American Journal of Case Reports

ISSN 1941-5923
© Am J Case Rep, 2016; 17: 459-461
DOI: 10.12659/AJCR.897158

Received: 2015.12.17
Accepted: 2016.04.05
Published: 2016.07.06

Level of HE4 is Correlated with Diagnosis of Struma Ovarii: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEFG Stavros Diavatis
DEF Alexis Papanikolaou

Department of Obstetrics and Gynecology, Papageorgiou General Hospital, Thessaloniki, Greece

Corresponding Author: Stavros Diavatis, e-mail: stavrosdiavatis@yahoo.com
Conflict of interest: None declared

Patient: Female, 75
Final Diagnosis: Ovarian teratoma
Symptoms: Chronic pelvic pain
Medication: —
Clinical Procedure: Tumor resection
Specialty: Oncology

Objective: Rare disease

Background: Struma ovarii is a rare ovarian teratoma with non-specific clinical presentation that can mimic malignancy, especially when combined with the presence of ascites. Since the surgical procedures performed for benign and malignant tumors are quite different, pre-operative differential diagnosis is key. In this case report we compare the levels of biomarkers CA 125 and HE4 in the differential diagnosis of a suspicious ovarian tumor.

Case Report: A 75-year-old woman with a palpable mass at the left adnexa, ascites, and high levels of CA 125, underwent a subtotal abdominal hysterectomy and bilateral salpingo-oophorectomy. Histology reported benign struma ovarii.

Conclusions: Even though transvaginal ultrasound and CA 125 levels suggested malignancy, HE4 measurements correctly diagnosed benignity.

MeSH Keywords: CA-125 Antigen • Ovarian Neoplasms • Struma Ovarii

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/897158

Background

Monodermal teratomas are a rare subtype of ovarian teratomas, composed predominantly or solely of a single tissue type, with the 3 main types being struma ovarii, carcinoid tumors, and neural tumors. Struma ovarii (goiter of the ovary) represents 0.5–1% of all ovarian tumors and approximately 2–3% of all teratomas [1,2]. Although the sparse presence of thyroid tissue is not uncommon in germ cell tumors, a teratoma is histologically classified as struma ovarii when 50% or more of its tissue consists of mature thyroid cells [1–3]. As a result of its rarity and non-specific clinical presentation, struma ovarii diagnosis can be challenging. Treatment is surgical resection either by open surgery or laparoscopy. The typical preoperative approach combines ultrasonography, CT/MRI scan, and use of serum tumor biomarkers in an attempt to differentiate malignancy. The final diagnosis is made by the post-operative histological report. Recently, a new serum biomarker HE4 (Human Epididymis protein 4) is being utilized and appears to be promising in the differential diagnosis of adnexal masses. The accuracy of HE4 in diagnosing epithelial ovarian tumors is well documented in the medical literature [4,5], but very few reports address germ-cell tumors. We therefore present a case of struma ovarii and assess if the measurement of HE4 helped the preoperative diagnosis.

Case Report

A 75-year-old woman, para 8, was admitted complaining of chronic pelvic pain and flatulence for 2 months. Her medical history included mild congestive cardiac failure due to coronary heart disease, with a past surgical history of percutaneous transluminal coronary angioplasty and an appendectomy. Her family history was negative for gynecological cancer. Transvaginal ultrasound revealed mild ascites and a solid mass measuring 6.34×5.91 cm arising from the left ovary (Figures 1, 2). The morphological evaluation of the tumor suggested high risk of malignancy and the sonographer's opinion was that malignancy could not be ruled out, although the possibility of a teratoma was indeed considered. MRI was inconclusive. Routine biochemistry was unremarkable. The patient was clinically euthyroid, with TSH value at 3.40 μIU/ml, free T_3 at 2.15 pg/ml, and free T_4 at 1.05 ng/dl. Evaluation of tumor markers showed high CA 125 at 264 U/mL (normal range 0–35 U/mL), CA 19-9 at 19.25 U/mL (normal range 0–37 U/mL), and HE4 at 57.1 pmol/L (normal range 0–150 pmol/L). The patient underwent exploratory laparotomy through a lower midline incision, with the option of a debulking procedure should the results of the frozen section reveal malignancy. Upon entering the abdominal cavity, a moderate quantity of free fluid was aspirated and sent for cytological examination. A 7×5×4 cm tumor was found on her left ovary, weighing 84 g, with smooth

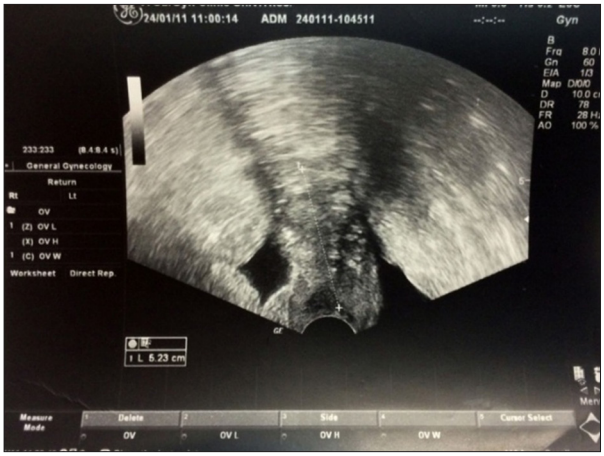

Figure 1. Transvaginal ultrasound image. Solid tumor of the left ovary.

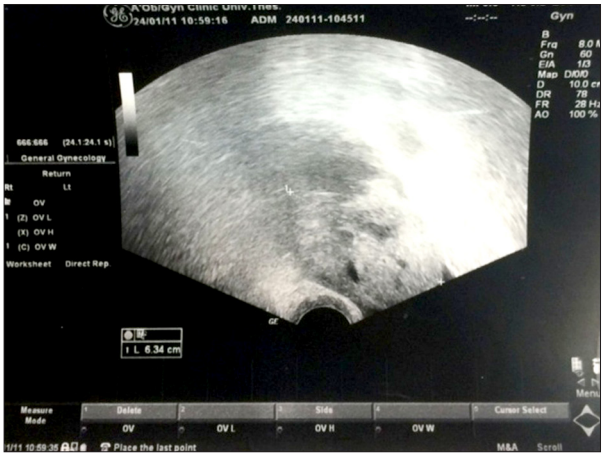

Figure 2. Ascites and echogenic foci in the tumor.

surface and gelatinous composition. The uterus, right adnexa, and the rest of peritoneal cavity were checked and found to be clear of any suspicious lesions. The frozen section showed struma ovarii with no signs of malignancy, and the operation was completed with subtotal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy. The postoperative recovery was uneventful. The permanent pathology report and the cytology examination of the ascites found no malignant cells, and the patient was discharged on the sixth postoperative day. At her follow-up examinations at 3 and 6 months, no ascites was detected, thyroid hormones were normal, and the level of all serum biomarkers had decreased to normal range.

Discussion

Struma ovarii usually presents in the fifth decade of life. A vast majority of these tumors are benign and carry a good prognosis. Rarely (5–8%) are there symptoms of thyroid hyperfunction, even thyrotoxicosis, which alerts the clinician to the

condition [3]. The tumor can even manifest as pseudo-Meigs' syndrome [6]. Preoperative differential diagnosis can be confusing even for experienced oncologists because most struma ovarii clinical features and echo patterns mimic ovarian cancer. According to the literature, malignancy occurs in 5% of cases [1–3] and the histological criteria are the same as for thyroid gland carcinoma. Advanced-stage malignant struma ovarii treatment is the same as the ovarian cancer surgical protocol, with some centers performing additional thyroidectomy, I-131 radiotherapy, and chemotherapy [2,6]. In our case, the main factor that led us to decide on open rather than laparoscopic surgery was the CA 125 value. As a result, a more extensive operation was performed and the patient's post-operative hospital stay and recuperation were prolonged. Although CA 125 is considered the criterion standard for differentiating adnexal tumors, its levels can be affected by various pelvic inflammatory diseases, uterine fibroids, liver ailments (including hepatitis and cirrhosis), and endometriosis, making correct diagnosis challenging. Some authors recommend caution when using CA 125 as a standalone diagnostic modality for ovarian tumors [7,8]. Biomarker HE4 seems to be a more accurate tool for diagnosing patients with suspicious ovarian tumors. There are many recent reviews reporting that, either as a single biomarker or in combination with CA 125 (ROMA algorithm), Human Epididymis protein 4 shows higher sensitivity/specificity in the pre-operative diagnosis than CA 125 alone [7–9]. In a systemic review of women with suspected gynecologic disease, HE4 demonstrated a higher specificity (93% *vs.* 78%) and similar sensitivity (79%) to CA125 when distinguishing benign disease from ovarian cancer [10]. In our case, HE4 correctly diagnosed benignity, and it seems that the value was not affected by the presence of ascites. However, due to the high false-positive rate in use of CA 125, if we were to calculate the Risk of Ovarian Malignancy Algorithm (ROMA) combining CA 125 and HE4, the outcome would be 54.9% malignancy (high risk).

Conclusions

In our case of a suspicious ovarian tumor, high levels of CA 125 led us to select laparotomy rather than laparoscopy. Although HE4 suggested benignity, lack of adequate clinical experience using this relatively new biomarker led our surgeons to favor CA 125 results over HE4. This is just one case where CA 125 and HE4 yield conflicting values in diagnosing struma ovarii. Analysis of more cases and a longer period of follow-up will be necessary to determine whether Human Epididymis protein 4 can improve the accuracy of ovarian teratomas diagnosis.

Conflict of interest

The authors declare no conflict of interest.

References:

1. Ning Y, Kong F, Cragun JM, Zheng W: Struma ovarii simulating ovarian sertoli cell tumor: A case report with literature review. Int J Clin Exp Pathol, 2013; 6(3): 516–20
2. Zhu Y, Wang C, Zhang GN et al: Papillary thyroid cancer located in malignant struma ovarii with omentum metastasis: A case report and review of the literature. World J Surg Oncol, 2016; 14(1): 17
3. Park CH, Jung MH, Ji YI: Risk factors for malignant transformation of mature cystic teratoma. Obstet Gynecol Sci, 2015; 58(6): 475–80
4. Lin J, Qin J, Li X, Dong P, Yin B: Diagnostic value of human epididymis protein 4 compared with mesothelin for ovarian cancer: A systematic review and meta-analysis. Asian Pac J Cancer Prev, 2012; 13(11): 5427–32
5. Wang J, Gao J, Yao H et al: Diagnostic accuracy of serum HE4, CA125 and ROMA in patients with ovarian cancer: A meta-analysis. Tumour Biol, 2014; 35(6): 6127–38
6. Riaz S, Bashir H, Hassan A et al: Metastatic radioiodine avid struma ovarii associated with pseudo-Meigs' syndrome. J Ayub Med Coll Abbottabad, 2015; 27(3): 731–34
7. Zhang Y, Qiao C, Li L et al: Serum HE4 is more suitable as a biomarker than CA125 in Chinese women with benign gynecologic disorders. Afr Health Sci, 2014; 14(4): 913–18
8. Dodge JE, Covens AL, Lacchetti C et al: Management of a suspicious adnexal mass: A clinical practice guideline. Curr Oncol, 2012; 19(4): e244–57
9. Zhen S, Bian LH, Chang LL, Gao X: Comparison of serum human epididymis protein 4 and carbohydrate antigen 125 as markers in ovarian cancer: A meta-analysis. Mol Clin Oncol, 2014; 2(4): 559–66
10. Cohen JG, White M, Cruz A, Farias-Eisner R: In 2014, can we do better than CA125 in the early detection of ovarian cancer? World J Biol Chem, 2014; 5(3): 286–300