

The diagnostic problems in patient with ascites, elevated Ca 125 level and autoantibodies against nuclear antigens and smooth muscle antigens mimicking advanced ovarian carcinoma – case study

Problemy diagnostyczne u pacjentki z wodobrzuszem, podwyższonym poziomem Ca 125, przeciwciałami przeciwjądrowymi i przeciwciałami przeciw mięśniom gładkim przypominającym raka jajnika – przypadek kliniczny

Szajnik Marta¹, Nowak-Markwitz Ewa¹, Szczepański Mirosław², Spaczyński Marek¹, Linke Krzysztof³, Żeromski Jan²

¹ Department of Gynecologic Oncology,

² Department of Clinical Immunology,

³ Department of Gastroenterology and Human Nutrition, University of Medical Sciences, Poznan, Poland

Abstract

The paper describes a case of 26-year-old patient primarily suspected to suffer from the ovarian or peritoneum cancer due to high level of Ca 125 antigen and ascites. During exploratory laparotomy, neoplastic process was excluded, which was confirmed by histopathological examination. Further diagnostic tests were performed.

The patient was not infected with hepatitis B or C virus, and there was no biochemical evidence of liver disease. Detailed, wide biochemical and immunological investigations detected antinuclear and anti smooth muscle autoantibodies in the blood serum. Afterwards, the patient was admitted to the Department of Gastroenterology and autoimmune chronic hepatitis was confirmed.

Key words: **ovarian neoplasms / ascites / CA-125 antigen / autoantibodies /**

Adres do korespondencji:

Ewa Nowak-Markwitz
Klinika Onkologii Ginekologicznej, Uniwersytet Medyczny,
ul. Polna 33, 60-535 Poznan, Poland
e-mail: ewamarkwitz@poczta.fm
tel. +48 61 8419330;
fax: +48 61 8419690

Otrzymano: 03.03.2008

Zaakceptowano do druku: 25.04.2008

Szajnik M, et al.

Streszczenie

Artykuł ten opisuje przypadek 26-letniej pacjentki, u której pierwotnie podejrzewano rozwijającego się raka jajnika lub pierwotnego raka otrzewnej, na co wskazywał wysoki poziom Ca 125. W trakcie laparotomii zwiadowczej wykluźono proces nowotworowy, co zostało potwierdzone badaniem histopatologicznym. Następnie rozszerzono badania diagnostyczne, mające wyjaśnić przyczynę wysokiego poziomu Ca 125.

Wykluczono zakażenie wirusem zapalenia wątroby typu B lub C. Nie było żadnych biochemicznych wykładników choroby wątroby.

Za pomocą szczegółowych testów biochemicznych i immunologicznych wykryte zostały autoprzeciwciała przeciwjadrowe i przeciwko mięśniom gładkim. Ostatecznie pacjentka została przyjęta do Kliniki Gastroenterologii i została rozpoznana chroniczne zapalenie wątroby o podłożu autoimmunologicznym.

Słowa kluczowe: **nowotwory jajnika / wodobrzusze / Ca 125 / autoprzeciwciała /**

INTRODUCTION

Cancer antigen (Ca) 125 is not a specific tumor marker and it can be synthesized by normal and malignant cells of different origin [1, 2]. Ca 125 is used for the diagnosis and follow up of patients with ovarian and peritoneum cancer [3].

Autoantibodies are produced in the course of organ-specific and non-organ specific autoimmune diseases. The panel of detected autoantibodies corresponds to the type of autoimmune disorder [4]. In the course of autoimmune hepatitis type I, autoantibodies directed against nuclear antigens and smooth muscle antigens can be detected. Our paper describes a case of 26-year old woman with high level of Ca 125 and autoantibodies against nuclear and smooth muscles antigens.

No malignant disease was found on extensive imaging studies and during abdominal exploration. Pre-operatively, it was difficult to determine whether the clinical signs were induced by liver disease.

CASE PRESENTATION

A 26-year old woman suspected of the ovarian cancer was operated in the Department of Gynecologic Oncology because of very high level of Ca 125 and 3-week history of abdominal pain, vomiting, nausea, fever, general weakness with ascites without hepatosplenomegaly. Previously she had felt well; she had never smoked and drunk alcohol. Laboratory findings showed blood hemoglobin 6,6 mmol/L, hematocrit

0,326 L/L, WBC count was 8,9 G/L, platelet 228 G/L, creatinine 0,69mg/dl. Liver function test and blood electrolytes were normal, erythrocyte sedimentation rated to 4mm, CRP 0,13 mg/dl. Hepatitis B surface antigen and antibodies anti hepatitis C virus were negative. In view of the gross ascites, serum Ca 125 was checked and proven to be greatly raised at 388 IU/ml (normal <35 IU/ml). Other markers: human chorionic gonadotropin (hCG), alpha-fetoprotein (AFP) and carcinoembryonic antigen (CEA) were negative. Chest x-ray was normal. CT scan of the abdomen and pelvis showed massive ascites without any abnormal masses. Pancreas, liver and ovaries were found to be normal. Transvaginal ultrasound revealed normal right and left ovary, normal uterus, and massive ascites. Transabdominal ultrasound showed normal liver, kidney and ascitic fluid in peritoneum.

Since the cause of the raised serum Ca 125 remained unclear, and spread minimal neoplastic process was suspected, exploratory laparotomy was decided upon. During laparotomy, visible focus of cancer tissue was not detected. The liver was macroscopically unchanged. The biopsies from both ovaries, and peritoneum, the appendectomy and partial resection of great omentum were performed in agreement with ovarian cancer protocol. No malignancy of the ovary or any other organs of the abdomen was found, which was confirmed by histopathological examination. Four liters of fluid were evacuated from peritoneal cavity and the cytology was also negative for malignant cells.

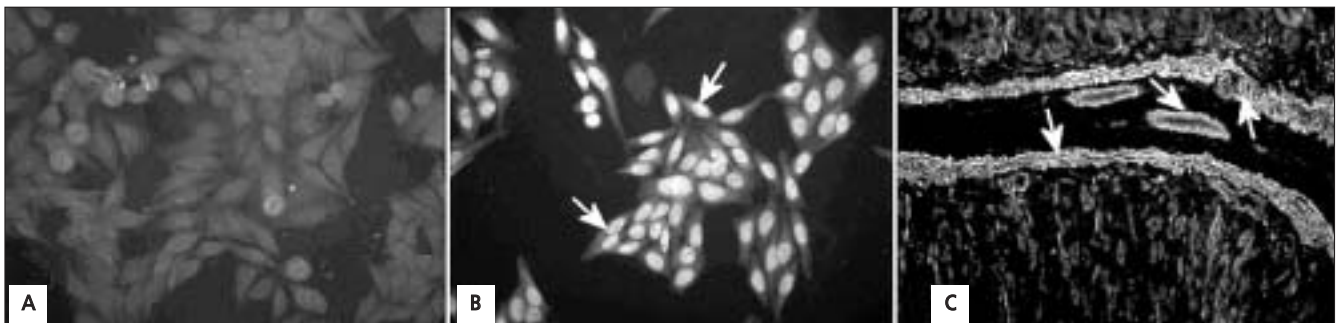


Figure 1. Autoantibodies directed against: nuclear antigens and smooth muscle antigens in patient's serum detected by indirect immunofluorescence on the sediment of Hep-2 cells line and on the section of primate stomach: A – negative control (without patient's serum) (x200); B – positive reaction: anti-nuclear antibodies with homogenous pattern of fluorescence (arrows) (x200); C – positive reaction: anti-smooth muscle antibodies seen on muscularis mucosa and vessel walls (arrows) (x200).

The diagnostic problems in patient with ascites, elevated Ca 125 level and autoantibodies...

After laparotomy, many specific biochemical and immunological investigations were carried out. Indirect immunofluorescence method was used to detect autoantibodies in the blood serum. Results of this study showed occurrence of autoantibodies against nuclear antigens (ANA) (in the titration 1:40, with homogenous pattern of fluorescence) and against smooth muscles antigens (SMA) with high intensive fluorescence. (Figure 1).

Because of ascites and detected autoantibodies in the blood serum, the gastroenterologist's opinion was sought. The opinion suggested some type of autoimmune chronic hepatitis. Afterwards, the patient was admitted to the Department of Gastroenterology. Because of normal liver function test and blood electrolytes, the liver biopsy was not performed and the patient was not treated with the use of glucocorticosteroids.

The patient is still under care of the gastroenterologist and the occurrence of autoantibodies and liver function tests will be assessed in every two months. Up to now, the patient remains in a good general condition. There is no recurrence of ascites but slightly high – 45-75mIU/mL of CA 125 level has been observed.

DISCUSSION

Ca 125 is increased in physiologic and patologic conditions. Over 80% of histologically proven ovarian carcinoma patients demonstrate high level of Ca 125. It is also produced by both healthy and malignant cells of mesothelial (pleural, peritoneal) and non-mesothelial origin (amniotic membrane, cervical epithelium).

Elevated serum Ca 125 level has therefore been reported in various conditions, involving these cells, including i.e. ascites in the course of inflammatory process [1]. Moreover, elevated serum Ca 125 levels were detected in over 50% of patients with hepatic disease [5].

Autoimmune hepatitis (AIH) is characterised by female predominance, hepatitis, and hypergammaglobulinaemia. Typically, the disease responds well to corticosteroid therapy, and clinical, laboratory, and histological remission can be achieved in about 60% of patients within 18 months. Three types of AIH have been distinguished, based on immunoserological findings. A definite diagnosis requires exclusion of viral, alcoholic, drug induced and hereditary liver disease. Type 1 AIH is the most common form of the disease worldwide and is associated with antinuclear antibodies (ANA) and/or smooth muscle antibodies (SMA). Type 2 AIH affects mainly children and is characterised by antibodies against liver/kidney cells microsome type 1 (anti-LKM1). Type 3 AIH is the least known form and has been characterised by antibodies to soluble liver antigen/liver-pancreas antigen (anti-SLA/LP) [6].

Our case apparently might correspond to type I of AIH but it is by no means clear.

CONCLUSION

Our paper illustrated the case of a patient, where malignant disease was strongly suspected. It seems to be worth assessing autoantibodies in cases with elevated level of Ca 125 and with ascites, because the reason of this can be the autoimmune process. Thus, it may be possible to avoid invasive procedures like exploratory laparotomy.

ACKNOWLEDGMENTS

This work was supported by grant for scientific research to Ewa Nowak-Markwitz. (N0 2064/PO11/2007/132) from the Ministry of Science, Poland.

References

1. Daoud E, Bodor G. CA-125 concentrations in malignant and nonmalignant disease. *Clin Chem.* 1991, 37, 1968-1974.
2. Bergmann J, Bidart J, George M, [et al.]. Elevation of CA 125 in patients with benign and malignant ascites. *Cancer.* 1987, 59, 213-217.
3. Eltabbakh G, Belinson J, Kennedy A, [et al.]. Serum CA-125 measurements > 65 U/mL. Clinical value. *J Reprod Med.* 1997, 42, 617-624.
4. Lernmark A. Autoimmune diseases: are markers ready for prediction? *J Clin Invest.* 2001, 108, 1091-1096.
5. Topalak O, Saygili U, Soy Turk M, [et al.]. Serum, pleural effusion, and ascites CA-125 levels in ovarian cancer and nonovarian benign and malignant diseases: a comparative study. *Gynecol Oncol.* 2002, 85, 108-113.
6. Ben-Ari Z, Czaja A. Autoimmune hepatitis and its variant syndromes. *Gut.* 2001, 49, 589-594.