Trakia Journal of Sciences, Vol. 12, Suppl. 1, pp 299-301, 2014

Available online at:
http://www.uni-sz.bg

**ISSN 1313-7050 (print)**
**ISSN 1313-3551 (online)**

# IMP3 EXPRESSION AND ENDOMETRIAL CANCER – FIRST STEPS IN SMALL GROUP INVESTIGATION

**V. Velev*, J. Ananiev, M. Gulubova**

Department of General and Clinical Pathology, Medical Faculty, Trakia University, Stara Zagora, Bulgaria

**ABSTRACT**

Insulin-like growth factor-II mRNA-binding protein 3 (IMP3) is a new factor and protein with major role in embryogenesis and carcinogenesis of some malignant tumors.

We investigate immunohistochemicaly the expression of IMP3 in 16 cases of EC. We evaluated the correlation between the collected data and clinical and pathological parameters of investigated patients. The results were compared with clinical and pathological parameters of investigated patients.

After analysis of the results we found expression of IMP3 in 10 (62.5%) cases were patients. Fifty percent from IMP3 positive cases were from EC type I and the other 50%- type II EC. We found that 60% from the patients in tumor stage T3-T4 were high expression of IMP3 ($\chi 2=2.56$; $p=0.051$).

Despite the small group of cases we may stated that in endometrial adenocarcinomas, IMP3 expression is found in more aggressive disease.

**Key words:** IMP3, endometrial cancer, tumor size

## INTRODUCTION

Endometrial cancer (EC) is one of the most common cancers in urogenital system of women. A thorough understanding of the epidemiology, pathophysiology, and management strategies for this cancer allows the obstetrician-gynecologist to identify women at increased risk, contribute toward risk reduction, and facilitate early diagnosis and prognosis [4].

Insulin-like growth factor-II mRNA-binding protein 3 (IMP3) known in previous publications as L523S or KOC (K-homologous domain containing protein o verexpressed in c ancer), is a newly identified oncofetal RNA-binding protein that binds [6, 7].

IMP3 is reported to be involved in cell growth, adhesion, invasion, and migration and is a prognostic marker associated with metastatic progression as demonstrated in several studies of renal cell carcinoma [1].

***Correspondence to**: *Valentin Velev, MD, Department of General and Clinical Pathology, Medical Faculty, Trakia University, Armeiska str.11, Stara Zagora, 6000, Bulgaria, e-mail: va.velev@abv.bg*

In the current study we present our attempt to correlate IMP3 expressing tumor cells and TNM staging, the clinical stage and the tumor progression.

## MATERIALS AND METHODS

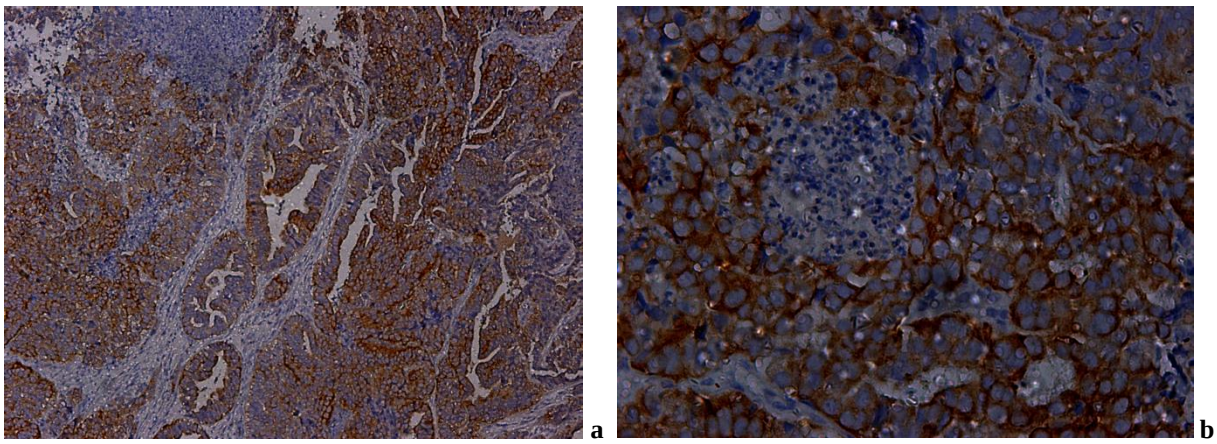
For this retrospective study, archival formalin-fixed, paraffin-embedded specimens from 16 patients with endometrial cancer who had been treated surgically between 2000 and 2012 year at the University Hospital of Stara Zagora, Bulgaria, were recruited. The patients population consisted in 16 females aged between 32 and 82 years (median 62,4 years). Tumor grading and staging was performed according to the TNM classification. Histological grading was performed on hematoxyllin and eosin-stained sections. Patients did not receive chemotherapy or radiation therapy before surgery.

For immunohistochemical staining, the paraffin blocks were prepared using tumor tissues from the periphery of the tumor adjacent to the normal tissues. Paraffin sections 5 μm thick were dewaxed in two xyllenes for 1 h, and were rehydrated in ethanol. Later, they were washed

in 0.1 M phosphate buffered saline (PBS), pH 7.4, incubated in 1.2 % ydrogen peroxide in methanol for 30 min, and rinsed in 0.1 M PBS, pH 7.4, for 15 min. Then the slides were incubated in a humid chamber for 60 min with Monoclonal Mouse Anti-Human IMP3 , dilution 1:100 (M3626, DAKO, Denmark). antibody. After washing three times in PBS, the slides were incubated with DAKO-REAL™ En-Vision™ detection system (DAKO) for 60 min, then visualized with diaminobenzidine and counterstained with hematoxylin. We used breast cancer tissue known to exhibit high levels of marker for positive control and for negative control, the primary antibody was replaced with PBS.

## RESULTS

The analysis of IMP3 expression showed that 10 (62.5%) cases were positive for IMP3 marker **(Figure 1a,b).**



**a** **b**

**Figure 1a,b.** Strong cytoplasmic expression of IMP3 in tumor epithelium / x100; x200/

Fifty percent from IMP3 positive cases were from EC type I and the other 50%- type II.

We found that 60% from the patients in tumor stage T3-T4 were high expression of IMP3 ($\chi 2=2.56$; $p=0.051$).

No statistically significant correlation between it parameter IMP3 and age, distant metastasis, stage and etc

## DISCUSSION

In our study we found that more aggresive EC showed high expression of marker IMP3.

Overexpression of IMP3 in many malignancies has been identified by some as an emerging biomarker of diagnostic and clinical significance [3]. A big part of studies including IMP3 expression in human tissue, have used i mmunohistochemical method logies, frequently examining the intensity of staining and the proportion of positively staining cells. For example , in one study of renal cell carcinoma, quantitative IMP3 immuno-histochemical staining results, as assessed by a computerized image analyzer, were combined with tumor stage to yield a system to predict the development of tumor metastases [2].

In the other article, Wang et al. detect the expression of IMP3 and make correlation with clinicopathological features in gastric cancers specimens and different gastric lessions [5]. Out of 92 cases of adjacent normal mucosa, 10 with dysplasia demonstrated weak expression of IMP3 and 82 without dysplasia showed negative expression. A comparison of IMP3 expression in this cases showed stronger immunohistochemical reactivity in gastric cancer ($P < 0.05$). High expression of IMP3 was found to be associated with lymphoid metastasis, high Ki-67 labelling index, and patient poor outcome ($P < 0.05$). There was a significant TNM stage difference between cancers with and without IMP3 expression ($P < 0.05$). Tumors with higher stage showed higher level of IMP3 expression [5].

Our results corresponding with data of many other authors. Despite the small group of cases we may stated that in endometrial

adenocarcinomas, IMP3 expression is found in more aggressive disease.

**REFERENCES**


1. Feng W, Zhou Z, Peters JH, Khoury T, Zhai Q, Wei Q, Truong CD, Song SW, Tan D. Expression of insulin-like growth factor II mRNA-binding protein 3 in human esophageal adenocarcinoma and its precursor lesions. *Arch Pathol Lab Med.* 2011 Aug;135(8):1024-31.
2. Jiang Z, Chu PG, Woda BA, et al. Combination of quantitative IMP3 and tumor stage: a new system to predict metastasis for patients with localized renal cell carcinomas. *Clin Cancer Res* 2008; 14:5579-84.
3. Kapoor S. IMP3 : a new and impor tant bio marker of systematic malignancies. *Clin Cancer Res* 2008;14:5640, author reply 5640-1.
4. SGO Clinical Practice Endometrial Cancer Working Group, Burke WM, Orr J, Leitao M, Salom E, Gehrig P, Olawaiye A, Brewer M, Boruta D, Villella J, Herzog T, Abu Shahin F; for the Society of Gynecologic Oncology Clinical Practice Committee. Endometrial cancer: A review and current management strategies: Part I. *Gynecol Oncol.* 2014 Jun 4. pii: S0090-8258(14)00978-0.
5. Wang L, Li HG, Xia ZS, Lü J, Peng TS. IMP3 is a novel biomarker to predict metastasis and prognosis of gastric adenocarcinoma: a retrospective study. *Chin Med J* (Engl). 2010 Dec;123(24):3554-8.
6. Wang T, Fan L, Watanabe Y, et al. L523S, an RNA-binding protein as a potential therapeutic target for lung cancer. *Br J Cancer* 2003;88:887–894.
7. Yantiss RK, Woda BA, Fanger GR, et al. KOC (Komology Domain Containing Protein Overexpressed in Cancer): a novel molecular marker that distin-guishes between benign and malignant lesions of the pancreas. *Am J Surg Pathol* 2005;29:188–195.