SUMMARY

Basal cell carcinoma (BCC), with the cutaneous form of squamous cell carcinoma (CSCC), are classified as a non-melanoma skin cancer (NMSC). It originates from basal epidermal cells and is a locally malignant, slowly growing tumor which can lead to destruction and deformation of surrounding tissues. BCC is currently the most common malignant tumor in Caucasians and accounts for 29% of all cancers, and 80% of all NMSCs worldwide. A constant increase in the incidence of NMSCs has been observed in the recent years. Despite the recent advances in treatment, numerous cases of resistance are still observed.

Multiple reports have highlighted the role of insulin-like growth factor-1 (IGF-1) and the IGF-1 pathway which includes insulin-like growth factor binding protein, insulin-like growth factor-1 and insulin-like growth factor receptor 1 (IGFBP/IGF-1/IGF1R) in the carcinogenesis. The correlation between increased IGF-1 concentration and decreased IGFBP concentration has been confirmed in the pathogenesis of numerous tumor types, e.g., breast cancer, prostate cancer, colorectal cancer and lung cancer. According to previous studies, IGF-1 plays an important role in maintaining homeostasis in the epidermis. Evidence collected to date includes a study conducted in mice which demonstrated a significantly higher IGFBP-2 concentration in BCC tissue compared with normal tissue, suggesting that this element of the IGFBP/IGF-1/IGF1R pathway can play an important role in the pathogenesis of BCC. The aim of the study was to evaluate the expression and concentration of selected components of the IGFBP/IGF-1/IGF1R pathway in human plasma and BCC tissue.

Twenty-nine patients routinely operated due to BCC were enrolled in the study. Control group consisted of 14 patients operated due to non-neoplastic conditions or benign lesions. *Western Immunoblot* was used to assess the expression of IGF-1, IGFBP-3 and IGFBP-5 in plasma and tumor tissue. The concentrations of the IGFBP/IGF-1/IGF1R pathway components in blood plasma and BCC tissue were assessed using *ELISA*.

The study showed that BCC most frequently occurs in people over 75 years of age. They were diagnosed mainly with advanced forms of cancer, which may be the cause of the high recurrence rates of BCC. The expression of IGF-1, mainly occurs as

complexes in plasma and BCC tissue. The presence of IGFBP-3 and IGFBP-5 in these complexes was confirmed. Moreover, the study demonstrated a lower expression of IGF-1 in BCC tissue compared with the plasma of patients with BCC. Patients with a large tumor had a significantly lower plasma IGF-1 concentration than those with a smaller tumor. Other clinical features: duration of disease, superficial/nodular form, primary or recurrent tumor, single or multiple lesions, as well as location of BCC did not have any significant influence on concentrations of the evaluated parameters in plasma or tumor tissue. The IGF-1, IGFBP-3 and IGFBP-5 concentrations were higher, and IGF1R was lower in plasma than in tumor tissue in both groups of patients. Lower concentrations of IGF-1, IGFBP-5 and IGF1R were observed in tumor tissue than in normal skin. No significant differences were found between the concentration of IGFBP-3 in tissue or components of the IGF-1/IGFBP/IGF1R pathway in the plasma of participants with and without BCC.

Conclusions:

1. Late diagnosis and the consequent extension of tumor, as well as its localization on the scalp, indicate the need for implementing early diagnosis programs of skin cancer, including BCC, in elderly people.

2. The recurrence rate of BCC of almost 20% suggests the need to implement more radical treatments, plan frequent follow-ups and develop new therapeutic options.

3. The evaluated components of the IGFBP/IGF-1/IGF1R pathway in plasma cannot serve as markers of disease duration, risk of recurrence or effectiveness of the treatment as their concentrations do not differ significantly in people with and without BCC.

4. The lower IGF-1 concentrations in the plasma of people with larger tumors suggests recruitment of IGF-1 into the tumor tissue and its role in the development of BCC. The higher concentration of IGFBP-5 in healthy skin compared with BCC tissue may suggest its protective effect. Detailed understanding of these correlations may contribute to development of new BCC treatment in future.