Eur J Cancer, Vol. 27, No. 9, pp. 1180–1181, 1991.
Printed in Great Britain
0277-5379/91 $3.00 + 0.00

Letters

Tumour-associated Trypsin Inhibitor and CA-125 during Treatment of Mucinous Ovarian Cancer in 2 Patients

Ole Mogensen

RECENT REPORTS [1, 2] have established the superiority of the tumour-associated trypsin inhibitor (TATI) [3] over CA-125 [4] in the differential diagnosis of mucinous ovarian tumours. TATI levels were increased in 60–80% of the patients whereas only 40–50% had elevated CA-125 levels. However, the use of TATI as a follow-up marker during treatment of patients with mucinous ovarian cancer has so far only been described in 1 case [1] and its effectiveness therefore needs further elucidation.

We have measured TATI and CA-125 levels during treatment (monthly courses of cisplatin 60 mg/m^2, doxorubicin 40 mg/m^2, cyclophosphamide 500 mg/m^2) of FIGO stage III mucinous ovarian cancer in 2 patients who developed progressive disease. The tumour response was evaluated clinically by a gynaecological examination before each course. Blood samples were drawn before the courses and stored as serum at −80°C until analysis. TATI and CA-125 levels were measured in serum by commercially available assays (TATI: Farmos Group, Oulunsalo, Finland; CA-125: Abbott Laboratories, Chicago). The instructions given by the manufacturers were followed. The upper limit of normal values for TATI was 21 μg/l [3] and for CA-125 35 U/ml [4].

In the first patient, before the start of chemotherapy the TATI and the CA-125 levels (Fig. 1) were normal (15 μg/l and 22 U/ml, respectively) and the CA-125 content remained normal (up to 8 U/ml) throughout the 12 months of treatment. The TATI level increased during therapy and gradually rose to 205 μg/l at the time of the diagnosis of progressive disease. The first abnormal value was registered after two courses of treatment and 5 months later persistent tumour was established at second look laparotomy. The TATI level increased rapidly after the second look, and progressive disease was diagnosed by ultrasonography 7 months later.

In the second case, the first blood sample was drawn before the primary operation. The preoperative TATI and CA-125 values (Fig. 2) were both abnormal (32 μg/l and 110 U/ml, respectively), but the values normalised after the operation. The TATI level remained normal (up to 17 μg/l) throughout the 7 months of chemotherapy. At the time of clinical progression the marker had risen to 23 μg/l and to 177 μg/l 1 month later. The first increased CA-125 value (38 U/ml) was demonstrated after four courses of chemotherapy and the antigen gradually rose to 122 U/ml during subsequent treatment. Thus, progressive disease was predicted by the CA-125 analysis 3 months before the first abnormal TATI value.

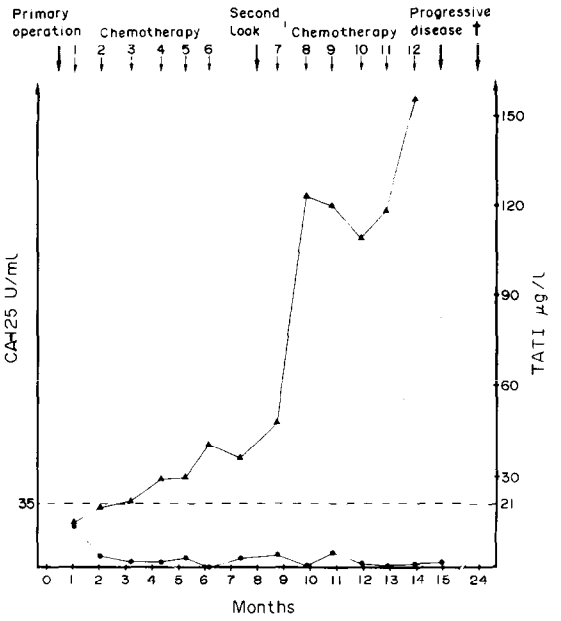

Fig. 1. TATI (▲—▲) and CA-125 (●—●) values during treatment of patient A. Progressive disease at TATI value = 205 μg/l.

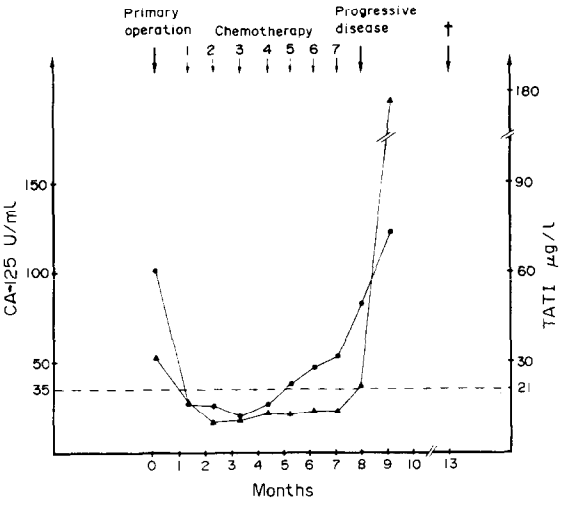

Fig. 2. TATI (▲—▲) and CA-125 (●—●) values during treatment of patient B.

The mechanism responsible for false negative TATI and CA-125 values during therapy is unknown. TATI and CA-125 marker levels did not fluctuate in parallel, which on the one hand suggests that the levels are not produced by one and the same tumour cell subpopulation and on the other hand that different tumour cell subpopulations exhibit a varying sensitivity to chemotherapy. This may explain why one marker (produced by tumour cells resistant to therapy) increased during treatment while the other (produced by more therapy-sensitive cells) was false negative. Studies comparing serum levels of TATI and CA-125 to the marker producing cells identified by immunohistochemical methods may further elucidate this problem.

The present results supplement the recent reports [1, 2] and suggest that TATI holds significant prognostic information in mucinous ovarian cancer.

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Revised 8 Apr. 1991; accepted 26 Apr. 1991.

1. Halila H, Lehtovirta P, Stenman U-H. Tumour-associated trypsin inhibitor (TATI) in ovarian cancer. *Br J Cancer* 1988, **57**, 304.
2. Mogensen O, Mogensen B, Jakobsen A. Tumour-associated trypsin inhibitor (TATI) and cancer antigen 125 (CA 125) in mucinous ovarian tumours. *Br J Cancer* 1990, **61**, 327.
3. Stenman U-H, Huhtala M-L, Koistinen R, Seppälä M. Immunochemical demonstration of an ovarian cancer-associated urinary peptide. *Int J Cancer* 1982, **30**, 53.
4. Bast RC, Jr, Klug TL, John ES, *et al.* A radioimmunoassay using a monoclonal antibody to monitor the course of epithelial ovarian cancer. *N Engl J Med* 1983, **309**, 883.

Acknowledgement—The skilful assistance of Helle Andersen, laboratory technician is highly appreciated.

Eur J Cancer, Vol. 27, No. 9, p. 1181, 1991.
Printed in Great Britain
0277-5379/91 $3.00 + 0.00

Missed Diagnoses Revealed at Necropsy in Patients with Gynaecological Malignancies

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THE ADVENT of sophisticated diagnostic tests has reduced the number of necropsies in patients who die while in hospital, due to the conviction that this procedure is unnecessary for verification of diagnosis [1, 2]. Many clinicians, however, are rediscovering the benefits of necropsy [3–6]. Our experience of the past 10 years has demonstrated that necropsy can reveal unexpected findings, even in apparently simple cases. Of 704 patients treated for gynaecological neoplasms, 54 died in our hospital and necropsy was requested for 29 (54%) (Table 1).

Request forms were always filled out by oncology group clinicians, and contained detailed information about the clinical course. A clinician was almost always present at the necropsy. In 9 deaths due to postoperative complications, the clinical diagnosis was confirmed. In a patient with stage IIIC ovarian cancer, who died from a pulmonary embolism, a second primary neoplasm was found in the pancreas. The necropsies in the other 20 cases were done to confirm and evaluate better the spread of disease in patients who died of cachexia. In 2 of these cases necropsy revealed a missed major diagnosis [5].

Case 1 (65 years) was operated on in July 1987 for a stage IIIB heterologous mixed Mullerian tumour of the ovary, with residual tumour of less than 1 cm after surgery. She was given chemotherapy with cisplatin and doxorubicin. Second-look laparotomy at 6 months revealed only one random biopsy specimen (an adhesion) positive for tumour, so chemotherapy was discontinued. A smooth, painful centropelvic mass and fever developed in June 1988. Computed tomography (CT) confirmed the clinical suspicion of recurrence. Concomitant anaemia and thrombocytopenia were interpreted as being secondary to the recurrence. The patient died 1 month later and the necropsy revealed no tumour in the abdominal cavity. The progressively increasing abdominal mass proved to be a partly organised haemoperitoneum.

Table 1. Missed clinical diagnoses in 29 necropsies

Clinical diagnosis		Necropsy findings
Pulmonary embolism	6	In 1 case, second primary tumour of pancreas
Myocardial infarction	1	–
Peritonitis	1	–
Cerebral embolism	1	–
Progression	20	In 2 cases, major missed diagnosis: adherences with intestinal occlusion organised haemoperitoneum

Case 2 (49 years) underwent first surgery in September 1987 for a stage IV (pleural) serous papillary ovarian carcinoma with residual tumour of 10 cm (the omentum was not removable). On completion of chemotherapy with cisplatin plus cyclophosphamide (with pulmonary disease radiologically negative), a second-look laparotomy demonstrated a good partial response and permitted debulking of the residual omental disease. The patient then received consolidation with the same drugs; at the end of this treatment, in keeping with the protocol [7], a third-look laparotomy was done in February 1988 and demonstrated complete response to therapy. The patient did well until July 1988 when intestinal occlusion developed. CT showed abdominal relapse, confirming the suspicions raised at clinical examination. Palliative derivative surgery seemed useless because of diffuse peritoneal carcinomatosis. The patient died 2 months later, and necropsy revealed diffuse fibrous adhesions conglobating the large and small intestines; however, no tumour was found in the abdominal cavity. Only a microscopic residual tumour was present in the pleural cavity.

Thus modern technology has not eliminated the need for postmortem verification: diagnostic imaging may have serious difficulties in the differential diagnosis between neoplasia and some therapy complications [8]. Necropsy provides valuable medical audit and can uncover missed diagnoses which could be helpful for future practice. When possible necropsy should be performed in all cases, and an effort should be made to overcome the natural resistance of relatives.

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Revised 24 Apr. 1991; accepted 25 Apr. 1991.

1. Burrows S. The postmortem examination. Scientific necessity or folly? *JAMA* 1975, **233**, 441–443.
2. McKay MJ, Langlands AO. On the yield of new information from the selective requesting of post mortem examinations in oncology patients. *Eur J Cancer Clin Oncol* 1988, **24**, 1707–1714.
3. McPhee JS, Bottles K. Autopsy: moribund art or vital science? *Am J Med* 1985, **78**, 107–113.
4. Landelfeld CS, Goldman L. The value of autopsy in modern oncology. *Eur J Cancer Clin Oncol* 1989, **25**, 607–609.
5. Goldman L, Sayson R, Robbins S, Cohn LH, Bettmann M, Weisberg M. The value of the autopsy in three medical eras. *N Engl J Med* 1983, **308**, 1000–1005.
6. Peacock SJ, Machin D, Duboulay CE, Kirkham N. The autopsy: a useful tool or an old relic? *J Pathol* 1988, **156**, 9–14.
7. Pecorelli S, Babilonti L, Bolis G, *et al.* Randomized trial of dose-intensive regimens with weekly cisplatin (P) plus adriamycin (A) or cyclophosphamide (C) in advanced epithelial ovarian cancer (abstr.). *II Meeting IGCS*. Toronto 1989, 71.
8. Franchi M, La Fianza A, Babilonti L, *et al.* Clinical value of computerized tomography (CT) in assessment of recurrent uterine cancers. *Gynecol Oncol* 1989, **35**, 31–37.