Relapsed non-Hodgkin's lymphoma with high CA-125 mimicking ovarian tumour

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CASE REPORT

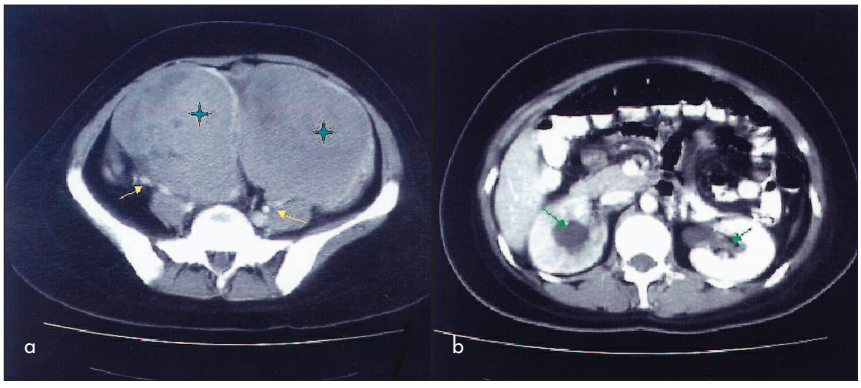
A 25-year-old woman was initially diagnosed to have stage IIB non-Hodgkin's lymphoma in April 1999 when she presented with shortness of breath and features of superior vena cava obstruction. She was treated with eight courses of CHOP (cyclophosphamide, adriamycin, vincristine and prednisolone) and showed complete response with disappearance of all the enlarged lymph nodes. She remained well for about 18 months until July 2001, when she presented again with shortness of breath, loss of appetite and loss of weight. Physical examination and investigations confirmed relapsed non-Hodgkin's lymphoma (huge mediastinal mass with right pleural effusion). She was then treated with salvage therapy with ICE (ifosfamide, carboplatin, etoposide). She was given six courses of ICE followed by irradiation to the mediastinum in view of the bulky disease. At the end of the radiotherapy, computed tomography of the thorax and abdomen showed no residual mediastinal mass or mediastinal lymph nodes, but bilateral ovarian tumours (*Figure 1a*) (the right ovarian mass measured 27 x 20 cm, left ovarian tumour measured 15 x 20 cm), and bilateral hydronephrosis (*Figure 1b*) were visible. Investigations showed markedly raised CA-125 (1216 U/ml) and lactate dehydrogenase (3147 umol/litre), and normal CEA and alpha-fetoprotein.

During open biopsies of the ovaries, multiple nodules were noted in the omentum. The histopathological examination of both ovarian (*Figure 2*) and omentum biopsies indicated non-Hodgkin's lymphoma, diffuse, large cell and B cell type. After the operation, the patient deteriorated rapidly with malignant ascites and massive pleural effusion, and died.

INTRODUCTION

CA-125 is a glycoprotein found in normal tissues derived from coelomic epithelia. It is a commonly used tumour marker for monitoring of epithelial ovarian cancer. Guppy and Rustin (2002) have shown that CA-125 is elevated in more than 90% of women with advanced ovarian cancer. High CA-125 has also been detected in non-gynaecological tumours, and reports by Apel and Fernandes (1995), Watanabe et al (1996) and Kubonishi et al (1997) have described CA-125 elevation in patients with non-Hodgkin's lymphoma.

Figure 1. Computed tomography of (a) the pelvis and (b) the abdomen. a shows the huge bilateral ovarian masses (star), which are predominantly solid, the adjacent pelvic vessels were displaced posterolaterally (arrow). b shows bilateral hydronephrosis (arrow), moderate on the right kidney and mild on the left kidney as a result of distal ureteric compression by the large lobulated ovarian masses.



DISCUSSION

CA-125 is a glycoprotein present within normal ovarian tissue and the epithelium of endometrium, endocervix and fallopian tubes. It is mostly associated with epithelial ovarian cancer and has been a very useful tumour marker to monitor the effect of treatment of the disease. However, high serum levels of CA-125 have also been reported in some non-ovarian adenocarcinomas, and non-malignant diseases involving the peritoneum.

Haematological malignancies are rarely associated with raised serum CA-125 levels. There are only a few sporadic case reports that report elevated serum CA-125 levels in non-Hodgkin's lymphoma. Apel and Fernandes (1995) initially reported a case of widespread intermediate-grade malignant lymphoma with extensive infiltration of the greater omentum and pelvic peritoneum associated with a markedly raised CA-125 level (380 U/ml). Subsequently, Watanabe et al (1996) reported an autopsy case of non-Hodgkin's lymphoma involving the pericardium and CNS with highly elevated CA-125 levels.

Kubonishi et al (1997) reported a case of Ki-1 (CD30-positive) lymphoma with multiple lymphomatous lesions in the heart, lungs, pancreas and massive pleural and peritoneal effusion, with an

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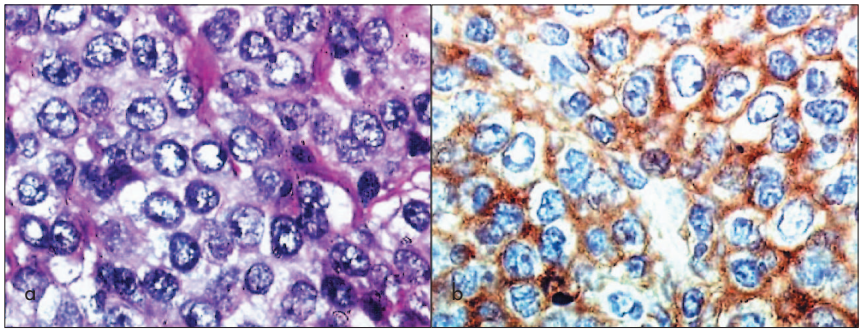

Figure 2. Histopathological diagnosis of the ovarian biopsy shows the presence of large cells with prominent nucleoli, (a) diffusely infiltrated in the biopsy specimen, which stained positive (b) for leucocyte common antigen. X 400.

unusually high serum CA-125 (3090 U/ml). Fehm et al (1998) evaluated 60 patients with several haematological malignancies and found elevated CA-125 concentrations in 3 out of 18 (16.6%) patients with acute leukaemia, 1 out of 5 (20%) patients with chronic myeloid leukaemia, 2 out of 9 (22.2%) patients with Hodgkin's lymphoma and 14 out of 28 (50%) patients with non-Hodgkin's lymphoma. Lazzarino et al (1998) and Ozguroglu et al (1999) reported increased serum CA-125 levels in 40% and 56% of patients with non-Hodgkin's lymphoma respectively. Kutluk et al (1999) found that (27/44) 61% of children with non-Hodgkin's lymphoma had elevated serum CA-125 levels.

CA-125 glycoprotein is derived from coelomic epithelial cells lining the pleural and peritoneal surface. The elevated CA-125 in non-Hodgkin's lymphoma correlates with the lymphoma infiltration of the coelomic epithelium (Apel and Fernandes, 1995; Watanabe et al, 1996; Fehm et al, 1998; Lazzarino et al, 1998; Kutluk et al, 1999; Ozguroglu et al, 1999). However, the mechanism by which lymphoma cells stimulate the secretion of CA-125 levels remains unclear. Ozguroglu et al (1999) demonstrated lymphoma cells stained negative with CA-125 but the reactive mesothelial cells were intensely positively stained.

Lymphokines, such as interleukin-1 beta and tumour-necrosis factor alpha, produced by lymphoma cells were suggested to be responsible for the stimulation of pleural or peritoneal mesothelial cells to secrete CA-125 level (Apel and Fernandes, 1995; Ozguroglu et al, 1999). Disease regression was also found to be associated with decrease or normalization of serum CA-125 levels (Fehm et al, 1998; Kutluk et al, 1999). Therefore, CA-125 may be a promising tumour marker in the assessment of invasive potential and therapeutic response in malignant lymphomas. HM

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