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OC-125 as a diagnostic aid in the cytological evaluation of ascitic cells in patients with ovarian carcinoma

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Summary. OC-125 is a monoclonal antibody raised against tumour cells from a patient with serous cystadenocarcinoma and reacting with an antigen CA-125 on the surface of ovarian epithelial cancer cells. We investigated whether immunohistochemical determination of CA-125 in cell samples from the peritoneal cavity could be used to discriminate between non-specific inflammatory changes in the mesothelium and malignant ovarian tumour cells. Three categories of patients were investigated: patients with disseminated serous or endometrioid ovarian carcinomas, patients with non-specific inflammatory changes in the peritoneal cavity and patients subjected to simple hysterectomy with no pathological changes in the mesothelium. In all cases of ovarian cancer CA-125 positive cells could be detected in the peritoneal fluid; none of the other categories showed positive reaction for CA-125. The results suggest that OC-125 may be a valuable adjunct in differentiating neoplastic from other cells in ascitic fluid from patients with some types of ovarian cancer.

Key words: CA-125 antigen – Histochemical study – Epithelial ovarian cancer – Diagnosis

Introduction

The clinical classification of patients with ovarian cancer is based on an evaluation of both the macroscopic dissemination and the presence of tumour cells in the ascitic fluid and/or in cell samples from the diaphragm. Intraperitoneal pathological conditions, both malignant and non-malignant, cause reactive changes in the mesothelial cells. When single or organized in small groups these cells can be hard to distinguish from highly differentiated carcinoma cells of the ovary, making diagnosis difficult.

OC-125 is a monoclonal antibody, developed by Bast et al. (1981) which reacts with an antigen, CA-125, present on the surface of most epithelial ovarian tumours. The antigen is present on the surface of benign and malignant epithelial tumours from the female genital tract (Fleuren et al. 1987; Nouwen et al. 1987) and may be common to all structures derived from the primitive coelomic epithelium.

The purpose of this investigation was to settle whether the presence of CA-125 on cells from ascitic fluid and/or from peritoneal cell samples could be used in the staging procedure of patients with ovarian cancer.

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Materials and methods

The samples for investigation of CA-125 reactivity were taken peroperatively from three categories of patients: Those with disseminated ovarian cancer (3 cases of serous and 3 cases of endometrioid carcinoma), from patients hysterectomized because of metrorrhagia whose mesothelium was expected to be normal (9 cases) and from patients operated for perforated appendicitis with reactive mesothelium (9 cases).

Cell samples and biopsies were taken from the peritoneum of all three categories of patients. From patients with ovarian cancer, cell samples from the diaphragm were also taken in addition to "touch preparations" from the tumour tissue itself. The smeared preparations of the cell samples were immediately spray-fixed and the biopsies were fixed in 10% buffered formalin and embedded in paraffin. Demonstration of CA-125 on the cells was made immunohistochemically by means of the monoclonal antibody OC-125 (CIS International (Compagnie ORIS Industrie S.A. France)) with an avidin biotin technique (Dakopatts, Copenhagen, Denmark) and using an antibody concentration recommended by CIS. The sections were thereafter incubated with 3,3-diaminobenzidine and slightly counterstained with Mayer's acid haematoxylin. All samples were taken at the Departments of Gynaecology and Surgery, Kolding Hospital and examined at the Institute of Pathology, Vejle Hospital.

Results

The biopsies and cell samples from patients with ovarian cancer all showed positive reaction for CA-125 (Figs. 1, 2). In contrast all biopsies and cell samples from patients appendecectomized or hysterectomized showed no reaction (Figs. 3, 4).

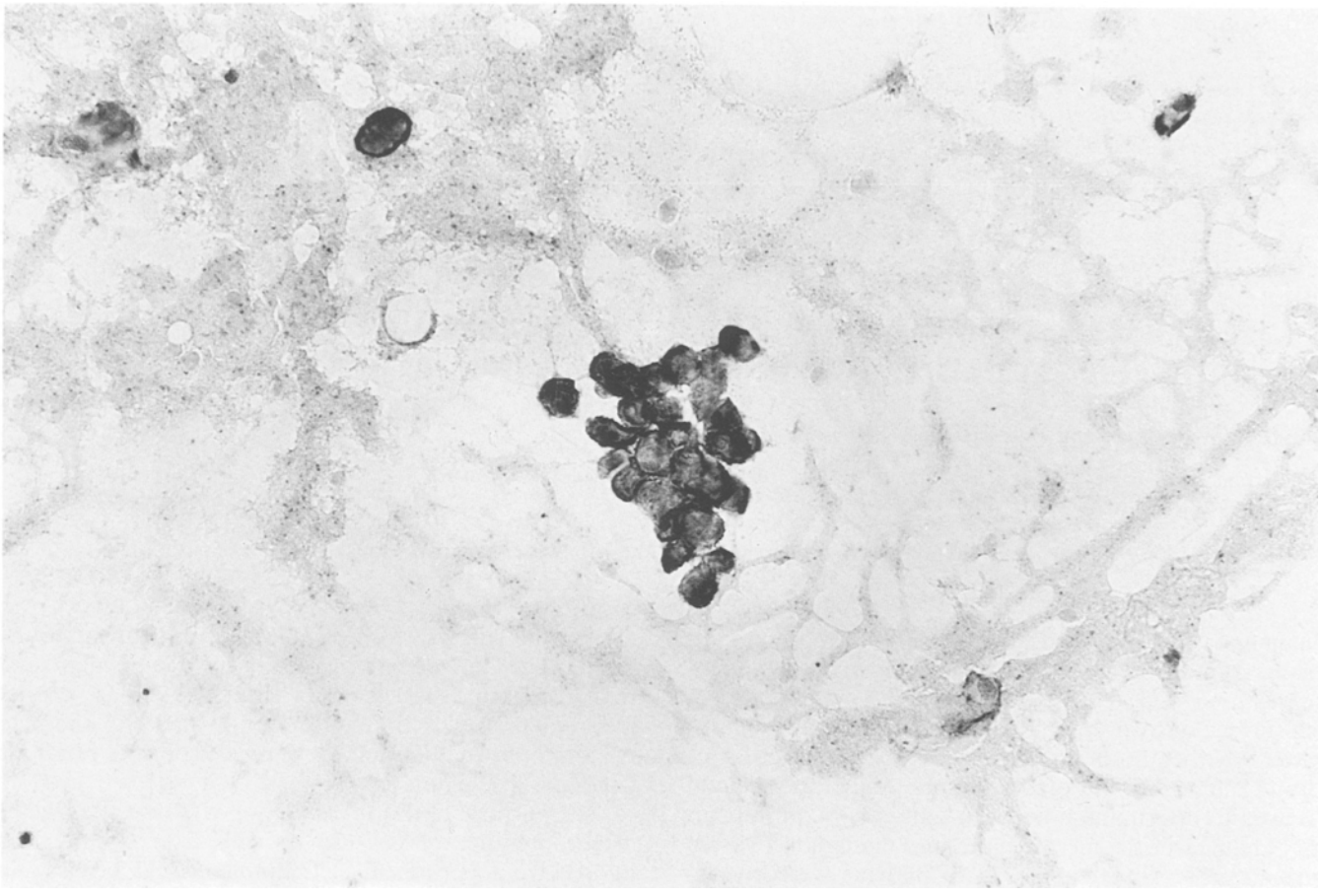

Fig. 1. Cell sample from the diaphragm showing strongly positive reaction with OC-125 on the tumour cells. ×400

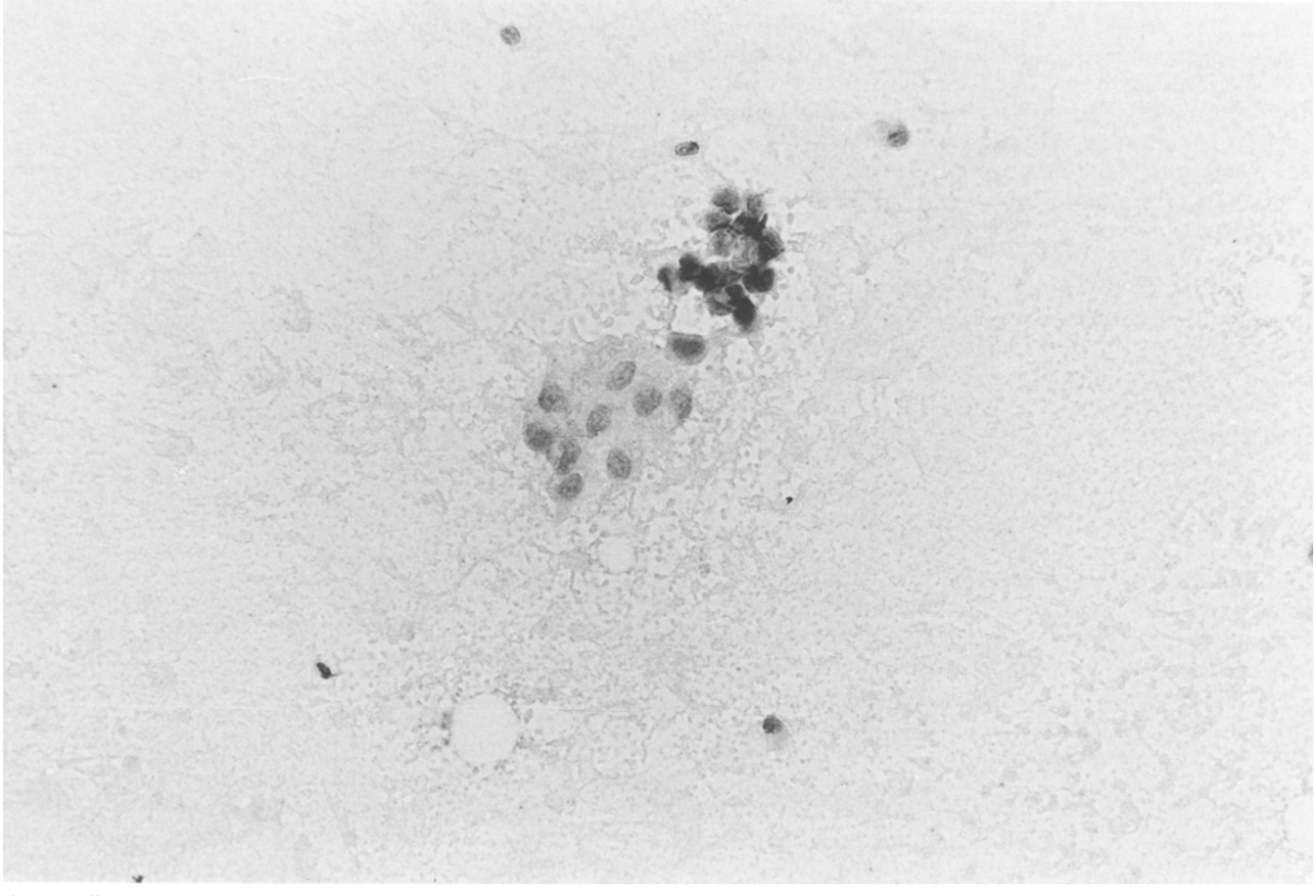

Fig. 2. Cell sample from the diaphragm (same patient as Fig. 1). Positive reaction with OC-125 on the tumour cells, whereas the mesothelial cells show negative reaction. ×400

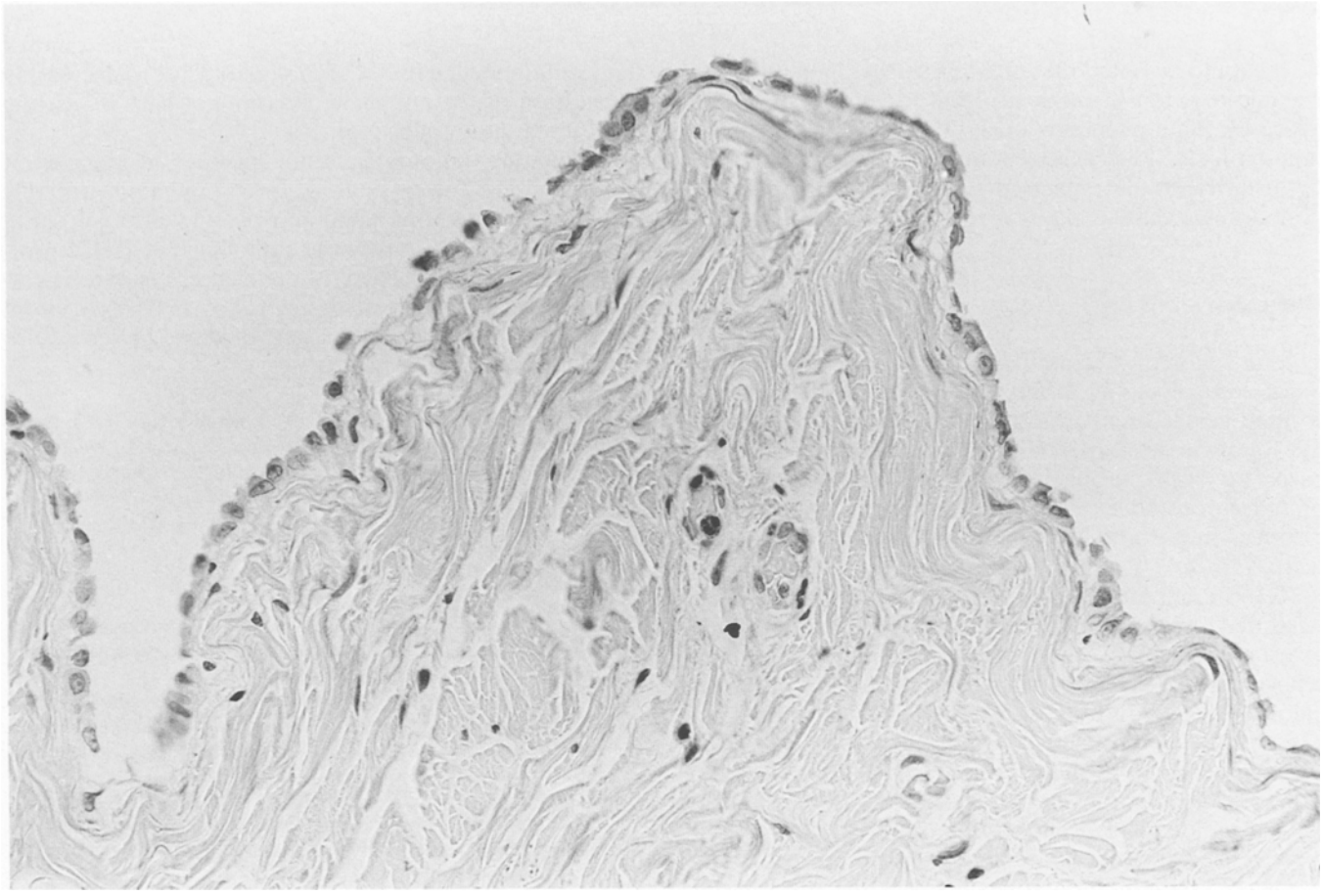

Fig. 3. Biopsy of mesothelium-covered omentum from patient with appendicitis acuta perforata. There is no reaction with OC-125 on the mesothelial cells, while some neutrophil leucocytes show non-specific positive reaction in the stroma. × 160

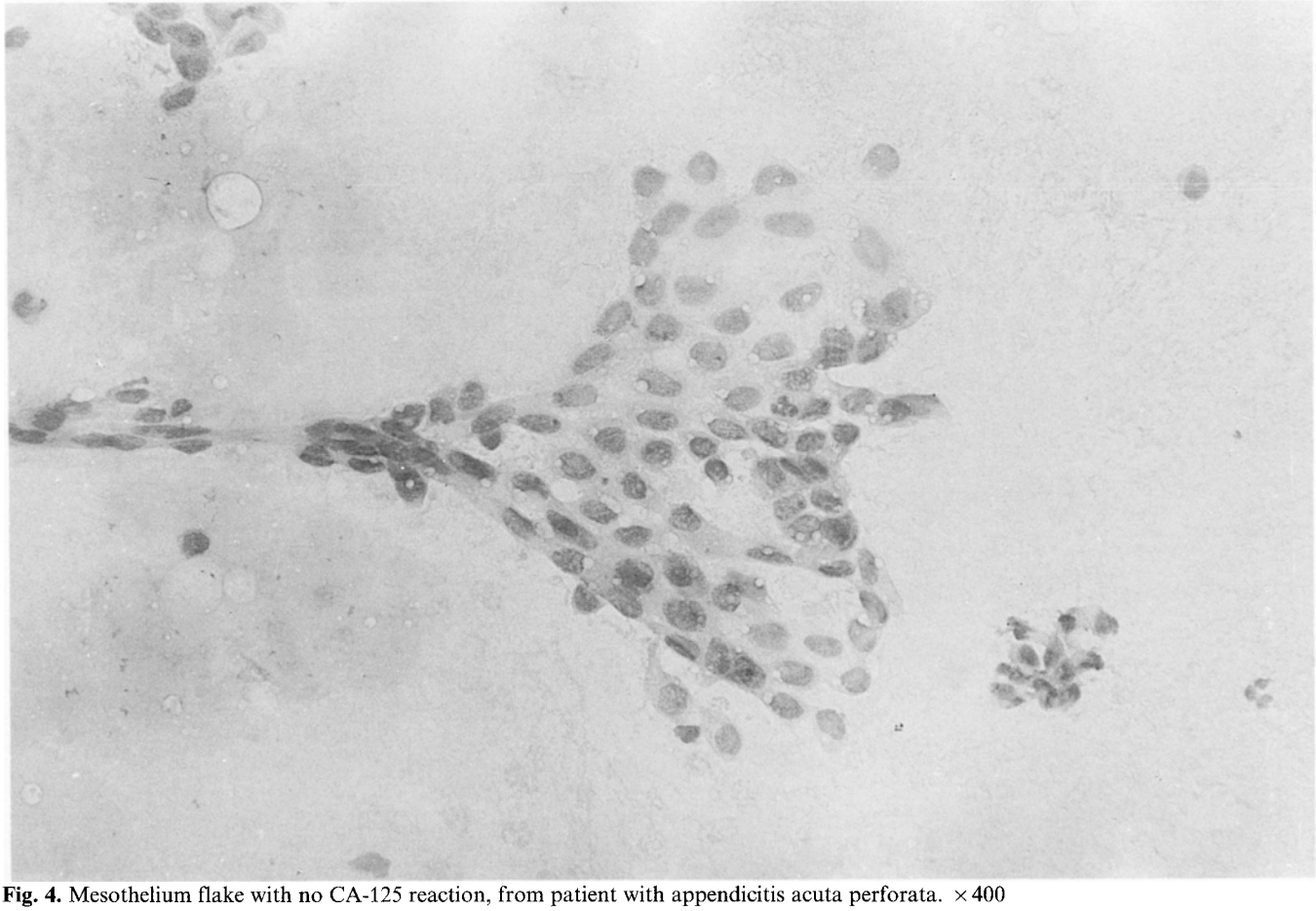

Fig. 4. Mesothelium flake with no CA-125 reaction, from patient with appendicitis acuta perforata. × 400

It should be noted that OC-125 showed positive cytoplasmic reaction in the neutrophil leucocytes in almost all cases. This phenomenon is well-known from other immunohistochemical reactions, and may be explained by insufficient neutralization of the endogenous peroxidase in these cells.

Discussion

The morphological identification of intraperitoneal tumour cells of highly differentiated ovarian carcinomas is often very difficult. As the primary classification and the follow-up of patients with cancer of the ovary are based on both the macroscopic dissemination and the presence of tumour cells in the ascitic fluid, this identification is important for reliable evaluation of these patients.

The present study showed that CA-125 can be demonstrated on the surface of serous and endometrioid ovarian carcinoma cells in both biopsies and smeared cell samples. It has previously been stated that mesothelial cells might bind OC-125 by unmasking of the CA-125 antigen when reactive (Kabawat et al. 1983). This was not observed in the present investigation. No positive OC-125 reaction was observed in the mesothelial cells of either the cancer patients or in the normal and reactive mesothelium of the appendectomized patients.

OC-125 cannot be used to disclose the presence of intraperitoneal tumour cells in all cases of ovarian carcinoma. Poorly differentiated tumours only give weak or no reaction at all with OC-125 possibly due to decreasing expression of the antigenic determinant with increasing dedifferentiation of the tumour.

Mucinous tumours were not included in the present study and the employment of OC-125 should probably be restricted to serous, endometrioid and clear cell carcinomas as only some mucinous tumours are OC-125 positive. In spite of these reservations the results of the present investigation suggest that OC-125 may be a useful supplement to the classification of most patients with ovarian carcinomas.

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