EVALUATION OF HEPARANASE PROCOAGULANT ACTIVITY AND TISSUE FACTOR PATHWAY INHIBITOR LEVEL IN UTERINE CANCER PATIENTS

Iglal Youssef Shaala, Akram Abdel Moneim Deghady, Mohammed Ahmed Meheissen,* Esraa Mohammed Mahmoud Hussien

Clinical and Chemical Pathology Department, Oncology and Nuclear Medicine Department,* Faculty of Medicine, University of Alexandria

Introduction

Endometrial cancer is considered one of the most common malignancies in females worldwide. The majority of endometrial cancers are estrogen related. Early detection of uterine cancer will provide the patient with better chance of survival while discovering the disease at late stage or after metastatic spread will significantly increase the morbidity and the risk of complications. Hemostasis is a complex physiological process and to achieve normal hemostasis, delicate balance between clotting cascade and fibrinolytic cascade is required to prevent thrombosis or hemorrhage. Heparanase is an endoglycosidase enzyme which cleaves heparane sulphate, it is expressed in human tumors. Heparanase upregulation correlates with increased tumor vascularity and poor postoperative survival of cancer patients so heparanase is implicated in angiogenesis and tumor progression. It is now well established that the prime trigger to blood coagulation is tissue factor (TF) that is exposed on the surface of fibroblasts as a result of vessel wall injury. TFPI binds to factor Xa and, in this combination, binds to and inhibits tissue factor / factor VIIa complex and activated FX (FXa) and thus TFPI is currently being included as a natural coagulation inhibitor.

Aim of the work

The aim of this work was to investigate the relation of both heparanase procoagulant activity and tissue factor pathway inhibitor level with thromboembolic complications and metastasis in uterine cancer patients.

Patients and Methods

The study was conducted on 90 subjects divided into two groups:

Group I: 70 patients with uterine cancer.

Group II: 20 selected healthy women with matched age as a control group.

All patients and controls included in the present study were subjected to the following:

1. Full history taking .
2. Complete physical examination.
3. Laboratory Investigations including:
   - Complete blood count (CBC).
   - Prothrombin time (PT).
   - D-Dimer
   - Heparanse procoagulant activity using Enzyme-linked immunosorbent assay (ELISA).
   - Tissue factor pathway inhibitor level using Enzyme-linked immunosorbent assay (ELISA).

Results

Table 1: Comparison between the three studied groups according to Heparanse

	Group I (n = 70)		Group II (n = 20)	H	p
	Without thromboembolic events (n = 56)	With thromboembolic events (n = 14)			
Heparanse					
Min. – Max.	1.80 – 13.22	9.06 – 19.75	0.95 – 5.48	45.395*	<0.001*
Mean ± SD.	6.05 ± 3.05	15.51 ± 2.46	3.08 ± 1.42		
Median (IQR)	5.21 (3.64 – 8.23)	15.56 (14.92 – 16.99)	2.71 (2.05 – 4.09)		
Sig. bet. grps.	p_1=0.001*, p_2<0.001*, p_3<0.001*				

IQR: **Inter quartile range** SD: **Standard deviation**

H: H for **Kruskal Wallis test,** Pairwise comparison bet. each 2 groups was done using **Post Hoc Test (Dunn's for multiple comparisons test)**

p: p value for comparing between the three studied groups

p_1: p value for comparing between **Without thromboembolic events** and **With thromboembolic events**

p_2: p value for comparing between **Without thromboembolic events** and **Group II**

p_3: p value for comparing between **With thromboembolic events** and **Group II**

*: Statistically significant at $p \leq 0.05$

Group I: Patients with uterine cancer **Group II: Healthy women as a control group**

Table 2: Comparison between the three studied groups according to TFPI

	Group I (n = 70)		Group II (n = 20)	H	p
	Without thromboembolic events (n = 56)	With thromboembolic events (n = 14)			
TFPI					
Min. – Max.	4.59 – 251.4	2.09 – 19.22	48.50 – 162.3	32.695*	<0.001*
Mean ± SD.	102.4 ± 69.79	5.14 ± 4.37	102.0 ± 30.35		
Median (IQR)	93.56 (39.82 – 165.7)	3.70 (2.94 – 4.91)	98.60 (84.60 – 120.4)		
Sig. bet. grps.	p_1<0.001*, p_2=0.780, p_3<0.001*				

p: p value for comparing between the three studied groups

p_1: p value for comparing between **Without thromboembolic events** and **With thromboembolic events**

p_2: p value for comparing between **Without thromboembolic events** and **Group II**

p_3: p value for comparing between **With thromboembolic events** and **Group II**

*: Statistically significant at $p \leq 0.05$

Group I: **Patients with uterine cancer**

Group II: **Healthy women as a control group**

Tissue factor pathway inhibitor level was decreased in patients complicated with thromboembolic events or metastasis.

Conclusion

According to the current study results it was concluded that:

Heparanase procogulant activity and pro-metastatic effect is proved as heparanase level was significantly elevated in uterine cancer patients complicated by thromboembolic or metastatic events.

Tissue factor pathway inhibitor has the ability to protect against thromboembolic events; as uterine cancer patients complicated with thromboembolic events were found to have a lower level of TFPI compared with other non-complicated cases and also with the control group.