHO criteria (serous 13, mucinous 1, endometroid 2, clear 2, undifferentiated 1). Immunohistochemical staining with OC125 murine monoclonal antibody (CIS, High Wycombe, Bucks) was performed on tissue sections (4 μm thick) obtained from formalin-fixed paraffin-embedded tissues using a peroxidase–anti-peroxidase technique. CA125 positivity of the tissue sections was assessed by one author (MB) on the basis of intensity and consistency of staining, using an arbitrary 0–3 scale for each variable which were then summated. A significant difference in CA125 positivity between the first and second specimen was defined as a change equal to, or greater than 2 in the summated score. The post-chemotherapy specimens were divided into three groups, i.e. increase, decrease or no change. Survival curves were drawn for each of these groups using the method of Kaplan and Meier [6] and the differences between the groups compared using the log-rank test [7]. Serial serum CA125 were performed in 6 patients (median of 4 samples per patient, range 2–7). Clotted whole venous blood samples were centrifuged within 4 h and the serum stored at −20°C until assayed in duplicate using a commercially available immunoradiometric assay (ELSA CA125™ CIS). A change of 50% in antigen level was considered significant.

Pre-chemotherapy serum CA125 levels were elevated in all patients (median 140 U/ml, range 80–560) in whom these were performed and were significantly decreased during treatment, falling below 35 U/ml in two cases.

Ninety-five per cent (18/19) of the tumours were CA125 positive. Tumour positivity was observed for all histological types. The only negative tumour was a Grade 3 endometrioid adenocarcinoma. There was no difference in immunostaining between primary tumour and metastatic disease.

Accepted 1 April 1988.
Correspondence and requests for reprints to: C.W.E. Redman, West Midlands CRC Clinical Trials Unit, Queen Elizabeth Medical Centre, Birmingham B15 2TH, U.K.

CA125 positivity in pre- and post-chemotherapy specimens did not differ in 13 cases. Six cases showed either an increase (3) or decrease (3). The median survival time for the study group was 15.8 (± 5.8) months. No significant association was noted between survival and change in CA125 positivity ($\chi^2_2 = 2.972$; $P = 0.2263$).

The fall in serum CA125 observed in patients responding to chemotherapy has been attributed not only to the reduction in tumour bulk as a whole but also specifically those cells that release CA125 [8]. In this study the cellular CA125 expression was reduced in only 16% of cases suggesting that there is not a selective killing of cells expressing this antigen.

Pre-treatment serum CA125 levels have not been shown to independently correlate with prognosis other than as an indicator of tumour burden and FIGO stage [9, 10] and therefore accords with our observation that changes in the expression of CA125 within the tumour did not influence prognosis, although the numbers are small and further study is required.

REFERENCES

1. Kabawat S, Bast RC, Weich WR, Knapp RC, Colvin RB. Immunopathologic characterisation of a monoclonal antibody that recognises common surface antigens of human ovarian tumours of serous, endometroid, and clear cell types. *Am J Clin Pathol* 1983, **79**, 98–103.
2. MacDonald F, Bird R, Stokes H, Russell B, Crocker J. The expression of CEA, CA125, CA 19-9, and human milk fat globule antigen in tumours of the ovary. *J. Clin Pathol* **41**, 260–264.
3. Goldie JH, Coldman AJ. A mathematical model for relating the drug sensitivity of tumours to their spontaneous mutation rate. *Cancer Treat Rep* 1979, **63**, 1727–1732.
4. Bast RC Jr, Klug TL, St John E *et al.* Monitoring human ovarian carcinoma with a combination of CA-125, CA 19-9, and CEA. *Am J Obstet Gynecol* 1984, **149**, 883–887.
5. Canney PA, Moore M, Wilkinson PM, James RD. A prospective clinical assessment of its role as a tumour marker. *Br J Cancer* 1983, **50**, 765–769.
6. Kaplan EL, Meier P. Non parametric estimation from incomplete observations. *J Am Stat Assoc* 1958, **53**, 457–462.
7. Peto R, Pike MC, Armitage P *et al.* Design and analysis of randomised clinical trials requiring prolonged observation of each patient. II analysis and observation. *Br J Cancer* 1977, **35**, 1–39.
8. Schilthuis MS, Aalders JG, Bouma J *et al.* Serous CA125 levels in epithelial ovarian cancer: relation with findings at second-look operations and their role in the detection of tumour recurrence. *Br J Obstet Gynaecol* 1987, **94**, 202–207.
9. Cruickshank DJ, Fullerton WT, Klopper A. The clinical significance of pre-operative serum CA125 in ovarian cancer. *Br J Obstet Gynaecol* 1987, **94**, 692–695.
10. Lavin PT, Knapp RC, Malkasian G *et al.* CA125 for the monitoring of ovarian carcinoma during primary therapy. *Obstet Gynecol* 1987, **69**, 223–227.