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*Letter to the Editor*



## Primary Regressive, But Metastasizing Melanoma!?

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### Abstract

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**BACKGROUND:** Cases of regressive melanomas represent a diagnostic and therapeutic challenge because time intervals between the presence of the primary tumour formation, the metastasis and the involution of the primary tumour may intertwine or occur at different times. The regression of cutaneous melanomas does not necessarily guarantee prevention from the development of locoregional or distant metastases. There are cases in which the prognosis of patients with the development of subsequent metastasis within regressive melanomas may be better depending on the number and location of metastases.

**CASE REPORT:** We are presenting a 42-year-old patient with two timed removals of enlarged inguinal lymph nodes within one year, as the subsequent histological examination identified histopathological data for metastasis of melanoma. BRAF testing was positive for BRAF mutation. Within the anamnesis, it was further clear that the patient had an irritated melanocytic lesion in the lateral right thigh area, which over the time disappeared and shortly after that, the enlargement of locoregional lymph nodes has been noted.

**CONCLUSION:** In the presented case prognosis and therapeutic options for treatment of patients with regression melanomas and subsequent development of lymph node metastasis have been discussed. Currently, there is no consentaneous opinion on the applicability of the early adjuvant therapy with targeted therapies or immunotherapy in patients with regressive and non-regressive type melanomas. We suggest and share the idea that early adjuvant therapy may be beneficial generally in patients with stage III melanomas.

### Dear Editor,

We present a 42-year-old man who was hospitalised 1 year ago in a surgical department for enlargement of right inguinal lymph nodes. The lymph nodes were surgically resected. The histological evaluation found metastatic melanoma. BRAF testing revealed a wild type genotype. After a thorough examination and PET Scan, the primary tumour was not identified. Twelve months later, PET/CT of the whole body was performed due to an enlarged lymph node in the inguinal area (clinically/palpatory and ultrasound), and the scans confirmed a single enlarged, metabolically active, right/inguinal lymph node. Surgical removal of the enlarged lymph node

from the proximal part of the right thigh was performed, below the inguinal fold (Figure 1a). The histological and immunohistochemical examination of the removed material identified a metastatic melanoma with infiltration through the lymph node capsule and perinodal soft tissues. The patient was visiting the Department of Dermatologic Surgery to clarify the diagnosis and to elucidate the further therapeutic regimen. During the clinical examination, a subungual pigmentation of the left foot's thumb was observed (Figure 1c), which was subsequently identified as a post-traumatic subungual hematoma. Concomitantly, the presence of a melanocytic lesion with peripheral involution, suspicious for regression melanoma was found in the right femoral region (Figure 1b and 1d). The patient also reported the

presence (6 years earlier) of a mole in the right femoral area, which was traumatically irritated and treated with "silver water", resulting in a complete disappearance. Immediately afterwards, the patient observed repeated swellings localized in the right inguinal area, and in the first 2-3 years they were reversible, but subsequently, the tumor formation increased and became painful for which it was surgically removed and identified as lymph node metastasis from melanoma. A re-excision of the regression lesion is contemplated with a view to discussing the benefits of adjuvant therapy.



Figure 1: a) Postoperative view after second surgical excision: surgical wound after inguinal lymph dissection to the right; b) and d) Clinical examination: melanocytic lesion with peripheral involution, clinically suspected for regression melanoma, located in the right femoral area; c) Subungual pigmentation of the left leg's thumb, identified as a post-traumatic subungual hematoma

Cases of regressive melanomas represent a diagnostic and therapeutic challenge [1]. The greatest difficulty in data interpretation and subsequent diagnosis is caused by cases of patients with metastatic melanoma with complete regression of the primary lesion [2]. The time intervals between the presence or emergence of the primary tumour formation, the metastasis and the involution of the primary tumour may intertwine or occur at different times. This often confuses clinicians and is the reason for subsequent inadequate diagnostic and therapeutic steps. Interesting is the fact that 1) the regression of melanomas do not necessarily guarantee the prevention/protection from the development of locoregional or distant metastases [3] and that [2] the

prognosis in some patients with metastasis within regressive melanoma may be better depending on the number and location of metastases (as in our case). In this regard, as important factors of major importance should be considered, on the one hand, primary tumour localisation, and, on the other, the location of metastasis development.

As areas of involvement from the primary tumour, the head and neck are probably associated with worse prognosis due to the more complicated and complex lymphatic drainage system (as well as the thoracic area), which in turn, in the case of metastatic involvement, is further problems due to the need for lymph dissection. An example of a possible predictive significance/relevance link between location and the subsequent prognosis is the recently described in the literature metastasis of the internal organs (such as gastrointestinal) in patients with regression type melanomas compared with metastases in the inguinal area (as seen in our patient) [4]. In the case of inguinal metastatic involvement, better overall prognosis and survival should be expected compared to disseminated intestinal involvement, for example. We describe a young patient with primary regression of melanoma and subsequent development of locoregional (inguinal) metastases. A re-excision of the regression lesion, located in the right thigh area, is planned, with the possible benefit of subsequent therapy remaining open.

New literature data suggest that early adjuvant therapy with targeted therapies or immunotherapy could provide greater benefits [5]. By definition, however, early adjuvant therapy is applied after resection of a primary melanoma, which opens the question of its applicability in the case of regression melanomas that are masked in the form of other skin diseases such as vitiligo [5], [6]. We propose an idea that early adjuvant therapy may be a key factor and also beneficial in patients with stage III melanomas in the case of completely eradicated metastatic tumours.

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