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

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Introduction

Ovarian cancer is considered one of the most common malignancies in females worldwide. Early detection of ovarian cancer will provide the patient with better chance of survival while discovering the disease at late stage 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 ovarian cancer patients.

Patients and Methods

The study was conducted on 86 subjects divided into two groups: Group I: 66 patients with ovarian 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 different five groups according to Heparanase (n = 86)

	Stage of disease and thromboembolic events (DVT)				Control (n = 20)	H	p
	Early without DVT (n = 15)	Early with DVT (n = 2)	Late without DVT (n = 39)	Late with DVT (n = 10)			
Heparanase (ng/ml)							
Min. – Max.	2.36 – 9.51	15.29 – 18.54	5.96 – 14.31	14.17 – 19.95	0.77 – 5.48	68.340*	<0.001*
Mean ± SD.	5.14 ± 2.29	16.92 ± 2.30	9.68 ± 1.88	16.61 ± 1.74	2.86 ± 1.42		
Median (IQR)	4.09 (3.56 – 6.56)	16.92 (15.29 –18.54)	9.32 (8.48 – 10.15)	16.73 (15.35 –17.85)	2.71 (1.73 – 3.85)		
p_0	0.106	<0.001*	<0.001*	<0.001*			
Sig. bet. grps.	p_1=0.001*, p_2<0.001*, p_3<0.001*, p_4=0.049*, p_5=0.957, p_6<0.001*						

Table (2): Comparison between the different five groups according to TFPI (n = 86)

	Stage of disease and thromboembolic events (DVT)				Control (n = 20)	H	p
	Early without DVT (n = 15)	Early with DVT (n = 2)	Late without DVT (n = 39)	Late with DVT (n = 10)			
TFPI (ng/ml)							
Min. – Max.	99.60 – 213.3	8.18 – 9.63	4.14 – 51.80	2.11 – 7.32	78.60 – 163.4	70.122*	<0.001*
Mean ± SD.	153.8 ± 40.09	8.91 ± 1.03	18.85 ± 13.10	3.97 ± 1.82	122.8 ± 22.20		
Median (IQR)	148.9 (117.6 –190.7)	8.91 (8.18 – 9.63)	16.53 (9.72 – 22.46)	3.31 (2.92 – 4.14)	123.4 (108.2 –139.8)		
p_0	0.374	0.013*	<0.001*	<0.001*			
Sig. bet. grps.	p_1=0.007*, p_2<0.001*, p_3<0.001*, p_4=0.419, p_5=0.373, p_6<0.001*						

Conclusion

Heparanase procogulant activity and pro-metastatic effect is proved as heparanase level was significantly elevated in ovarian cancer patients complicated by thromboembolic or at later stages of the disease. Tissue factor pathway inhibitor has the ability to protect against thromboembolic events; as ovarian 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.