Serum actin-binding proteins as markers of metastasis of larynx and laryngeal pharynx cancer

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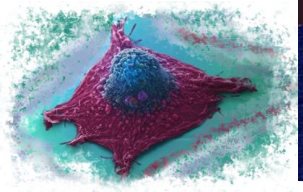
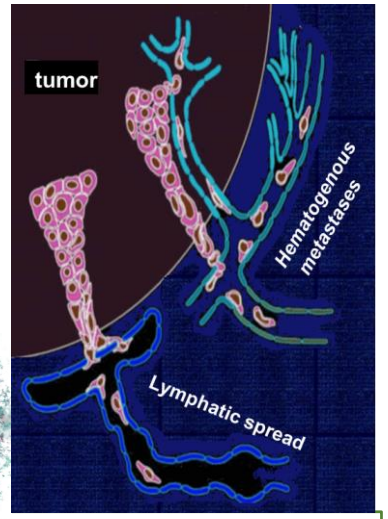
Motivation: High one-year mortality among patients with squamous cell carcinoma of the larynx and larynxopharynx L/L SCC is associated with a prolonged asymptomatic course and frequent metastasis . The solution to the problem of predicting metastasis of L/LSCC using minimally invasive techniques is relevant. The metastasis process is closely related to the remodeling of the cytoskeleton in tumor cell, which is mediated by actin binding proteins. At the moment, there is no data on the possibility of using the above listed ABPs circulating in the blood of patients with L/L SCC as markers for the prognosis of this disease. Earlier, we showed the possibility of determining the level of CAP1 in the tumor tissue and blood serum of patients with L/L SCC for predicting the course of the disease.

Aim: *T*he study was to study the relationship between the level of CAP1, cofilin 1, ezrin, fascin 1 and profilin 1 in the blood serum of patients with L/L SCC with the main clinical and morphological characteristics and to assess the possibility of their use as markers of metastasis

Cytoskeleton Remodeling

Actin binding proteins : cofilin (CFN1), profilin (PFN1), ezrin (EZR), fascin (FSCN1), and adenylyl cyclase-associated protein 1 (CAP1)





METHODS:

The material for analysis was the serum blood of 15 healthy volunteer and 57 patients with L/L SCC (T1-4N0-2M0) with histologically verified diagnosis. Material for the study was taken before the special treatment. Blood serum analysis was performed using ELISA kits (Human CFL1, FSCN1, EZR, PFN1 and CAP1) on a Microplate reader Multiskan FC 100 (ThermoFisher Scientific). The results in tables present as level of studying protein. The statistical analysis was carried out by software package Statistica 6.0.

I. RESULTS

In the serum of patients with L/L SCC the level of CAP1 was almost 5 times higher (p = 0.01) relative to the control group (fig.1).

The metastatic process was also characterized by a change in the level of serum ABPs (fig.2).

The level of FSCN1 was higher by almost 10 times (p = 0.05) and the level of CAP1 was 60% higher (p = 0.03) in the group with regional metastases. The level of PFN1 in patients with L/L SCC with metastases was lower by 30% (p = 0.05). Using the discriminant analysis method on the presented sample of patients, a metastasis prognosis model was obtained and is described by equation (1):

$$y = -23 + 3{,}7 * CAP1 + 1{,}43 * FSCN + 68 * PFN1 \qquad (1)$$

The sensitivity is 89%, the specificity is 62%; prognostic significance is 77%; p≤0,001.

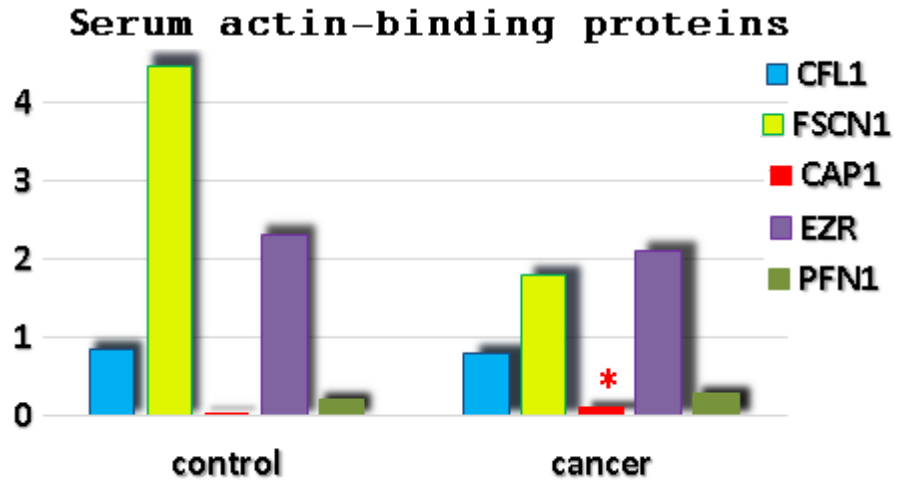


fig.1

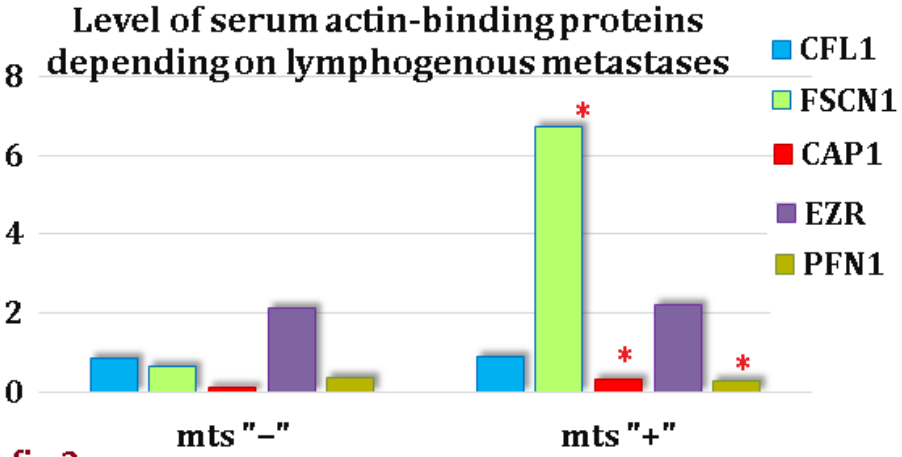
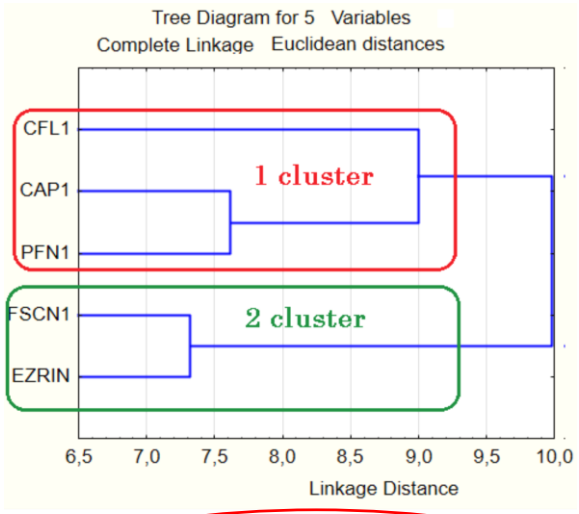
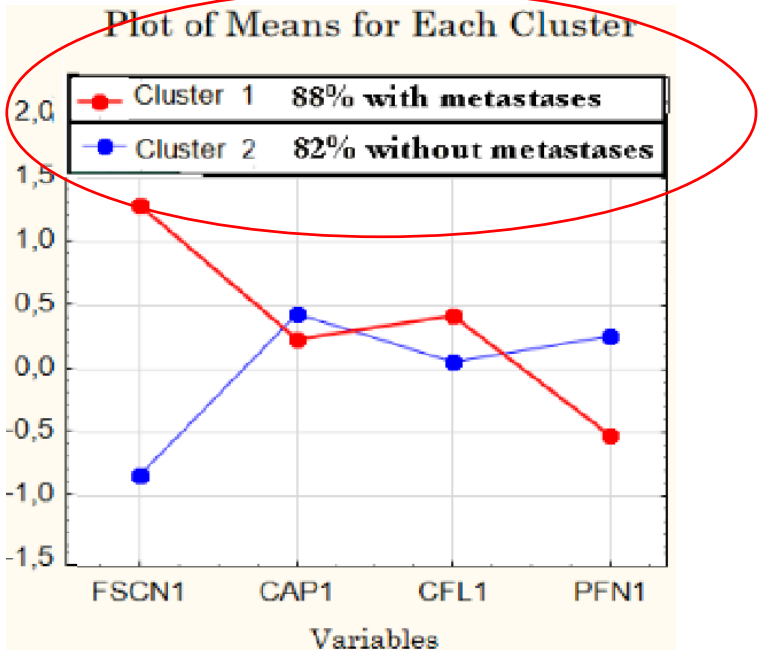


fig.2

Correlation analysis revealed a weak correlations between the levels of CAP1 - CFL1 (r=0,3, p=0.05), FSCN1- EZR (r=0.5; p=0.05) and FSCN1- PFN1 (r= - 0.4; p=0.05). For the group with metastases: FSCN1 and EZR (r = 0.5; p = 0.05), for the group without metastases: CAP1 and FSCN1 (r = - 0.5; p = 0.05) and FSCN1 and EZR (r = - 0.5; p = 0.05).

Hierarchical cluster analysis of ABP levels between metastasis and non-metastasis grups





CONCLUSION

- The data obtained in the presented sample of L/L SCC patients indicate a relationship between the level of serum ABPs and the stage of the disease, which may have prognostic value.
- The results, in general, do not contradict the literature data and indicate the possibility of using serum markers in clinical practice.
- Currently, several serum ABPs (CAP1, CFL1, PFN1 and FSCN1) have been identified as potential markers of metastasis of L/L SCC.
- For further conclusions about the clinical value of the proposed metastasis markers, further studies with an expanding sample of patients are needed.

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THANK YOU!

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