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# Successful repetitive treatments by electrochemotherapy of multiple unresectable Kaposi sarcoma nodules

*Jean-Rémi Garbay*[a,*], *Valérie Billard*[b], *Claire Bernat*[c,d], *Lluis M. Mir*[c,d], *Nassim Morsli*[c,d], *Caroline Robert*[e,*]

[a]*Department of Surgery, Institut Gustave-Roussy, 39 rue Camille Desmoulins, 94805 Villejuif Cédex, France*
[b]*Department of Anaesthesiology, Institut Gustave-Roussy, 39 rue Camille Desmoulins, 94805 Villejuif Cédex, France*
[c]*CNRS UMR 8121, Institut Gustave-Roussy, 39 rue Camille Desmoulins, 94805 Villejuif Cédex, France*
[d]*Univ Paris-Sud, UMR 8121, France*
[e]*Department of Dermatology, Institut Gustave-Roussy, 39 rue Camille Desmoulins, 94805 Villejuif Cédex, France*

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ABSTRACT

We report the successful treatment of a 66-year-old man with failure of conventional local and general treatments for Kaposi sarcoma. He had a poor quality of life because of large ulcerated lesions on both legs. After the first electrochemotherapy session, the largest and the most painful lesions were cleared. Later on, repetitive electrochemotherapy sessions combined with the alternate use of imiquimod application led to an excellent local control with no secondary effect. This case demonstrates that electrochemotherapy can be safely and successfully repeated, with persistent excellent antitumour effects.



## 1. Introduction

Most of the tumours treated by electrochemotherapy are cutaneous malignant melanoma nodules, breast cancer recurrences, or basal cell carcinomas.[1–4] However, the bases of the electrochemotherapy are such that similar responses are expected for the treatment of any cutaneous or subcutaneous tumour.[5] Experience on sarcomas is still very limited. We report here a case of complete clinical response obtained in a patient presenting multiple unresectable Kaposi sarcoma nodules of various sizes treated by electrochemotherapy.

## 2. Case report

In 1984, a 46-year-old Caribbean patient presented with a HIV-negative cutaneous Kaposi sarcoma with confluent nodules located on the legs and severe regional lymphoedema. Chemotherapy with vinblastin sulphate (7.5–10 mg/week) was performed from June 1984 to December 1984, with a total dose of 155 mg. Radiotherapy (41 Gy) on both legs was then performed with a boost on a large nodule located on the left poplitear region. In 1986 additional radiation therapy on the left internal thigh (36 Gy fractionated in 12 sessions) was performed.

In 1991 surgical excision of a left poplitear nodule was performed, showing a grade II soft tissue sarcoma, potentially linked to the previous radiotherapy. In 1998, multiple Kaposi sarcoma nodules recurred on both legs and the patient received a second line chemotherapy with liposomial daunorubicin (8 cycles; total dose 640 mg). After a good initial regression, stabilisation was obtained. One year later, in 1999, an upper left thigh recurrence occurred and two supple-

* *Corresponding authors:* Tel.: +33142114211.
E-mail addresses: garbay@igr.fr (J.-R. Garbay), crobert@igr.fr (C. Robert).
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mentary cycles of daunorubicin were delivered, followed by contact radiotherapy. Despite this treatment, a large plurinodular recurrence was in progression at the end of year 1999 with bilateral moderate lymphoedema. Chemotherapy was undeliverable because of a persistent neutropenia. The local destruction of one nodule was achieved by cryotherapy, and, because there was still no distant metastasis, therapeutic abstention was decided. In 2001, the patient presented a post-radic left ankle fracture.

In 2003 locoregional tumour progression was impressive, with large and often ulcerated nodules disseminated on both legs. Several lesions measured more than 3 cm, and functional consequences were increasing (Fig. 1A). Distant metastases were absent. The patient was referred to the ESOPE electrochemotherapy protocol. He was included for treatment and evaluation of 8 nodules less than 3 cm in diameter. He had compassionate treatment of the 3 largest ones. Even though he had numerous small nodules, eight nodules only were selected before the treatment for evaluation within the ESOPE protocol (Fig. 1A).

The first treatment session was performed on October 23, 2003, under general intravenous anaesthesia (propofol and remifentanil given in TCI mode) and controlled ventilation with $O_2$/air mixture through a laryngeal mask, limiting $FiO_2 < 40\%$ to avoid bleomycin toxicity. After intravenous injection of 27,000 IU of bleomycin in 30–45 s, Type III electrode (an hexagonal centred array of seven needles, used to apply 8 pulses of 730 V and 100 μs at a frequency of 5 kHz be-

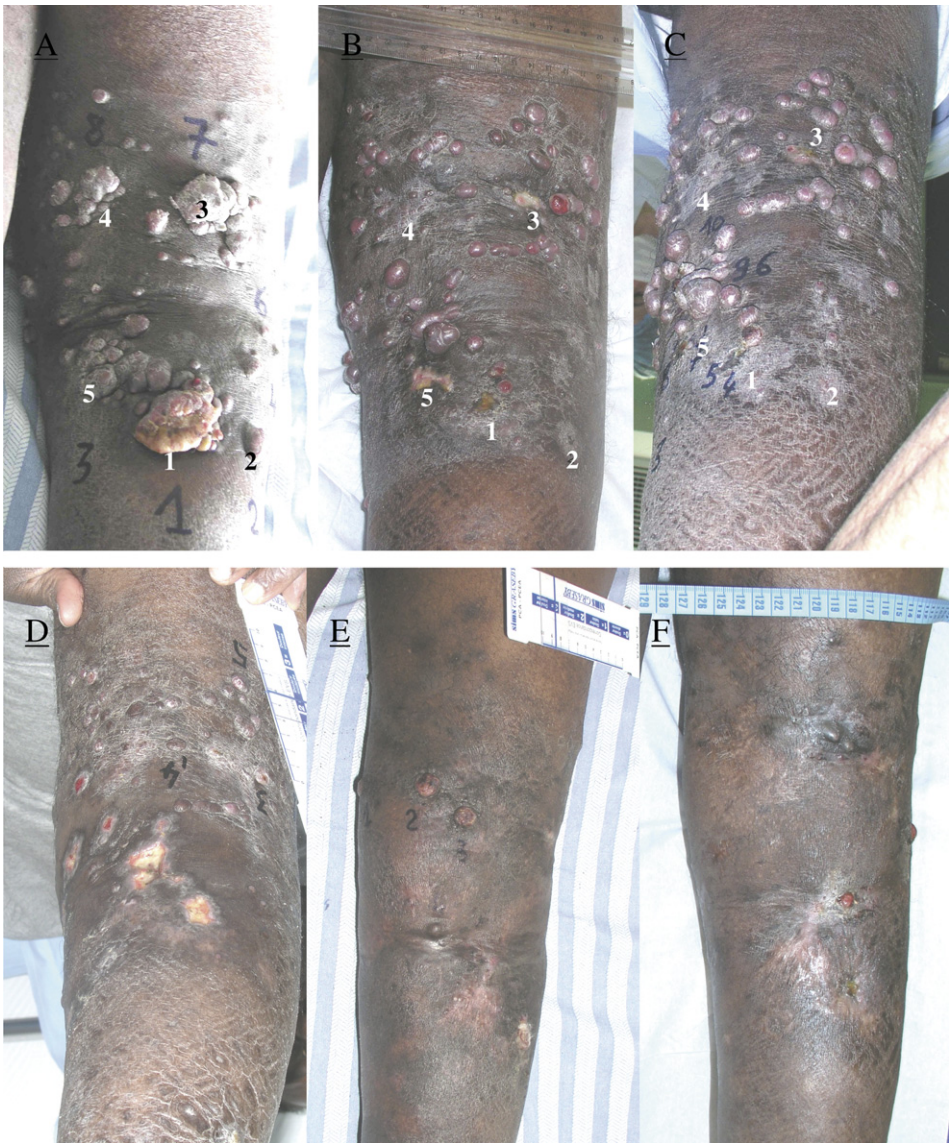


**Fig. 1 – Response of Kaposi sarcoma nodules to consecutive treatments by electrochemotherapy. Panel A: before the first session of electrochemotherapy; panel B: 3 months after the first session, showing the disappearance of the treated nodules and the growth of the untreated nodules; panel C: before the second electrochemotherapy session; panel D: 30 days after the second session, showing again excellent response of the treated nodules; panel E: situation of the patient's leg in February 2005, before the fifth electrochemotherapy session; panel F: situation of the patient's leg in March 2006, 2 years and a half after the first electrochemotherapy session.**

tween each pair of equidistant needles, 7.3 mm apart) was used to deliver 31 trains of pulses and type I electrode (two parallel metallic plates, 8 mm apart, used to apply 8 pulses of 960 V and 100 μs at a frequency of 5 kHz) was used to deliver 15 other trains of pulses. As a general rule, the trains of pulses (one train of pulses per nodule or per part of the treated nodule in the case of the large nodules) were delivered between 8 and about 30 min after the end of the bleomycin bolus injection. The electric pulses were generated by the CE labelled Cliniporator™ (IGEA S.r.l., Carpi, Italy). At day 15, a spectacular response was observed with complete necrosis of all treated nodules, even the largest ones. The patient suffered no pain and no lymphoedema progression was noticed. At 3 months, there was an excellent result with plane scars in place of the treated nodules, but progression of the non-treated ones (Fig. 1B).

The treatment of these latter nodules was thus decided. A second session was performed on February 12, 2004 (Fig. 1C) under the same modalities, i.e. general anaesthesia, 27000 IU of bleomycin iv and type III electrode. Thirty-four applications were made on the largest non-treated nodules. At day 30, almost all the treated lesions were rated as complete responses, while the others were still regressing (partial responses at that time) (Fig. 1D).

To complete the treatment performed during the second session, a third session was made on March 11 2004, always under general anaesthesia and with 27000 IU of bleomycin iv, requiring 27 applications with a type III electrode and 6 applications with a type II electrode (two parallel rows of 4 needles, 4 mm apart, 8 pulses of 400 V and 100 μs delivered at a frequency of 5 kHz). Again the complete response of the treated nodules was observed. At 3 months, the complete response of all the treated nodules was confirmed.

Later on, the presence of new millimetric nodules was noticed, outside the treated areas. Topical treatment with Imiquimod cream (Aldara, 3M Santé, Cergy Pontoise, France) resulted in complete response of two thirds of the nodules and partial response of the others. At the end of year 2004, there were only 9 progressive nodules on the right leg, with some non-progressive millimetric nodules. The complete response of all the nodules treated by electrochemotherapy was persistent.

In February 2005, a fourth session was made under general anaesthesia and 27000 IU of bleomycin iv, with a type III electrode for 16 applications and with a type II electrode for 2 applications (Fig. 1E). A surgical biopsy of the scar of one of the previously treated nodules was made, with negative histological analysis. At 1 month, complete response of all the treated nodules was observed again.

In June 2005, a fifth session under local anaesthesia was performed to treat 5 new lesions on the right leg and one nodule on the left leg, under general anaesthesia and with 27000 IU of bleomycin iv and ptype II electrode. At 2 months, treated lesions were in complete response but, once again, the presence of new lesions was detected outside the treated areas, on the right leg only.

Thus in September 2005, a sixth session under general anaesthesia was performed, with 27000 IU of bleomycin iv and 27 applications with type III electrode. One month later, complete response was observed. After the last session (and a total dose of bleomycin of 162000 IU of bleomycin), functional breath test was still normal.

In January 2006, Imiquimod was applied on new nodules located on the right leg with a good response. In March 2006, lesions were decreasing in size and no new lesion was noted. No distant metastasis was present (Fig. 1F).

## 3. Discussion

In 2003, this 66-year-old man was in a worrying situation, with failure of conventional local and general treatments for Kaposi sarcoma. He had a poor quality of life because of large ulcerated lesions on both legs.

After the first electrochemotherapy session, the largest and the most painful lesions were cleared.

Later on, repetitive electrochemotherapy sessions combined with the alternate use of imiquimod application led to an excellent local control with no secondary effect. The low doses of intravenous bleomycin allow repetitive sessions. It is still unknown whether the combination of electrochemotherapy and imiquimod has a synergistic effect and further studies using this combination will be necessary to evaluate the interest of such an association.

This case demonstrates that electrochemotherapy can be safely and successfully repeated, with persistent excellent antitumour effects. The patient is extremely grateful for this treatment and ready for other sessions if necessary.

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