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CASE REPORT

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Electrochemotherapy, as a novel therapeutic approach in the management of lentigo maligna, lentigo maligna melanoma, and acral lentiginous melanoma

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ABSTRACT

Purpose: Lentigo maligna (LM), lentigo maligna melanoma (LMM), and acral lentiginous melanoma (ALM) are characterized by irregular borders and manifest on highly visible and/or surgically challenging areas. The challenge in treating these melanomas lies in preserving function and achieving satisfactory esthetic outcomes while ensuring complete surgical excision with an appropriate safety margin. We report three cases of elderly patients with LM, LMM, and ALM treated with electrochemotherapy (ECT).

Materials and Methods: All patients were treated according to the European Standard Operating Procedures of Electrochemotherapy protocol. Bleomycin was administered intravenously, followed by electroporation to allow better drug uptake into the tumor cells. The safety margin was ensured by electrode repositioning, and follow-up was scheduled regularly.

Results: Our patients experienced favorable outcomes: two achieved a complete response, with one requiring adjuvant topical imiquimod for suspected residual disease, while the third patient achieved a partial response. No serious adverse events were observed, and cosmetic results were superior compared to extensive surgery.

Conclusion: ECT appears to be a safe and effective treatment alternative for LM, LMM, and ALM, especially in elderly patients where surgery may lead to significant morbidity. ECT can be used alone or in combination with other therapies, providing a wide safety margin and cosmetically favorable results.

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Bleomycin; electrochemotherapy; imiquimod; irradiation; melanoma

Introduction

Lentigo maligna (LM), lentigo maligna melanoma (LMM), and acral lentiginous melanoma (ALM) are challenging tumors to treat. They are characterized by ill-defined borders, often extensive involvement, and typically manifest on the face or the soles of the feet. The difficulty in treating these melanomas lies in the need to preserve function and achieve satisfactory esthetic outcomes while ensuring effective tumor control. According to the most recent NCCN guidelines, recommended surgical margins exceed 5 mm to ensure histologically negative margins, or Mohs microsurgery may be considered (1). However, elderly patients with larger lesions may not be suitable for extensive reconstructive surgeries, particularly in cosmetically sensitive areas of the face, as such procedures could lead to significant morbidity. This underscores the need for alternative treatment options, which currently include radiotherapy, topical imiquimod and other local ablative treatments (2).

Electrochemotherapy (ECT) combines electroporation with a chemotherapeutic drug. During treatment, an electric pulse is applied, temporarily increasing the permeability of the cell membrane and allowing chemotherapeutic agents to enter cells, which would otherwise have limited or no penetration. Once inside, these agents exert their cytotoxic effects, leading to cell death. Electroporation is reversible; when the electrical pulse stops, the cell membrane returns to its normal state.

ECT is an effective and commonly used treatment for tumors located on the skin or subcutaneously, including cutaneous metastases of malignant melanoma. Two prospective cohort studies (3,4) demonstrated the high efficacy of ECT in treating cutaneous metastases of melanoma malignum with overall response rates of 78%, and 82%, complete response rates of 58%, and 64% respectively, with no serious adverse events reported. For primary, unresectable melanoma, only a few cases of anorectal malignant melanoma treated with ECT have been reported (5). We present three cases of LM, LMM, and ALM successfully treated with ECT.

Materials and methods

The treatment in all three cases was performed in accordance to the international protocol (European Standard Operating Procedures of Electrochemotherapy [ESOPE]) (6) using a CE marked Cliniporator™ (IGEA Ltd, Modena/Carpi Italy) electric pulse generator under general anesthesia. Bleomycin was administered intravenously at a dose of 15,000 IU/m^2. Standard needle electrodes were used, with repositioning of the electrodes to treat the large lesions with a 15 mm safety margin. Eight electric pulses were delivered over 100 µs at a frequency of 5000 Hz and an amplitude of 1000 V/cm (according to the electrode distance) between 8 and 28 min after administering bleomycin. Follow-up visits were scheduled as needed, but at least every two months in the first six months.

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Results

Figure 1. Patient 1 before (a) and six months after ECT (b).

Case 1. The first patient was an 83-year-old female with histopathologically confirmed LM located above the right eyebrow (Figure 1(a)). The initial size of the lesion was 20×15 mm. Due to the size and location of the tumor, our multidisciplinary tumor board decided to perform ECT followed by the use of topical imiquimod. Imiquimod was applied topically five times a week for six weeks. Six months after ECT, a small, residual brown-pigmented macule was observed in the treated area (Figure 1(b)) so we decided to perform an excisional biopsy. The histological report confirmed the absence of any remaining tumor, with only melanophages present in the upper dermis, indicating a complete response (Figure 2).

Case 2. The second patient was a 79-year-old female with a large, histologically confirmed LMM pT1a (Breslow: 0.7 mm) extending from the left lower eyelid through the nasolabial fold, involving a large portion of her left cheek (Figure 3(a)). Initially, the patient received radiotherapy (6 MeV electron beam, 65.2 Gy). However, due to minimal clinical regression, it was decided to proceed with ECT, given the extensive tumor involvement on the face of the elderly patient. At that time, the tumor measured 50×50 mm with infiltrative

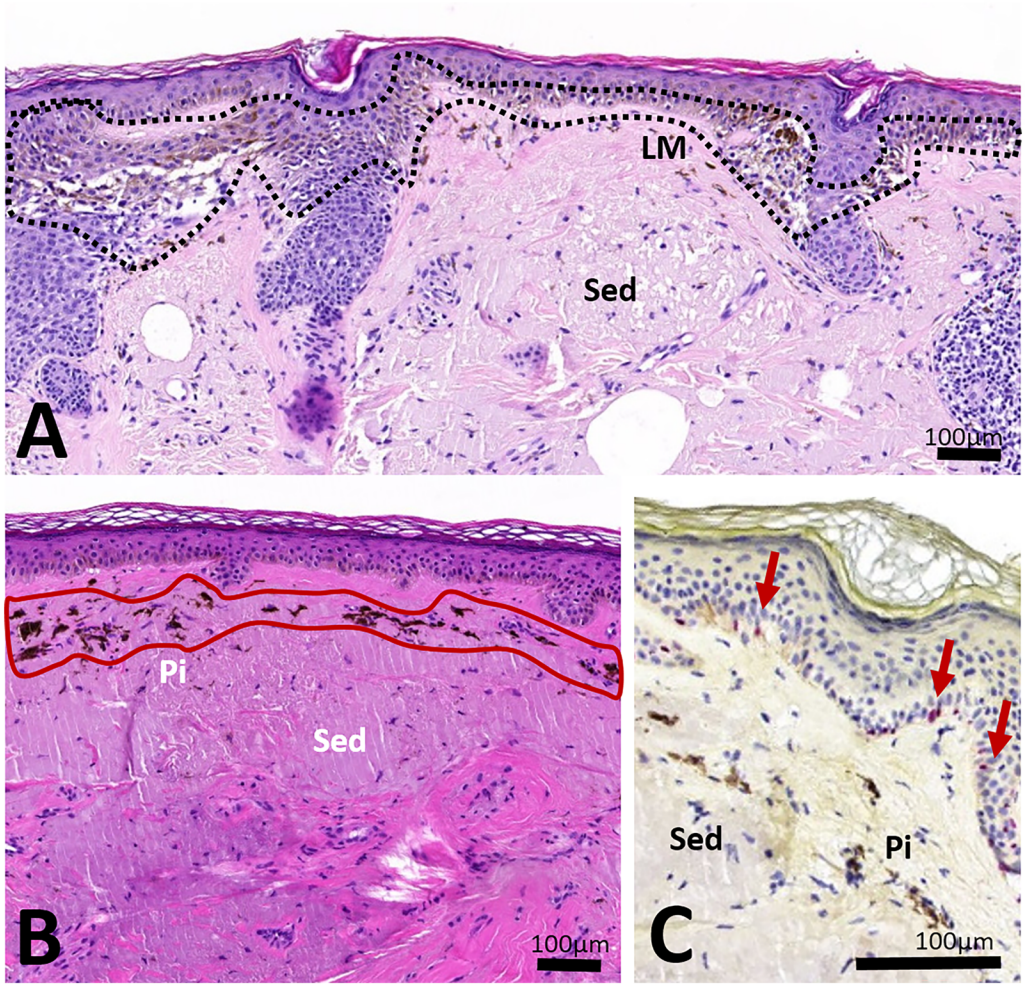

Figure 2. HE-stained representative pictures of the 'before' (A) and 'after' (B, C) status in patient 1. (A) Atypical lentiginous melanocyte proliferation with fuzing atypical nests (LM) and pronounced solar elacin degeneration (sed). (B) After ECT treatment, there was no residual tumor noted; only dermal melanophage accumulation remained along with piment incontinence (Pi). The SOX10-immunostained picture (C) showed the resident junctional melanocytes (arrows). OM 224x, A–B): H&E, C): SOX10 immunohistochemistry.

Figure 3. Patient 2 before (a) and six months after ECT (b). Complete response was achieved.

components. Six months after ECT, a complete response was achieved (Figure 3(b)). The patient declined further follow-up due to her advanced age and difficulties with travel.

Case 3. Our third patient was an 82-year-old male with ALM pTis on his right foot, involving two toes and part of the sole. The tumor measured approximately 40 × 35 mm before treatment. He also had a concurrent diagnosis of primary myelofibrosis, which did not require treatment at the time. Due to the involvement of both the toes and the sole, and the need for an alternative to extensive surgery, our tumor board decided to proceed with ECT. We performed two ECT sessions, three months apart. During the second session, two excisional biopsies were taken from the remaining pigmented macule. One specimen showed no signs of malignancy, while pagetoid spread in the other sample raised suspicion of residual disease. The patient exhibited a partial response six months after the first ECT treatment, during which he was advised to use topical imiquimod. However, he later began treatment for his primary myelofibrosis and did not return for further follow-up visits.

Only transient, local, low-grade side effects were observed including mild erythema, edema, and crusting.

Discussion

Managing LM, LMM, and ALM poses significant challenge due to their ill-defined margins, large sizes, and frequent localization in cosmetically and functionally sensitive areas. Our cases highlight ECT as a promising alternative treatment modality for these tumors, supported by histological results from post-ECT biopsies.

ECT, primarily used as a second-line or palliative option, employs bleomycin to target tumor cells while sparing healthy tissue (7). This enables treatment with a wide safety margin, preserving functionality and reducing complications. In our elderly patients, ECT provided a safer alternative to surgery while maintaining effectiveness.

ECT's ability to activate the immune response through non-thermal tumor ablation is particularly beneficial for immunogenic tumors like melanoma (8). It can be used alone, combined with other treatments, or repeated if necessary, and has shown efficacy even in previously irradiated tumors. Notably, the combination of ECT with topical imiquimod appears to enhance therapeutic outcomes. This aligns with the American Academy of Dermatology guidelines (9), which recommend imiquimod as an adjuvant therapy after surgery, noting that combination therapies outperform surgery alone. Additionally, ECT offers favorable cosmetic outcomes by preserving healthy tissue, making it less invasive and improving quality of life, especially for visible tumors.

However, ECT has limitations. This case series involves a small patient cohort, and longer follow-up is needed to assess long-term outcomes. Further studies with larger groups and extended observation are essential to optimize protocols and expand its clinical use.

Despite these challenges, ECT holds promise as a complementary or alternative therapy, especially for patients who are not candidates for surgery.

Ethical statement

This research was conducted in accordance with the Human Investigation Review Board, University of Szeged. All procedures involving human participants were approved by the Human Investigation Review Board, University of Szeged (ECT-REPRO-002, 29/02/2016).

Consent form

Informed consent was obtained from all individual participants included in the study. Additionally, consent was obtained for the use of photographs depicting human subjects.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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References

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Melanoma: cutaneous version 3; 2024. Available from: https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1492

2. Ungureanu L, Vasilovici AF, Trufin II, et al. Lentigo maligna treatment—an update. J Clin Med. 2024;13:2527. doi: 10.3390/jcm13092527.
3. Kunte C, Letulé V, Gehl J, et al. Electrochemotherapy in the treatment of metastatic malignant melanoma: a prospective cohort study by InspECT. Br J Dermatol. 2017;176(6):1475–1485. doi: 10.1111/bjd.15340.
4. Clover AJP, de Terlizzi F, Bertino G, et al. Electrochemotherapy in the treatment of cutaneous malignancy: outcomes and subgroup analysis from the cumulative results from the pan-European International Network for Sharing Practice in Electrochemotherapy database for 2482 lesions in 987 patients (2008-2019). Eur J Cancer. 2020;138:30–40. doi: 10.1016/j.ejca.2020.06.020.
5. Farricha V, Quaglino P, Brizio M, et al. Safety and efficacy of electrochemotherapy in a series of patients with nonmetastasized primary or recurrent anorectal malignant melanoma. Melanoma Res. 2021;31(1):76–80. doi: 10.1097/CMR.0000000000000699.
6. Gehl J, Sersa G, Matthiessen LW, et al. Updated standard operating procedures for electrochemotherapy of cutaneous tumours and skin metastases. Acta Oncol. 2018;57(7):874–882. doi: 10.1080/0284186X.2018.1454602.
7. Mir LM. Bases and rationale of the electrochemotherapy. Eur J Canc Suppl. 2006;4(11):38–44. doi: 10.1016/j.ejcsup.2006.08.005.
8. Maio M. Melanoma as a model tumour for immuno-oncology. Ann Oncol. 2012;S8:10–14.
9. Swetter SM, Tsao H, Bichakjian CK, et al. Guidelines of care for the management of primary cutaneous melanoma. J Am Acad Dermatol. 2019;80(1):208–250. doi: 10.1016/j.jaad.2018.08.055.