Correlative imaging study in the diagnosis of ovarian cancer recurrences

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Abstract. A correlative imaging study was carried out in 61 female patients previously treated for ovarian carcinoma. Upon suspicion of recurrence, abdominopelvic immunoscintigraphy (IS) using F(ab')2 fragments of indium-111-labelled OC 125 monoclonal antibody was performed in all patients. Ultrasonography (US) and computed tomography (CT) were performed 53 and 37 times, respectively. The diagnostic accuracy of the different imaging techniques was studied per site (abdomen and pelvis) and per patient. The diagnostic accuracy of planar scintigraphy (PS) was slightly lower than that of emission computed tomography (ECT): 66% vs 73% for abdomen, 65% vs 72% for pelvis, and 78% vs 84% in analysis per patient. The accuracy of IS (PS and ECT combined) was markedly better than that of US and CT for abdomen (IS = 73%; US = 30%; CT = 47%), pelvis (IS = 73%; US = 37%; CT = 52%) and analysis per patient (IS = 85%; US = 43%; CT = 59%). The results of IS and morphological imaging techniques (MIT: US and/or CT) were correlated with the frequency of recurrence. When IS and MIT were both negative, the frequency of non-recurrence was 14/23 for abdomen, 7/12 for pelvis and 8/13 in analysis per patient. On the other hand, when both IS and MIT were positive, the frequency of recurrence was high (9/9 for abdomen, 17/21 for pelvis and 24/26 for analysis per patient). It was also found that a positive IS associated with a negative MIT was still highly suggestive of recurrence (17/21 for abdomen, 16/22 for pelvis and 17/19 for analysis per patient). The results of this study strongly suggest that 111In-labelled OC 125 IS is accurate for the diagnosis of recurrence of ovarian cancer and provides complementary data to those obtained by MIT.

Key words: OC 125 monoclonal antibody – Immunoscintigraphy – Ovarian cancer – Diagnosis of recurrence – Correlative imaging


Introduction

Recurrences of ovarian cancer following complete surgical excision of primary tumour and polychemotherapy are not infrequent even in favourable cases of negative second-look surgery. Moreover, the prognosis remains poor, with a 5-year survival rate of roughly 50% (Neijt et al. 1986). Serial biological monitoring of serum CA-125 tumour marker may facilitate early detection of such recurrences before the appearance of clinical signs (Bast et al. 1984); however, serum CA-125 can be elevated in benign disease (Bergoran et al. 1987). Thus, the role of imaging techniques is to confirm and localize the recurrence. Promising immunoscintigraphic results have been obtained with OC-125 F(ab')2 fragments radiolabelled with iodine-131 (Chatal et al. 1987; Barzen et al. 1989; Maughan et al. 1990). However, for scintigraphic imaging [particularly emission computed tomography (ECT)], the radiophysical characteristics of 131I are less suitable than those of indium-111. A recent work (Vuillez et al. 1991) has shown that the reproducibility of inter- and intraobserver interpretation of scintigraphic images (especially ECT) after injection of 111In-OC-125 was better than with 131I-OC-125 and comparable to that of ultrasonography (US) and computed tomogra-
Immunoscintigraphy (IS). Preliminary evaluation studies of \(^{111}\)In-OC-125 carried out in patients with suspected recurrence of ovarian cancer were encouraging (Hunter et al. 1987; Peltier et al. 1989).

The aim of the present work was to compare immunoscintigraphy (IS) performed with F(ab')2 fragments of \(^{111}\)In-labelled OC-125 antibody with morphological imaging techniques, i.e. US and CT, for the diagnosis of recurrence of ovarian cancer.

Patients and methods

Patients. Sixty-one female patients (mean age 56 years, range 36–87 years) admitted for suspicion of recurrence of ovarian cancer were included in this study. Eight patients were FIGO stage I, 5 stage II, 37 stage III and 11 stage IV. After surgery for primary tumour, 50 patients underwent polychemotherapy and, in 14 of these cases, abdominal pelvic radiotherapy. Three of the 11 patients not treated by chemotherapy underwent abdominal pelvic radiotherapy.

Imaging was indicated in 55 patients (90%) by a rise in the CA-125 serum level (measured within the preceding 2 months) of more than 40 U/ml (mean 540 U/ml, range 43–5000 U/ml). For the six patients with a normal CA-125 serum level, the IS examination was based on previous inconclusive morphological (US or CT) findings.

Antibody labelling. The characteristics of OC-125 F(ab')2 fragments have already been reported (Bast et al. 1981; Chatal et al. 1987). Labelling with \(^{111}\)In was performed after coupling of F(ab')2 fragments of OC-125 antibody to two DTPA molecules using bicyclic anhydride of diethylene triamine penta-acetic acid (DTPA), as described by Hnatowich et al. (1985). The coupling yield was around 40%. Labelling was done using 370 MBq/ml of \(^{111}\)In-chloride (specific activity 74–185 MBq/mg) in acetate buffer (0.1 M, pH 5), giving a labelling yield of more than 90%.

Imaging technique. After informed consent was obtained for the procedure, an activity of 74–111 MBq of \(^{111}\)In-DTPA-OC-125 F(ab')2 fragments was administered intravenously for 20 min in an infusion of 100 ml of saline solution. No immediate or delayed reactions were noted.

Three days after injection of radiolabelled antibody fragments, abdominal pelvic planar scintigraphy (PS) and ECT were performed in 60 and 59 patients, respectively, using a large field of view gamma camera and a medium energy parallel-hole collimator (Sophy camera, Sopha Medical). These two acquisition modes were performed with the spectrometer setting on the two photopeaks of \(^{111}\)In (173 and 247 keV). Abdominopelvic PS was done in anterior and posterior views with a 10-min preset time. After tomographic acquisition, consisting of a 40-min step-by-step mode 360° elliptical rotation, 6-mm-thick transverse, sagittal and coronal sections were reconstructed using a Wiener filter.

Routine US and CT with intravenous contrast medium administration were performed in 53 (abdomen 53 times, pelvis 53 times) and 37 patients (abdomen 34 times, pelvis 35 times), respectively, during the month immediately preceding or following IS.

Interpretation and evaluation. Immunoscintigraphic images (PS, ECT) were interpreted blindly relative to those obtained with US and CT. PS and ECT were considered positive if they revealed one or more abnormal hot spot. IS was rated positive when PS or ECT was positive. IS was considered negative when both PS and ECT were negative.

US and CT were rated positive, provided that abnormal features suggesting the presence of a malignant lesion were visualized. As the diagnostic accuracy of US and CT is quite similar (Megibow et al. 1988; Silverman et al. 1988; Khan et al. 1983; Pussel et al. 1980), it was possible to define the entity of morphological imaging techniques (MIT), which corresponded to US and/or CT. MIT was rated positive if US and/or CT gave positive results, and negative if neither detected a lesion.

The different imaging methods were evaluated per site (abdomen and pelvis, which were separated by an imaginary line passing through the two anterosuperior iliac spines) and per patient. In patient analysis, IS, US, CT and MIT were considered positive when the abdominal or pelvic site was positive, and negative when no abnormality was demonstrated in the two sites.

The presence or absence of recurrence was confirmed by histological data (surgery and biopsy) in 40/61 patients (65%). In the other 21 patients, the presence or absence of recurrence was strongly suggested by the clinical course and changes in paraclinical data (CA-125 serum level, US, CT) during at least 6 months following imaging. This follow-up period was sufficiently long to ensure that the presence or absence of recurrence at the time of imaging was reliable.

In the per site evaluation, imaging methods were rated true-positive or false-positive when the abnormality shown was confirmed to be, respectively, cancerous or non-cancerous. They were rated true-negative or false-negative when no abnormality was visualized at a site and the final diagnosis respectively excluded or indicated the presence of recurrence at this site.

In the per patient analysis, imaging methods were considered true-positive when at least one of the positive sites was confirmed to be a recurrence and false-positive if neither of the positive sites was proved to be a recurrence. They were rated false-negative when at least one of the recurrences was not visualized. Immunoscintigraphy was considered determinant when it was the only imaging method truly to confirm (negative MIT) or disprove (positive MIT) a recurrence. It was considered complementary when results were truly (true-positive or true-negative) concordant with those of MIT.

Results

The sensitivity, specificity and accuracy of IS, US and CT according to site and per patient analysis are shown in Table 1.

Abdomen

PS was performed 60 times, resulting in 20/37 true-positive (TP), 17/19 true-negative (TN) and two doubtful findings. ECT was done 59 times, indicating 26/37 TP, 15/19 TN and one doubtful result. Combined results of PS and ECT were 27/39 TP and 16/20 TN. In two patients, the final abdominal diagnosis remained undetermined.

Fifty-three abdominal US explorations showed 5/40 TP, 11/12 TN and one doubtful finding. The results of 34 abdominal CT explorations were 8/25 TP and 8/9 TN.