European Journal of Obstetrics & Gynecology and Reproductive Biology 215 (2017) 141–147

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

Preoperative serum levels of YKL 40 and CA125 as a prognostic indicators in patients with endometrial cancer

Beata Kotowicz[a,*], Malgorzata Fuksiewicz[a], Joanna Jonska-Gmyrek[b], Michal Wagrodzki[c], Maria Kowalska[a]

[a] The Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Laboratory of Tumor Markers, Department of Pathology and Laboratory Diagnostics, Roentgen Street 5, 02-781 Warsaw, Poland
[b] The Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Department of Urology, Roentgen Street 5, 02-781 Warsaw, Poland
[c] The Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Department of Pathology and Laboratory Diagnostics, Roentgen Street 5, 02-781 Warsaw, Poland

ARTICLE INFO

Article history:
Received 8 April 2017
Received in revised form 8 June 2017
Accepted 12 June 2017
Available online xxx

Keywords:
Endometrial cancer
Prognostic factors
CA125
YKL-40 (CHI3L1)
Outcome

ABSTRACT

Objective: To evaluate the utility of YKL-40 and CA125 in endometrial cancer (EC) patients, and to determine their prognostic value in assessing the disease-free survival (DFS) and overall survival (OS).
Methods: We analyzed seventy-four EC patients, treated at a single institution and 25 healthy individuals. CA 125 serum level was evaluated in the Cobas 6000 system and YKL-40, using the ELISA method.
Results: Significantly increased serum level of YKL-40 and CA125 was in EC patients in FIGO I-IB when compared to healthy controls. CA125 was significantly higher in patients with more advanced FIGO stage vs. FIGO I, and also in patients with lymph node metastases vs. patients with no metastases. The obtained AUC for YKL-40 was higher than for CA125. There was, however, higher diagnostic sensitivity for YKL-40 in comparison to CA125, both in patients with type I and type II tumours. In patients who had disease progression, both the percentage of elevated concentration of CA 125 and YKL-40 was higher than in patients with remission. The Chi2 test demonstrated the statistically significant differences. The predictive value of CA125 in an aspect of DFS and OS was demonstrated.
Conclusions: A high diagnostic sensitivity of YKL-40 in the early stages of the disease suggests the possibility of using this biomarker at an early diagnostic phase of patients with EC. The patients with increased levels of YKL-40 before treatment are also at the higher risk of relapse. The determination of CA125 before surgery may be helpful in the evaluation of the regional lymph nodes, and is a poor prognostic factor for OS and DFS.

Introduction

Malignant tumours of the uterine body are the fourth most common location of neoplastic cases among women in Poland and the first among gynaecological neoplasms. According to the data from the National Cancer Registry in Poland, endometrial cancer was diagnosed in 5426 women in 2012 alone, and the number of deaths was 1162 [1]. This high incidence primarily relates to postmenopausal women. Main factors associated with increased risk of endometrial cancer include: nulliparity, genetic factors, late age of menopause, diabetes, obesity and hypertension. The mainstay of therapy in apparent stage I endometrial cancer is total hysterectomy and bilateral salpingo-oophorectomy without the vaginal cuff. In stage II disease, radical hysterectomy is not recommended, whereas complete cytoreduction with bilateral salpingo-oophorectomy and lymphadenectomy is required in advanced stages of the disease. In patients unfit for the recommended surgery and selected patients with low-risk EC, vaginal hysterectomy and salpingo-oophorectomy can be considered. In some medically unfit patients, radiotherapy or hormone replacement therapy can be considered. During the lymphadenectomy procedure systematic removal of pelvic and paraaortic nodes to the level of renal veins should be performed. Currently, the main challenge is to be able to predict before the surgery the risk of the disease progression, including the assessment of the lymph nodes and the prediction of the course, which affects therapeutic decisions. The use of advanced imaging techniques (MRI, CT) is a routine management in the preoperative diagnosis of these

* Corresponding author at: Laboratory of Tumor Markers, Department of Pathology and Laboratory Diagnostics, Cancer Center and Institute of Oncology, 02-781 Warsaw, Roentgen Street 5, Poland.
E-mail address: bkotowicz@coi.pl (B. Kotowicz).

http://dx.doi.org/10.1016/j.ejogrb.2017.06.021
0301-2115/

patients. Using the panel of marker tests along with the results of imaging examinations can help to identify patients with advanced disease, before the planned surgery. The utility of serum CA125 measurements, which is a key prognostic biomarker in ovarian cancer treatment, has been so far demonstrated to be limited in patients with endometrial cancer. The elevated CA125 level may suggest the presence of cancer cells in the regional lymph nodes [2,3]. Moreover, high values of CA125 are associated with the spread of the disease and a high degree of malignancy, and therefore could have a prognostic value [4–6]. As with other markers that are used in early clinical stages of the disease, its diagnostic sensitivity is not satisfactory. Thus, further research is needed to identify novel biomarkers that can be used in the initial diagnosis of endometrial cancer, as well as to monitor the progression of the disease. YKL-40 biomarker, also known as chitinase-3-like 1 protein (CHI3L1) having a molecular weight of 40 kDa, was identified in the early 90's. It is a glycoprotein, heparin and chitin-binding, anti-apoptotic factor and a growth factor in different cell types and has been of special interest in recent years, because of its pro-angiogenic properties by stimulating endothelial cell factors, like VEGF.

It has been shown that chondrocytes and synovial cells in rheumatoid arthritis, as well as neutrophils and tumour cells express and release YKL-40 into the blood. Previous studies have demonstrated that changes in the concentration of this biomarker play an important role in the remodelling of connective tissue and stimulate cell migration, which is associated with increased metastatic potential of tumour cells [7–9]. Thus elevated concentrations of this marker in serum have been identified in patients with different types of tumours. A number of studies have demonstrated the prognostic value of YKL-40, especially in melanoma, breast cancer, colon cancer, lung cancer, ovarian cancer and endometrial cancer [10–15].

The aim of the study was to evaluate the utility of the new biomarker-YKL-40 in patients with endometrial cancer and the standard CA125 tumour marker, and to determine their prognostic value in assessing the disease-free survival (DFS) and overall survival (OS).

Material and methods

The study enrolled 74 patients with histologically confirmed endometrial cancer treated in one centre, the Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology in Warsaw, from 2007 to 2010. The patients' age ranged from 42 to 84 years (median age 61 years), including 6 women before and 68 after menopause. During the follow-up period, 19 patients developed relapse (26%) and 16 patients died (22%). The clinicopathologic characteristics of the study group are shown in Table 1.

Before surgery, patients were subjected to the pelvic MRI (magnetic resonance imaging) and abdominal ultrasound (US) or CT (computed tomography) of the pelvis and abdomen to determine the initial stage of the cancer. All patients underwent surgical treatment, which involved the removal of the uterus and appendectomy – total abdominal hysterectomy and ilio-obturator lymphadenectomy. The final determination of the stage and histopathological diagnosis was based on the assessment of postoperative material. The clinical stage of cancer was determined according to the FIGO classification. The type of cancer was identified on the basis of the histopathological examination of postoperative material; type I – 60 patients and type II – 14 patients. The clinical follow-up of the patients was carried out until the year 2016. Control examinations involved evaluation of the clinical condition of the patient, based on the standard gynaecological examination, ultrasound or CT of the abdomen and pelvis and chest X-ray.

Table 1
Clinicopathological characteristics of endometrial cancer patients included in the study.

PARAMETERS	Number of Patients	Percentage of patients%
Menopausal status		
premenopausal	6/74	8
postmenopausal	68/74	92
FIGO		
IA-IB	50/74	68
II	8/74	11
IIIA-IIIC2	12/74	16
IVA-IVB	4/74	5
Type		
I (endometrial)	60/74	81
II (serous, clear cell, solidum, papillare, other)	14/74	19
Histological grade/G/		
G1	21/74	28
G2	50/74	68
G3	1/74	1
Gx	2/74	3
Lymph node status (N)		
negative	64/74	86
positive	10/74	14
Recurrence		
No	52/71	73
Yes	19/71	27
Survival status		
Alive	58/74	78
Dead	16/74	22

Abbreviations: FIGO – International Federation of Gynecology and Obstetrics.