Case report

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CUTANEOUS MELANOMA IN A PATIENT WITH MULTIPLE SCLEROSIS: CASE REPORT AND REVIEW OF LITERATURE

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Skin melanoma is a malignant tumour with aggressive behaviour. Regional or systemic metastases represent a form of spreading, however, the time of appearance should not be strictly defined. We present a case of the patient with skin melanoma, also suffering from multiple sclerosis, under a long-lasting high dose corticosteroid therapy. The primary tumour was 1.7mm thick (T2a), but the clinical course was highly aggressive with massive subcutaneous and lymphatic metastases involving even the popliteal nodes. Several surgeries were performed as the only therapeutic choice, in circumstances in which interferon could not be applied because of multiple sclerosis. The patient died 16 months after establishing the diagnosis, in the stage of generalized disease. It should be debated that aggressive clinical course could be associated with immunosupression, however, we still cannot draw definite conclusions. *Acta Medica Medianae 2012;51(4):47-50.*

Key words: *cutaneous melanoma, multiple sclerosis, rapid progression*

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Introduction

Malignant skin tumours have a high incidence among all malignant tumours worldwide. Majority of those tumours have origin in epithelial cells of the skin (basal cell carcinoma, squamous cell carcinoma). Although cutaneous melanoma is not malignancy with the highest incidence rate with around 5% of all malignant neoplasms worldwide (1), it represents a tumour with high malignant potency. Because of its aggressiveness, it is often diagnosed in advanced stages. Surgical treatment and reconstruction planning make it also a medical issue of a high clinical significance. In certain cirmustances, even when treated according to the protocol, it can be furious and hazardous.

We present a case of the patient with skin melanoma, who also suffered from multiple sclerosis, discussing up-to-date oncologic rules and the influence of immunosupresion on the initial course.

Case report

A female patient, 45 years old, was admitted to the Clinic of Plastic and Reconstructive Surgery, Clinical Centre Niš, for a radical excision of a pigmented skin tumour, highly suspicious for melanoma. The patient was diagnosed with multiple sclerosis 10 years earlier, and was on corticosteroid therapy. The pigmented tumour, suspected of melanoma, was located on the upper left thigh. The surgery was performed under local anaesthesia and mild sedation. Tumour was radically excised with margins of 2cm, and the wound was directly closed. The wound healed without any complications. In the pathology report, the tumour was defined as cutaneous melanoma, Clark III, Breslow thickness 1.7mm, without ulceration, (clinical Stage Ib: T2a N0 M0) according to the AJCC system (2).

Six months after the first surgery, the patient was admitted to the Clinic, having the regional spread to the left inguinal lymph nodes. CT scan did not reveal spreading into the parailiac nodes. Inguinofemoral dissection was performed under general anaesthesia. Three months after dissection, the patient was admitted again. There were major local metastases on the upper left thigh (Figure 1), and enlarged popliteal lymph nodes. Cosmetic operation was planned and performed under general anaesthesia. Local metastases were excised, and popliteal node dissection was performed. Skin defect was reconstructed using split thickness graft from the opposite thigh (Figure 2). The wound healed by secondary intention where margins of defect healed by delayed epithelisation. After three months we found progressive deterioration of health condition with the local metastases (Figure 3). On the abdominal CT, we detected massive iliac and aortal lymphatic spread. Surgery was not performed. Patient died 16 month after

melanoma excision, having lung and liver metastases.

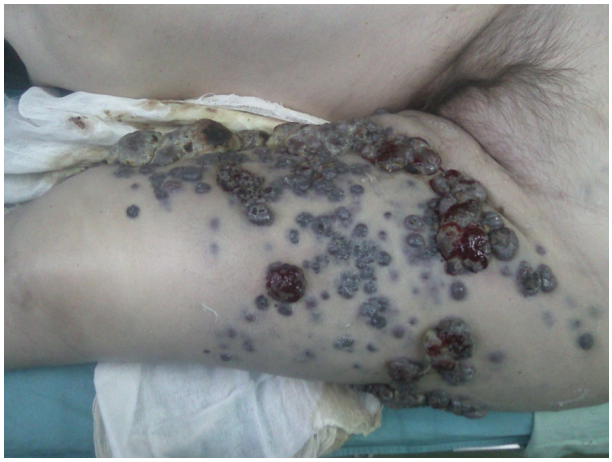

Figure 1. Metastatic disease in the skin of the left thigh

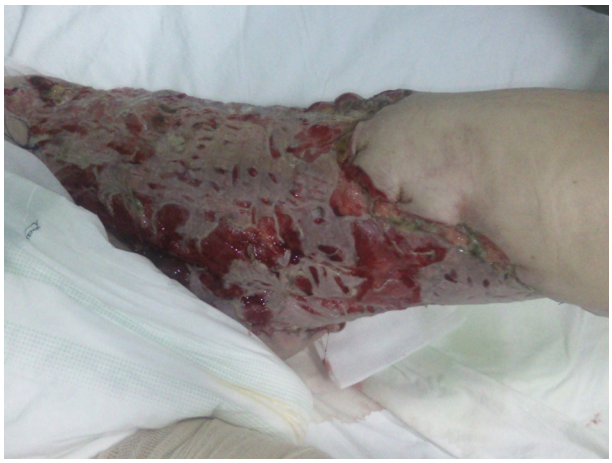

Figure 2. Early postoperative view, almost the entire thigh was degloved and the defect was covered with split-thickness skin graft. In the same procedure, the dissection of popliteal nodes was done.

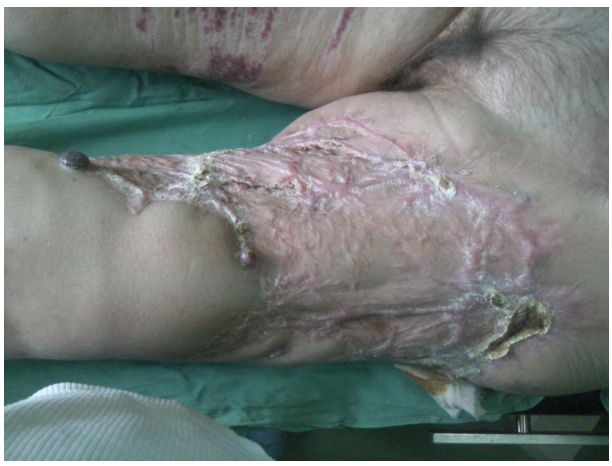

Figure 3. Three months after surgery, the wound healed well, but new local metastases were evident on the surrounding skin. At this moment, the disease has already disseminated

Discussion and review of literature

Melanoma is malignancy of pigment-producing cells (melanocytes) located predominantly in the skin but also found in the eyes, ears, gastro-intestinal tract, leptomeninges, and oral and genital mucous membranes. Skin melanoma was firstly described in 1812 by Rene Laennac (3). It is known for its highly malignant potency. Local, regional and distant metastases are not rare. In the USA, melanoma incidence has increased by 3.1% annually throughout the last 20 years, reaching in 2007 the level of 27.5/ 100.000 in Caucasians, and 11.1/100000 in African-American population. Its incidence grows faster than the incidence of any other cancer (4). There are a lot of risk factors for melanoma, which are widely described in the literature. Two among them differentiate - genetic abnormalities and ultraviolet radiation (UVR) exposure (5,6).

Although melanoma has been known for centuries, its therapy has not changed for a long time. According to the oncologic rule, the key therapy includes early diagnosis, and radical excision of the melanoma during the early stage, in which case there is a 90% to 99% chance of curing the disease (7,8). Very often, prompt diagnosis is not possible, and therefore we cannot predict whether the surgical excision will provide good medical outcome.

Metastatic melanoma is by far the most aggressive form of skin cancer with median overall survival (OS) of 8 to 18 months (9). Prognosis for unresectable metastases or for advanced-stage melanoma is poor, due to its resistance to chemotherapy and irradiation, aggressive behaviour, and rapid metastasizing propensity. A 5-year survival rate is 78%, 59%, and 40% for patients with stage IIIA, IIIB and IIIC, respectively. One-year survival rate decreases from 62% to 53% and 33% for Stages M1a, M1b and M1c, respectively (7).

Until 2012, there were only a few approved and recommended therapy modalities for advanced-stage melanoma recommended by US Food and Drug Administration. Usual therapy modalities included chemotherapy protocol with dacarbazine (DTIC) and high dose interleukin 2 (HDIL 2), but they did not increase the median OS, and both of them were limited by a low response rate (10-15%, and 6- 10 % respectively) (10,11). Treatment with IL-2 in combination with interferon-α2b (IFN-α2b) as adjuvant immunotherapy achieves a response in 10–20% of patients (8). Unfortunately, all of these responses are generally short-lived and associated with high toxicity. Over time, many therapeutic modalities have been explored, and none of them is promising. Encouragingly, in the recent years, the identification of the main genetic aberrations and signalling pathways involved in oncogenesis and disease progression has resulted in the development of novel, more effective therapeutic approaches (6).

Another question arises concerning surgical therapy of the olygometastatic processes in melanoma. A 2011 phase 2 study included 77 patients who underwent complete resection of the metastatic disease and demonstrated a relapse free survival of five months, and around one third of the patients survived the following three years (12).

As presented patient was on corticosteroid therapy, IFN-□2b was not a treatment option. Rapid appearance of the local and regional metastases may be related to her prior immunodeficiency state, when corticosteroids were administered also during the surgical treatment of melanoma. Furthermore, because of the lack of deeper understanding of molecular interactions, we cannot discuss possible course which could have been taken if the corticosteroid therapy had been stopped and standard treatment IL-2 and IFN-α2b had been started.

Conclusion

Cutaneous melanoma and its advanced-stage forms present a systemic disease of great complexity which are to be further investigated on molecular, but also on biological and clinical levels. Case-related treatment brings out a lot of difficulties, mostly because of the incidence of the disease, which is growing on annual bases. Even though prognosis with advanced-stage disease is not favourable, with recent therapeutic advances there are chances for better survival. With such a therapeutic complexity, the treatment of patient with two or more unrelated diseases makes the decision even more complex. It requires deeper knowledge of all issues, possible interactions on disease-treatment relation, and necessarily, further investigation of therapeutic modalities.

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MELANOM KOŽE KOD BOLESNIKA SA MULTIPLOM SKLEROZOM: PRIKAZ SLUČAJA I PREGLED LITERATURE

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Melanom kože je maligni tumor agresivnih osobina. Regionalne ili sistemske metastaze predstavljaju formu širenja bolesti, ali tačno vreme pojavljivanja ne može se jasno definisati. Predstavljamo slučaj bolesnice sa melanomom kože, koja boluje od multiple skleroze i koja je na dugogodišnjoj terapiji kortikosteroidima. Primarni tumor bio je debljine 1,7mm (T2a), ali je klinički tok bio izuzetno agresivan sa masivnim potkožnim i limfatičkim metastazama, koje su uključivale čak i zatkolene limfne noduse. Izvedeno je više hirurških zahvata, kao jedini terapijski izbor, u uslovima u kojima interferon alfa nije mogao biti primenjen zbog multiple skleroze. Bolesnica je umrla 16 meseci nakon dijagnoze u stadijumu generalizovane bolesti. Diskusija o slučaju bi trebalo da prati agesivni tok, koji može biti povezan sa imunosupresijom, ali to nije moglo biti jasno zaključeno. *Acta Medica Medianae 2012;51(4):47-50.*

Ključne reči: *melanom kože, multipla skleroza, brzo napredovanje*