The raising cancer incidence is among the most serious medical and social problems of our time. According to the Cancer Register of Ukraine, the annual mortality from malignant processes is close to 100 thousand cases, and the annual morbidity reaches 160 thousand cases (0.2 and 0.32% of the country population, respectively). 7.5–8% of cancer cases are related to the cancer of upper respiratory tract (URT), which incidence has increased by 1.6 times during last 10 years [1]. As it is commonly accepted, the early detection of a disease is a key to its effective therapy. However, cancer is usually detected by its late clinical manifestations, and no universal index for early cancer detection has been found so far [2]. However, according to the data of some researchers, not a single index but a combination of several cancer-related biochemical alterations in components of haemostatic system (HS), could be considered promising [3].

It is well known that HS consists of two oppositely directed enzymatic sub-systems, which provide the formation of fibrin clot and its lysis. The majority of enzy-matic HS components are trypsin-like proteinases that are synthesized as inactive pro-enzymes with their following processing into active forms via high-selective enzymatic cleavage. In turn, these activated proteinases are activators for other pro-enzymes, pro-factors and are under strict control of high-selective protein inhibitors [4, 5]. Disturbances of this highly regulated systems lead to the disturbance of various physiological processes that are aligned with numerous diseases. Malfunction of proteolysis significantly disturbs both fibrin clotting and fibrinolysis, complement and kinine systems [6, 7], and causes tissue damage and uncontrolled tumor growth [8–12]. Cancer cells are known to produce proteolytic enzymes, which affect haemostasis as well as promote tumor invasion and metastasis [13, 14]. Non-functional proteolysis plays a prominent role in post-operative complications, such as thrombosis and bleeding, recurrence and metastasis [15–17]. It should be underlined that a number of HS components is directly involved into cancer development [18–20]. Therefore, in the present work we aimed to analyze whether comprehensive assessment of HS components, in particular, indices of coagulation and fibrinolytic systems along with functionally related proteins, could be an informative tool for prediction of disease progression in patients with URT cancer.

**MATERIALS AND METHODS**

**Patients.** In the study, 10 patients with primary laryngeal cancer of II stage and 25 patients with URT cancer of III stage were enrolled. The patients were cured in SI “O.S. Kolomiychenko Institute of Otolaryngology of National Academy of Medical Sciences of Ukraine” in 2008–2010. The patients underwent surgical treatment, those with URT cancer of III stage...
RESULTS AND DISCUSSION

The main indices of plasma coagulation system of the patients and healthy donors are presented in Table 1. The most significant changes were recorded in the patients with URT cancer of III stage: the contents of fibrinogen, AT-III, and level of amiodolytic thrombin-like activity increased by 1.8-, 1.2- and 1.6-fold, respectively. Also, in this group PT was significantly higher than in healthy donors. In the patients with laryngeal cancer of II stage increased PT and fibrinogen content are noted, whereas the level of amiodolytic thrombin-like activity was close to that in control group. In both groups of the patients the content of soluble forms of fibrin wasn’t different from the normal level. We have conclude that pre-treatment levels of fibrinogen, AT-III, and amiodolytic thrombin-like activity in the group of patients with III stage of malignancy were significantly higher than in patients with II stage as well as in control group. These differences may be evaluated as the evidence for the dependence of these haemostatic indices of the stage of disease.

<table>
<thead>
<tr>
<th>Groups of patients</th>
<th>Content of fibrinogen, g/l</th>
<th>Dissoluble fibrin, mg%</th>
<th>Prothrombin time, s</th>
<th>Content of AT-III, %</th>
<th>Amiodolytic thrombin-like activity, nmol p-NA/ (min∙ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy persons</td>
<td>4.0 ± 0.3</td>
<td>29.0 ± 1.0</td>
<td>119.0 ± 6.6</td>
<td>18.0 ± 3.0</td>
<td></td>
</tr>
<tr>
<td>(control group)</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.02</td>
<td>p &lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>n = 10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>URT cancer of II stage</td>
<td>3.1 ± 0.2</td>
<td>4.0 ± 0.8</td>
<td>28.0 ± 1.4</td>
<td>107.0 ± 5.0</td>
<td></td>
</tr>
<tr>
<td>(n = 25)</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.02</td>
<td>p &lt; 0.02</td>
<td>10.2 ± 2.0</td>
<td></td>
</tr>
<tr>
<td>Patients with URT cancer of III stage</td>
<td>2.2 ± 0.1</td>
<td>4.3 ± 0.4</td>
<td>23.5 ± 0.8</td>
<td>100.0 ± 2.7</td>
<td></td>
</tr>
<tr>
<td>(n = 24)</td>
<td></td>
<td></td>
<td></td>
<td>9.6 ± 1.0</td>
<td></td>
</tr>
</tbody>
</table>

Note: statistically significant differences with control group are marked by corresponding p value.

It is known that cancer cell secretion of proteolytic enzymes causes the destruction of intercellular matrix thus creating favorable conditions for tumor invasion. The activity of proteases are dependent both on the level of their production and of their blocking by specific inhibitors [27, 28]. The levels of activity of proteolytic enzymes and the content of protease inhibitors (α2M and α1IP) in blood plasma of the patients are presented in Table 2. According to these data, in the group of patients with URT cancer of III stage the levels of PRA and elastase-like amiodolytic activity are significantly higher than the corresponding levels in healthy donors, while the content of α2M is significantly reduced. PRA in patients with UTR cancer of II stage was also significantly increased, but lower than in the patients with stage III of the disease. The elastase-like amiodolytic activity in patients with UTR cancer of II stage just tended to be increased in comparison to the control group, while the content of α2M was reduced in contrary to that in patients with III stage. The level α1IP in patients with II stage of URT cancer wasn’t different from its reference value.
Could all these data be considered useful for the evaluation of UTR cancer progression? Combined use of the studied indices allowed create an effective approach based on evaluation of pre-treatment level of amidolytic thrombin-like activity, the content of fibrinogen and α2M. At the same time, the levels of amidolytic elastase-like and PRA remain valuable indicators of the general condition of the patients, but they were less informative in regard of prognosis of disease course in post-treatment period. That’s why it seems reasonable to use an additional index accounting the differences between the thrombin-like activity and contents of fibrinogen and α2M of each patient from their normal levels ([Fg], [Thr] and [α2M]). The formula for calculation of such index (let’s name it “index H”) is as follows:

\[ H = \frac{[Fg]}{[Thr]} / [α2M] \]

By calculation of individual parameters of the patients with URT cancer using this formula with following use of the methods of variation statistics for both groups of patients, the average value of H index for the group of patients with complications was 6.35 ± 1.67 vs 2.65 ± 0.53 for group patients in remission (p < 0.05).

In conclusion, the results of combined use of pre-treatment indices of HS and functionally related proteins of blood plasma in patients with II and III stages of UTR cancer evidence on association of these indices with the disease progression. The level of thrombin-like amidolytic activity, α2M and fibrinogen contents in blood plasma of the patients with URT cancer of III stage could be used as valuable index for cancer recurrence and metastasis at post-treatment period.

**REFERENCES**


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