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Long lasting complete response in melanoma treated by electrochemotherapy

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ABSTRACT

The optimal treatment of multiple cutaneous and subcutaneous metastases of melanoma still remains unresolved. There are many different possible treatment modalities. We present a case of melanoma on the calf in which multiple cutaneous and subcutaneous metastases were treated by electrochemotherapy with cisplatin. They completely responded for eight years. After eight years two new metastatic nodules occurred and were treated by electrochemotherapy with cisplatin and again complete response was achieved. The case presents the advantages of electrochemotherapy of multiple cutaneous and subcutaneous metastases of melanoma, its relative simplicity, its minimal side effects and the possibility to treat recurrent disease as many times as needed, with long lasting complete responses.

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1. Introduction

The multiple cutaneous and subcutaneous metastases of melanoma are a condition which is difficult to treat with curative intent. There are different modalities in use. When nodules are conveniently located the surgical excision is performed. Radiotherapy,¹ isolated limb perfusions and infusions² and laser therapy could be employed when surgery is not feasible. Another possible modality is electrochemotherapy.^{3–5}

We present a case of a patient with multiple cutaneous and subcutaneous metastases of the melanoma treated by electrochemotherapy with cisplatin. With this treatment long standing complete response was obtained.

2. Case report

Fifty-seven years old female patient was operated upon in 1992, with wide excision of a melanoma of Breslow thickness 1.3 mm on the anterior side of left ankle. No further treat-

ment was given at that time. Patient fared well until January 1997 when multiple cutaneous and subcutaneous nodules (16 nodules) were observed on right calf, verified by fine needle aspiration biopsy as metastases of melanoma (Fig. 1). The size of the nodules ranged from 4 × 4 mm to 17 × 18 mm in diameters. The US of the abdomen and chest X-rays did not show any signs of metastases. From February to May 1997 the patient was treated by electrochemotherapy. Altogether five sessions were performed. First three sessions were performed with weekly intervals. The fourth session was performed 2 weeks after the third one. The fifth one was performed in May 1997 when new 16 × 16 mm metastasis on the inner side of right thigh emerged. The treatment was performed by intratumoural injection of cisplatin (cis-diamminedichloroplatinum II; Platinol, Bristol-Myers Squibb, Vienna, Austria) in concentration of 1 mg/100 mm³ of tumour nodule. The interval between cisplatin injection and the application of electric pulses was 1–2 min. Square wave electric pulses of 100 μs, 910 V amplitude (amplitude/electrode distance ratio

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Fig. 1 – Response of melanoma tumour nodules to single treatment by electrochemotherapy using cisplatin. Nodules were treated with intratumoural injection of cisplatin and 1-2 min afterward exposed to electric pulses. Two months after treatment crusts are visible on some of the treated nodules, which fell off. Good cosmetic effect without visible scarring 6 and 8 years after treatment without recurrences.

1300 V/cm) and frequency of 1 Hz were delivered through 2 stainless steel electrodes with inner distance between them 7 mm, using an electric pulse generator Jouan GHT 1287 (Jouan, St. Herblain, France). Nodules larger than 7 mm in diameter were treated with several runs of electric pulses administered in adjacent positions to assure adequate coverage of the whole tumour area. By August 1997 all metastases were in complete response except the tumour on the ankle which grew to 6 cm with superficial ulceration. This nodule was then treated by excision and cryosurgery of the base. Its histology revealed the metastasis of epitheloid melanoma with infiltration of the resection surface. By November 1997 the wound was completely healed by secondary intention and all nodules treated by electrochemotherapy were in complete response. The treated nodules were at first erythematous and slight oedema was observed, which remained for two weeks. Thereafter a superficial crust was formed on the treated nodules which fell off in approximately in 4-8 weeks (Fig. 1). After the crust fell off, the skin in the treated area

was slightly depigmented with minimal retraction. However, these changes in the skin disappeared with time as during regular follow ups the primary position of the treated nodules was difficult or impossible to locate (Fig. 1).

Patient was in complete response till August 2005, when two subcutaneous metastases on right leg emerged, one was located below the knee (7 × 7 mm) and the second above it (13 × 11 mm). They were treated by electrochemotherapy with cisplatin with the same drug dosage and electrical parameters as in the first course of treatment using the electric pulse generator CLINIPORATOR™ (IGE A srl. Carpi, Italy). The same development of the treatment response was observed and in November 2005 complete response was observed.

3. Discussion

Case presented is showing that multiple cutaneous and subcutaneous metastases of melanoma could be treated by

electrochemotherapy with cisplatin with long lasting complete response of eight years.

The multiple cutaneous and subcutaneous metastases of melanoma are believed to be the result of intralymphatic spread of tumour cells. Therefore the longstanding complete remission is difficult to obtain and cures are very rare. The treatment modality which is the most appropriate if nodules are few and conveniently located is surgical excision. It is obviously limited by the ability to obtain skin closure, which is sometimes achieved with skin grafting. When surgical excision is not feasible and tumours are located on the extremities, isolated limb infusion and perfusion could be the option. The drawback of the procedure is its relative complexity imposing that it could be performed in few cancer centers with resources and competence. Although the isolated limb perfusion might have high complete response rate as 90%, remission rate is high as 50%, the corresponding median limb disease free interval is of only short duration, 9.5 months.⁶ When it comes to recurrence after limb perfusion a second limb perfusion might be done which is even more technically demanding than the first one.⁷ In some centres laser evaporation of melanoma nodules is performed which is resulting in defects which are healed by secondary intention for quite some time and are prone to infection.⁸

All these drawbacks of different modalities of treatment of multiple cutaneous and subcutaneous metastases of melanoma might be overcome with electrochemotherapy taking long lasting complete response as its definite advantage. The electrochemotherapy is an easy, fast and effective procedure which can be repeated as much as needed. Furthermore the wounds are not healed by secondary intention as tumours are diminishing in its size. All these advantages are presented in our case.

Furthermore, this case clearly demonstrates that electrochemotherapy can be repeated several times with equally good antitumour effectiveness indicating that melanoma cells in new emerging metastases did not have acquired resistance to cisplatin.

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