

The correlation ship between the number of platelets and endometrial pathology

Alexandru CIULCU¹, Nicolae BACALBASA^{2,3}, Irina BALESU⁴, Claudia STOICA^{5,6}, Lucian POP⁷, Valentin VARLAS^{2,8}, Cristina MARTAC⁹, Andrei VOICHITOIU^{2,7}

¹ Department of Obstetrics and Gynecology, "Cantacuzino" Clinical Hospital, Bucharest, Romania

² Department of Obstetrics and Gynecology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

³ Department of Visceral Surgery, Center of Excellence in Translational Medicine, Fundeni Clinical Institute, Bucharest, Romania

⁴ "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

⁵ Department of Anatomy, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

⁶ Department of Surgery, Ilfov County Emergency Hospital, Bucharest, Romania

⁷ Department of Obstetrics and Gynecology, "Alessandrescu-Rusescu" National Institute of Mother and Child Care, Bucharest, Romania

⁸ Department of Obstetrics and Gynecology, Filantropia Clinical Hospital, Bucharest, Romania

⁹ Department of Anesthesiology, Fundeni Clinical Institute, Bucharest, Romania

ABSTRACT

Introduction. Circulating platelets play an essential role in the immune system and furthermore in tumor development and proliferation. Therefore, the correlation ship between different neoplasia and the number of platelets has been widely studied.

The aim of the current paper is to investigate the correlation ship between platelet number and tumoral endometrial transformation.

Material and methods. Between January 2022 and June 2022 22 patients with endometrial hyperplasia or endometrial cancer were submitted to surgery. The serum levels of platelets were determined and compared to those reported in a similar group of patients in whom the endometrial lining was normal.

Results. Patients diagnosed with endometrial cancer presented a significantly higher number of platelets as well as a significantly higher platelet volume when compared to patients diagnosed with endometrial hyperplasia and respectively to those in whom a normal endometrial lining was found.

Conclusions. The serum number of platelets and their volume seem to be positively correlated with the aggressivity of the tumoral transformation of the endometrial lining and should be therefore considered as part of the elements which should be analyzed when discussing the best therapeutic option in such patients.

Keywords: endometrial cancer, endometrial hyperplasia, platelet number, platelet volume

INTRODUCTION

Tumoral transformation of the endometrium represents one of the most commonly encountered health problem affecting women worldwide [1-3]. Fortunately,

it usually induces the apparition of abnormal uterine bleeding which worries the patients and determine them to have a gynecological check-up. Most often in such cases a degree of endometrial tumoral transfor-

Corresponding authors:

Nicolae Bacalbasa

E-mail: nicolae_bacalbasa@yahoo.ro

Article History:

Received: 22 June 2022

Accepted: 24 June 2022

mation is encountered, varying between simple endometrial hyperplasia, complex endometrial hyperplasia and endometrial cancer [4-6]. In such cases, depending on the type of endometrial transformation, different therapeutic options have been proposed, ranging from observation to radical surgery consisting of total hysterectomy with bilateral adnexectomy and lymph node dissection. In order to establish which cases could benefit most from a conservative treatment and which ones should be treated aggressively, multiple paraclinical factors such as tumoral markers have been analyzed [7,8]. Recently, beginning from the hypothesis that the level of the serum platelets as well as their volume seem to be correlated with the presence of different neoplastic transformations, attention was focused on determining whether a positive correlation ship can be established between these parameters and tumoral transformation of the endometrial lining [9-11]. The aim of the current paper is to analyze the relation on a group of 22 patients diagnosed with endometrial hyperplasia or endometrial cancer.

MATERIAL AND METHODS

After obtaining the approval of the Ethics Committee no 88/2022, data of patients submitted to surgery for endometrial hyperplasia or endometrial cancer between January and June 2022 were retrospectively reviewed; finally, there were 22 such cases, in all of them the final diagnostic being confirmed at the final histopathological studies. The serum number and volume of platelets were compared between the two groups; meanwhile, they were compared to those obtained in a control group in which the endometrial lining presented a normal aspect at hysteroscopy.

RESULTS

The mean age of patients included in the current study was of 56 years among patients diagnosed with endometrial cancer, 49 years among patients diagnosed with endometrial hyperplasia and respectively

45 years among patients diagnosed with normal endometrial lining ($p=0,03$). Finally there were 14 patients diagnosed with endometrial cancer and eight cases diagnosed with endometrial hyperplasia; the control group included 22 patients with abnormal vaginal bleeding submitted to diagnostic hysteroscopy but in whom a normal endometrial lining was observed. Meanwhile patients diagnosed with endometrial cancer had a significantly higher body mass index when compared to those with endometrial hyperplasia and respectively with endometrial lining ($38,3 \text{ kg/m}^2$ versus 28 kg/m^2 and 23 kg/m^2 , $p=0,02$). Another factor which was significantly associated with the presence of endometrial transformation was the serum level of CA125 (270 U/ml versus 44U/ml and 16U/ml) ($p=0.05$). When studying the correlation ship between the levels of hemoglobin or the number of white blood cells and the presence of endometrial tumoral transformation. However, when studying the correlation ship between the platelet count and the presence of endometrial cancer or hyperplasia, a significant correlation ship was observed ($490.000/\text{microl}$ versus $350.000/\text{microl}$ and 233.000 microl , $p=0,001$). Meanwhile another significant correlation ship was seen between the platelet volume and the type of tumoral transformation ($p=0.003$). Details regarding the correlation ship between these parameters are presented in Table 1.

All 22 patients were further submitted to surgery consisting of total hysterectomy with bilateral adnexectomy for cases diagnosed preoperatively with endometrial hyperplasia and respectively to total hysterectomy with bilateral adnexectomy and pelvic lymph node dissection for patients with initial diagnostic of endometrial cancer. In all cases the histopathological studies confirmed the presence of endometrial hyperplasia and respectively endometrial cancer, the main histopathological subtypes being the following: simple endometrial hyperplasia in six cases, complex endometrial hyperplasia in two cases, endometroid adenocarcinoma in 12 cases, clear cell adenocarcinoma in 8 cases and endometroid sarcoma in two cases. Among these histopathological subtypes there was no significant correla-

TABLE 1. The correlation ship between the platelet count and the presence of endometrial cancer or hyperplasia

Parameter	Endometrial cancer (14 cases)	Endometrial hyperplasia (8 cases)	Normal endometrial lining (22 cases)	p value
Age (years)	56	49	45	$p=0,03$
BMI (kg/m^2)	38,3	28	23	$p=0,02$
CA125 (U/ml)	270	44	16	$p=0,05$
Hb (g/dl)	10,8	11,3	12	$p=0,08$
WBC(/microl)	7700	7200	8220	$p=0,09$
Platelet number	490.000	350.000	233.000	$p=0,001$
Platelet volume	11,1	9,9	8,1	$p=0,003$

tion ship between the number or dimension of platelets and respectively the histopathological result.

DISCUSSIONS

Endometrial tumoral transformation has become a serious health problem affecting women worldwide especially in the last decades; therefore once an increasing trend was observed in regard to weight gain and apparition of obesity especially in postmenopausal women, an increasing level of the number of cases presenting endometrial transformation was observed [12,13]. Therefore, it has been widely demonstrated that a higher amount of adipose tissue will lead to the apparition of an increased amount of estrogen which will stimulate cellular proliferation at the level of the endometrial lining leading to the apparition of endometrial hyperplasia and even endometrial cancer [13]. In this respect, attention was focused on identifying different biological markers which might underline the predisposition to the apparition of these neoplastic transformations. Initially, a strong correlation ship was observed between the risk and clinical stage of endometrial cancer and the serum level of CA 125 [14-16]; however, there were studies which came to demonstrate that this relationship cannot be demonstrated routinely; moreover, a significant number of patients with endometrial cancer presented normal serum values of CA125 [17]; therefore, attention was focused on identifying other paraclinical tests which might be correlated with the apparition of such neoplasms.

Recently, a significant number of articles were focused on studying the possible correlation ship between the number of the circulating platelets, their volume, their diameter and the co-existence of different neoplasms [18-20]; therefore, it is well known the fact that the platelets themselves have a stimulating role on tumorigenesis and on tumoral dissemination. Certain authors came to demonstrate that a higher number of

platelets presenting a higher volume and diameter contain in fact a higher number of granules with mediators which stimulates cancerogenesis and progression of the disease [21].

An interesting study published on this issue was conducted by Karateke et al. and was published in 2015; the study included 194 patients with abnormal vaginal bleeding who were diagnosed after performing an endometrial biopsy with endometrial hyperplasia in 55 cases, endometrial cancer in 34 cases and respectively with normal endometrial lining in 105 cases. Similarly to our study, the authors underlined the fact that endometrial cancer patients were significantly older when compared to the other groups and had a significantly higher volume of the circulating platelets; meanwhile, neither their study or our study did find a statistically significant correlation between the level of hemoglobin or of the circulating number of white blood cells; however in their study the number of platelets itself was not significantly correlated with the severity of the endometrial tumoral transformation [22]. However, the study was limited by the low number of cases.

This limitation regarding the low number of cases is also present in our study; however, the strength of our paper consisted of the fact that in all cases presenting an abnormal endometrial lining the final diagnostic was confirmed after performing the hysterectomy and was not only obtained by an isolated endometrial biopsy.

CONCLUSIONS

The number and dimensions of platelets seem to be strongly correlated with tumoral transformation of the endometrial lining. Therefore, these parameters might serve as potential biomarkers in order to identify the patients at risk to develop further malignant transformation and to improve the implementation of the concept of personalized medicine.

Conflict of interest: none declared

Financial support: none declared

REFERENCES

- Amant F, Moerman P, Neven P, Timmerman D, Van Limbergen E, Vergote I. Endometrial cancer. *Lancet*. 2005;366(9484):491-505.
- Moore K, Brewer MA. Endometrial Cancer: Is This a New Disease? *Am Soc Clin Oncol Educ Book*. 2017;37:435-442.
- Cust AE, Allen NE, Rinaldi S, Dossus L, Friefenreich C, Olsen A et al. Serum levels of C-peptide, IGFBP-1 and IGFBP-2 and endometrial cancer risk; results from the European prospective investigation into cancer and nutrition. *Int J Cancer*. 2007;120(12):2656–2664.
- Kaaks R, Lukanova A, Kurzer MS. Obesity, endogenous hormones, and endometrial cancer risk: a synthetic review. *Cancer Epidemiology Biomarkers and Prevention*. 2002;11(12):1531–1543
- Dashti SG, English DR, Simpson JA, Karahalios A, Moreno-Betancur M, Biessy C et al. Adiposity and Endometrial Cancer Risk in Postmenopausal Women: A Sequential Causal Mediation Analysis. *Cancer Epidemiol Biomarkers Prev*. 2021;30(1):104-113.
- Clarke MA, Long BJ, Del Mar Morillo A, Arbyn M, Bakkum-Gamez JN, Wentzensen

- N. Association of Endometrial Cancer Risk With Postmenopausal Bleeding in Women: A Systematic Review and Meta-analysis. *JAMA Intern Med.* 2018;178(9):1210-1222.
8. Murali R, Delair DF, Bean SM, Abu-Rustum NR, Soslow RA. Evolving Roles of Histologic Evaluation and Molecular/Genomic Profiling in the Management of Endometrial Cancer. *J Natl Compr Canc Netw.* 2018;178(8):201-209.
 9. Terzic M, Aimagambetova G, Kunz J, Bapayeva G, Aitbayeva B, Terzic S et al. Molecular Basis of Endometriosis and Endometrial Cancer: Current Knowledge and Future Perspectives. *Int J Mol Sci.* 2021;22(17):9274.
 10. Baranyai Z, J6sa V, T6th A, Szilasi Z, Tihanyi B, Zar6nd A et al. Paraneoplastic thrombocytosis in gastrointestinal cancer. *Platelets.* 2016;27(4):269-75.
 11. Ishizuka M, Nagata H, Takagi K, Iwasaki Y, Kubota K. Preoperative thrombocytosis is associated with survival after surgery for colorectal cancer. *J Surg Oncol.* 2012;106(7):887-891.
 12. Sylman JL, Mitrugno A, Tormoen GW, Wagner TH, Mallick P, McCarty OJT. Platelet count as a predictor of metastasis and venous thromboembolism in patients with cancer. *Converg Sci Phys Oncol.* 2017;3(2):023001.
 13. McCullough ML, Patel AV, Patel R, Rodriguez C, Feigelson HS, Bandera EV et al. Body mass and endometrial cancer risk by hormone replacement therapy and cancer subtype. *Cancer Epidemiol Biomarkers Prev.* 2008;17:73–79.
 14. Cosgrove CM, Backes FJ, O'Malley D, Bixel KL, Suarez AA, Fowler JM et al. Endometrial Cancer: Who Lives, Who Dies, Can We Improve Their Story? *Oncologist.* 2021;26(12):1044-1051.
 15. Kurihara T, Mizunuma H, Obara M, Andoh K, Ibuki Y, Nishimura T. Determination of a normal level of serum CA125 in postmenopausal women as a tool for preoperative evaluation and postoperative surveillance of endometrial carcinoma. *Gynecol Oncol.* 1998;69:192–6.
 16. Ginath S, Menczer J, Fintzi Y, Ben-Shem E, En-Shem E, Glezerman M et al. Tissue and serum CA125 expression in endometrial cancer. *Int J Gynecol Cancer.* 2002;18:372–375.
 17. Chung HH, Kim JW, Park NH, Song YS, Kang SB, Lee HP. Use of preoperative serum CA-125 levels for prediction of lymph node metastasis and prognosis in endometrial cancer. *Acta Obstet Gynecol Scand.* 2006;85:1501–5.
 18. Dotters DD. Preoperative CA 125 in endometrial cancer: Is it useful? *AJOG.* 2000;182(6): 1328-1334.
 19. Ye Q, Wu Z, Xia T, Liu D, Yang Y, Tang H. Pre-treatment thrombocytosis predicts prognosis in endometrial cancer: A meta-analysis of 11 studies. *Exp Ther Med.* 2020; 19:359–366.
 20. Giannella L, Menozzi G, Di Monte I, Venturini P, DePace V, Boselli F et al. Preoperative platelet count as index of the grading in endometrial carcinoma. *Minerva Ginecol.* 2008;60:273–279.
 21. Nie D, Yang E, Li Z. Pretreatment thrombocytosis predict poor prognosis in patients with endometrial carcinoma: A systematic review and meta-analysis. *BMC Cancer.* 2019;19:73.
 22. Mantovani A, Allavena P, Sica A, Balkwill F. Cancer related inflammation. *Nature.* 2008;454:436-44.
 23. Karateke A, Kaplanoglu M, Baloglu A. Relations of Platelet Indices with Endometrial Hyperplasia and Endometrial Cancer. *AJCP.* 2015;16: 4905-4916.