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CA 125 Tumor-associated Antigen in a Patient with Multivisceral Tuberculosis

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Twenty seven year-old Bahraini female presented with three weeks history of intermittent fever and general malaise not responding to conventional treatment. A CT scan of the chest and abdomen was performed for pleural effusion detected on a chest radiograph. This revealed omental cake and peritoneal seedling with minimal ascites with a small cystic ovarian mass.

Tuberculosis was considered as a possible diagnosis although an elevated CA 125 tumor marker serum level suggested the diagnosis of disseminated ovarian malignancy or gastrointestinal malignancy.

A fine needle aspiration and a diagnostic laproscopy revealed the presence of the typical epitheloid cell granuloma and central caseation confirming the diagnosis of disseminated tuberculosis. Treatment with quadruple anti-tuberculous therapy shown a dramatic improvement in both the clinical pictures as well as a remarkable drop in CA 125 levels.

CA 125 tumor associated antigen is known to be a useful screening test for ovarian, breast and other gynaecological malignancies however our experience with this case proved that it can be used as a useful marker for the clinical response to treatment in multivisceral tuberculosis.

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Serum CA 125-associated antigen is a tumor marker commonly associated with malignant tumors of ovary, endometrium, lung and breast tumors and also in some benign gynaecological tumors. CA 125-associated antigen is mainly used as a diagnostic and screening tool for ovarian tumor[1] however it is also elevated in some benign inflammatory conditions of the pleura and peritoneum[2,19]. We report a case of multi visceral tuberculosis and raised level of serum CA125 associated antigen mimicking

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ovarian cancer in a young female patient. We believe that our case report will add to the few clinical case reports of such an occurrence in the medical literature that can help understand CA 125 antigen.

THE CASE

A previously healthy 27-year-old Bahraini female was admitted to Salmaniya medical complex with three weeks history of daily intermittent fever. She attended several clinics and received different antibiotic treatment. The fever was as high as 40° C and was associated with generalized malaise, fatigue and lassitude lasting for 2-3 hours and subsided by paracetamol tablets. She denied any history of weight loss but admitted to loss of appetite during her feverish period. She complained of non-localized minimal abdominal discomfort; which was described by the patient as distension. There were no other gastrointestinal and genitourinary symptoms, no significant past medical or surgical illnesses.

The patient is single and has no history of hereditary or communicable diseases. She had minimal non-troublesome cough, which she had not sought any treatment for. The physical examination was unremarkable; she had no pallor, clubbing, or lymphadenopathy. Her abdomen was soft and no significant physical sign were demonstrated. The auscultation of the chest revealed adequate normal vesicular breath sounds and no added sounds. The cardiovascular and central nervous system review was unremarkable. A provisional diagnosis of tuberculosis versus lymphoma was made. Because of her complaint of a non-specific cough, a routine chest radiograph was taken. This showed blunting of both pleural angles suggestive of minimal pleural effusion.

Full blood count, blood sugar, urea, electrolyte, and liver function tests were all within normal range. The erythrocyte sedimentation rate (ESR) was 80mm in the 1st hour. Serum tumor markers showed a ß-hCG and alpha-fetoprotein within normal limits but raised CA125 associated antigen level 900 micrograms/L, (normal value 23-50), ovarian carcinoma was considered. Ultrasound of lower abdomen revealed free fluid in the pelvis and pouch of Douglas; the uterus was noted to be bulky and the endometrial cavity was filled with fluid. A complex cyst measuring about 3.5x4.5 cm was seen at the left ovary, this showed isodense/hypodense area with no demonstrable calcification or septation. The right ovary and both fallopian tubes were reported as normal. An ultrasound guided diagnostic abdominal paracentecesis cytology revealed reactive mesothelial cells, lymphocytes and histiocytes, but no malignant cells were seen. Gram stain, culture, and AAFB (alcohol acid-fast bacilli) stain of the ascitic fluid were negative. Computerized Tomogram Scan of the chest and abdomen showed bilateral minimal pleural effusion and ascites. An omental cake was seen at the anterior aspect of the abdomen; this was rather shaggy and dirty in appearance suggestive of omental infiltration or seedling. The liver, hepatobiliary ducts, pancreas, both kidneys and spleen were normal. No abdominal or pelvic lymphadenopathy was detected. Fiber-optic bronchoscopy examination was normal, and the bronchial washout was negative for AAFB stain and malignant cells.

Abdominal laparoscopic examination showed inflammatory adhesions spread over liver, spleen, small bowel and abdominal wall. The omentum was inflamed, thickened and shortened with multiple small nodules. Deposits of whitish nodules were seen within the abdominal wall peritoneum. There was a minimal amount of ascitic fluid. The laparoscopic findings suggested tuberculosis. Omental biopsy showed a characteristic epitheloid cell granuloma with central caseation, Langhan's giant cell reaction and peripheral collar of lymphocytes. Ziehl-Neelsen stain detected an alcohol acid-fast bacillus in a giant cell. The culture of ascitic fluid six weeks later grew mycobacterium tuberculosis, which was confirmed by PCR (polymerase chain reaction). A final diagnosis of multivisceral tuberculosis was made.

The patient immediately started on quadruple antituberculous therapy (Rifampecin 600-mg, Isoniazid 300-mg, Ethambutol 1g and Pyrazinamide 2g) daily for two months followed by four months of isoniazid 300 mg and rifampicin 600 mg as continuation phase therapy. She became afebrile on the third day of treatment. After two weeks of antituberculous therapy, serum CA125 dropped to 227 microgram/L and at the end of six months of treatment it dropped to 5 micrograms/L.

DISCUSSION

Fever of unknown origin (FUO) in a healthy 27 years old woman raises the possibility of infection or malignancy especially lymphoma. However, in some early series collagen vascular diseases has been implemented as a possible cause. Most studies agree that infections, especially extrapulmonary tuberculosis, remain the leading cause of FUO[3].

In the case presented, the patient presentation with FUO, abdominal pain, ascites, raised CA 125 and an ovarian cyst detected by ultrasound raised the suspicion of an ovarian malignancy[4]. Although ovarian cancer is uncommon before the age of 40, it remained a possible diagnosis in our patient. Most patients with ovarian cancer are first diagnosed when the disease has already spread beyond the true pelvis.

The possibility of chronic infection like Tuberculosis was also considered in our patient and the normal fiber-optic bronchoscopy did not exclude pulmonary tuberculosis. The initial ascitic fluid analysis was non-conclusive and since the pleural effusion size was small, a final diagnosis of peritoneal tuberculosis was made based on an omental biopsy, obtained by laparoscopic omental biopsy.

Tuberculosis is a major communicable health hazard in many countries; but in Bahrain prevalence rate of TB is estimated to be low (1.9% in year 2000)[5]. It is not clear how our patient contracted tuberculosis, but she most likely did so through her respiratory tract, which led to pleural effusion and hematological spread to the abdomen. It is unlikely that she contracted TB through gastrointestinal route, since the gastrointestinal tract is an uncommon port of entry, and usually involves colonization of the colon with subsequent invasion of the local lymph node and spreading into the peritoneal cavity by perforation or ulceration.

CA 125 is a glycoprotein antigen expressed by tissues of coelemic epithelium including the ovarian epithelium, fallopian tubes, endometrium and endocervix as well as the mesothelial lining cells of peritoneum, pleura, and pericardium. Any physiologic or pathologic reaction of these cells that are of the same origin including menstruation, inflammation of any cause, trauma, or tumoral involvement, cause an increase of serum CA 125 level[18]. Chronic inflammation of mesothelial cells of peritoneum, pleura and pericardium, may also cause a similar response[6].

Cancer antigen (CA 125) is a high molecular-mass carbohydrate antigen whose concentration is increased in most of the ovarian epithelial tumors and is also utilized in the follow-up of patients with ovarian cancer[1].

It is a nonspecific marker for malignancy, and may be elevated in a number of benign gynecological (e.g. endometriosis, ovarian thecoma, uterine fibroids) and non-gynecological disorders (e.g. alcoholic

hepatitis, pancreatitis and peritonitis) [7,17]. Healthy people have CA 125 level <35 U/ml, 80-85% patient with epithelial ovarian cancer have a level of CA 125 >35 u/ml[6, 17].

CA 125 elevation in tumors of the ovary, colorectal and breast malignancies has implemented its use as a screening and monitoring tool for assessing response to treatment[1].

The combination of raised Serum CA 125 associated antigen and tuberculosis of peritoneum and pleura has been described previously in the literature although not extensively. We report an additional case demonstrating the association between multivisceral tuberculosis and FUO, pleural effusion, ascites and elevated CA- 125. More reports are being published which suggest the increasing use of CA 125 for monitoring response to antituberculous therapy. L. Penna presented a case of intra-abdominal miliary tuberculosis presenting as disseminated ovarian carcinoma with ascites and raised CA 125. She reviewed the medical literatures and found only two previously reported cases of peritoneal TB associated with a raised CA 125[11,12].The association between CA 125 and peritoneal tuberculosis had been documented in the literature as case reports[8-10, 13-16] and as a case control study[17].

Serum CA 125 and pelvic ultrasonography have been suggested by some, to be accurate enough to include in yearly screening for ovarian cancer although we know as in our case this is a very non-specific tumor markers and cannot in itself be specific enough to permit a diagnosis of malignancy to be made, but once a malignancy has been diagnosed and shown to be associated with elevated levels of a tumor marker, the marker can be used to assess response to treatment[1,7].

We agree with the cases reported in the medical literature on how high serum CA 125 in symptomatic patients can mimic ovarian malignancy in patients although this was not the case in our patient. Therefore tuberculosis has to be considered in the differential diagnosis list. Serial serum level may be used as an effective marker in the diagnosis and following up of patients with tuberculous peritonitis[15-17]. We report a case of multivisceral tuberculosis and raised serum CA 125-associated antigen level mimicking ovarian cancer, as the first case in Bahrain. The subsequent clinical therapeutic response was correlated with serum level of CA 125-associated tumor marker antigen.

CONCLUSION

Serum CA125 associated antigen can be used as a marker for clinical improvement and response to treatment in multivisceral TB.

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