A case of ovarian sarcoidosis mimicking malignancy

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Summary

We present a case of systemic sarcoidosis with ovarian and peritoneal involvement. The atypical clinical presentation of the disease has lead to a problem of the differential diagnosis with ovarian cancer.

A 72-year-old female was admitted because of low grade fever, fatigue and dilatation of the abdomen. Clinical and laboratory evaluation of the patient revealed moderate right pleural effusion, ascites, diffuse ovarian infiltration, presence of enlarged intra-abdominal lymph nodes and a substantially high value of serum CA 125. Histological examination after laparotomy was indicative of ovarian sarcoidosis.

Key words: Ovarian sarcoidosis; Peritoneal sarcoidosis; CA-125, Ovarian cancer.

Introduction

Sarcoidosis is a systemic granulomatous disease that primarily affects the lung and the lymphatic system. Diagnosis of the disease requires the demonstration of typical lesions (non-caseating epithelioid cell granulomas) in more than one organ system and the exclusion of other disorders known to cause granulomatous disease. Sarcoidosis usually presents with bilateral hilar lymphadenopathy, pulmonary infiltration and skin and ocular lesions. The liver, spleen, lymph nodes, salivary glands, heart, nervous system, muscles, bones and other organs may be involved. The course and prognosis correlates with the mode of onset and the extent of the disease [1].

There are only a few case reports of ovarian and peritoneal sarcoidosis in the literature. We present a case of systemic sarcoidosis with ovarian and peritoneal involvement accompanied by a marked elevation of serum CA-125.

Case Report

A 72-year-old female was admitted to the hospital because of low grade fever, fatigue, mild respiratory distress and dilatation of the abdomen. The patient had been well until about 20 days before, when she started to feel weak, anorexic and febrile (temperature up to 37.8°C). During the next few days she noticed that her belly was progressively distended and two days before admission she became mildly dyspnoic.

On physical examination her temperature was 37.5°C, blood pressure 110/70 mmHg and heart rate was 88 beats/min. Her respiratory rate was 18 breaths per minute. Breath sounds were diminished at the left lung base but normal elsewhere. There was evidence of ascites.

Hematological and biochemical routine laboratory tests (Table 1) were unremarkable apart from mild normochromic and normocytic anemia and an increase of erythrocyte sedimentation rate (ESR = 55 mm/hr). The urine examination was normal as was the ECG. A CT scan of the chest, upper and lower abdomen was performed and revealed moderate right pleural effusion, a large amount of ascites, hepatomegaly and enlargement of both ovaries. Enlargement of the intraabdominal lymph nodes (lower paraaortical and mesenteric) was also found. No signs of lung lesions or hilar lymphadenopathy were present. Both pleuritic and peritoneal fluids were exudates. No malignant cells were found in either fluid in cytological examination nor were any acid fast bacilli detected in the fluid. Gastroscopy was performed and was negative apart from mild gastritis. A diffuse (nonmonoclonal) increase of gamma globulin was found in serum protein electrophoresis (albumin: 52.7%, α_1: 3.3%, α_2: 13.8%, β: 9.8%, γ: 20.7%). Tests for rheumatoid factor, ANA and anti-DNA were negative. A tuberculin skin test was negative. The serum tumor marker CA-125 was found to be substantially increased: 477 U/ml while other tumor markers were normal: CEA: 0.5 ng/ml, α_1FP: 1.0 ng/ml, CA19-9 U/ml: 23. CA 15-3 U/ml: 86 CA 125 U/ml: 477.

According to the findings, ovarian malignancy was considered to be the likely diagnosis. Laparotomy was performed in order to establish diagnosis by histological examination. During the surgical procedure though, both ovaries and the peritoneum were found to be infiltrated by granulomatous tissue. An infiltrating tissue biopsy revealed the presence of non-caseating

Table 1. — *Hematological and biochemical tests on admission.*

Hct	35.3%	Creatinine	0.9 mg/dl
Hgb	11.3 mg/dl	AST	14 U/l
MCV	81.3 fl	ALT	19 U/l
MCH	26.6 pg	ALP	239 U/l
MCHC	32.5 g/dl	γGT	18 U/l
WBC	6220/mm^3	Uric acid	4.8 mg/dl
Neut	67%	Total proteins	6.6 g/dl
Lymph	22%	Albumin	3.5 mg/dl
Mono	10%	Total cholesterol	165 mg/dl
Heos	1%	Triglycerides	102 mg/dl
PLT	409,000/mm^3	Total bilirubin	1.07 mg/dl
ESR	55 mm	Direct bilirubin	0.48 mg/dl
Prothr. time	12.1 sec (INR: 1.04)	Amylase	110 U/l
Gluc	91 mg/dl	K^+	3.9 mEq/l
Urea	24 mg/dl	Na^+:	141 mEq/l
Ca^{++}:	9.2 mg/dl		

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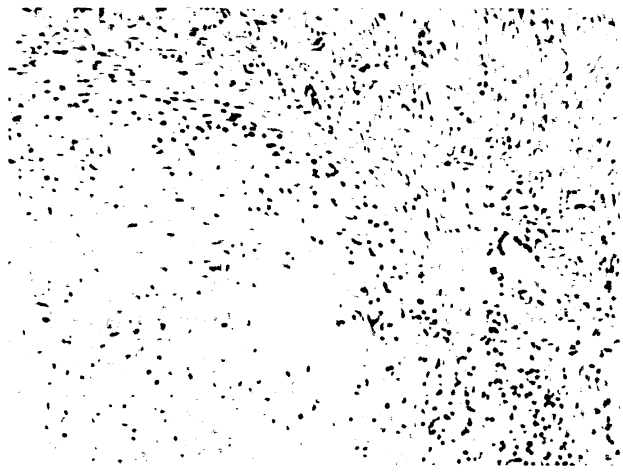

Figure 1. — Epithelioid granuloma (bottom left) of the left ovary.

granulomas. Granulomas consisted of epithelioid cells and giant cells with lymphocytes being present in the center. Some giant cells contained cytoplasmic inclusions (Figure 1). Peritoneal biopsy revealed partial infiltration by the same granulomatous tissue. All the above histological characteristics are strongly consistent with sarcoidosis. A PCR test for detection of mycobacterium tuberculosis was negative.

In order to confirm the diagnosis of systemic sarcoidosis we performed a scalene fat pad biopsy, which was also indicative of the disease. In addition, the plasma SACE (serum angiotensin converting enzyme) value was slightly increased (71 U/ml). Bronchoscopy was not performed because of the normal lung appearance in the CT scan. Corticosteroids were given to the patient (prednisone 1mg per kg of ideal body weight) and the symptoms subsided rapidly. Four months later she was feeling in good health and her laboratory tests as well as the chest X-ray and the CT scan of the abdomen were normal. Serum CA-125 value had returned to normal. Five years after diagnosis there have been no signs of disease relapse.

Discussion

Ovarian sarcoidosis is a very rare condition. A review of the international literature brought up only four case reports of ovarian involvement by sarcoid tissue. In all cases the uterus was involved as well [2]. More frequently (but still rarely), uterus involvement is reported. The peritoneum is the least common site of involvement in sarcoidosis. The presence of granulomatous disease in these sites should initiate a thorough investigation for potential etiologies by both the pathologist and clinician. Etiologies of granuloma fraction must include tuberculosis, coccidiomycosis, foreign body reactions and inguinal lymphogranuloma [3]. Bacteriologic proof is essential to differentiate these from sarcoidosis. Even though there are few reported cases of sarcoidosis involving the female genital tract and the peritoneum, it is possible that the incidence may be higher. For one reason, lesions may be misdiagnosed as tuberculosis. The second reason, symptoms may be so varied as to lead some physicians to feel that they are not related to the presence of granulomatous disease [3].

The CA125 monoclonal antibody recognizes multiple antigen determinants on a glycoprotein found in coelomic epithelium during embryonic development [4]. Approximately 80% of patients with nonmucinus epithelial ovarian cancer have elevated serum levels of CA125 [4]. Elevated levels of this tumor marker have also been reported in patients with endometriosis and pelvic inflammatory disease, during menstruation and pregnancy, and after laparotomy [5]. However, the expression of CA125 by normal mesothelial cells suggests that any disease, benign or malignant, causing inflammation of the peritoneum may result in an elevation of serum CA125 [4]. Peritoneal infiltration by tuberculosis is a rare but well established condition, which is often accompanied by an increase in tumor marker CA125 [6].

In our case, ascites, ovarian infiltration, enlargement of intraabdominal lymph nodes and increased serum value of CA125 were all consistent with ovarian malignancy as the most probable initial diagnosis. After laparotomy was performed though, the granulomatous tissue found in both the ovaries and peritoneum was indicative of tuberculosis. Histological examination led to the diagnosis of sarcoidosis. The possibility of tuberculosis was excluded based on the histological features (non-caseating epithelioid granulomas), negative PCR, and, to a lesser extent, the negative tuberculin skin test and negative results of direct examination and cultures of the pleuritic and peritoneal fluid. In addition, positive histological findings of a scalene fat pad biopsy strongly supported the diagnosis of sarcoidosis.

We conclude that the differential diagnosis of polyorogonitis as well as ovarian infiltration by granulomatous tissue should include sarcoidosis as a rare but possible and curable cause.

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