Regional metastatic melanoma. Aspects of treatment and prognostic factors

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Chapter II

Carbon dioxide laser for cutaneous melanoma metastases: indications and limitations

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Chapter II

ABSTRACT

Background: Cutaneous melanoma metastases pose a therapeutical challenge to the treating surgeon. The value of carbon dioxide (CO₂) laser as an alternative treatment modality is evaluated.

Methods: A total of 469 in-transit or satellite lesions were treated by carbon dioxide (CO₂) laser vaporisation in 15 patients. The treatment was performed mostly on an outpatient basis, under local anaesthesia.

Results: The technique was easily mastered and quickly performed. Wound healing and patient acceptance were good. A major drawback, however, proved to be the unexpected high incidence of recurrences at the lasered sites.

Conclusions: In our opinion CO₂ laser treatment may be considered as a palliative option in patients with a moderate to extensive amount of cutaneous metastases, whose lesions preferably are < 10 mm. For extremity lesions this treatment has a place after failure of isolated limb perfusion. CO₂ laser treatment cannot be considered a first-line option unless the issue of local recurrences is solved.
INTRODUCTION

A typical expression of regional dissemination in melanoma consists of cutaneous or subcutaneous lesions, commonly referred to as satellites or in-transit metastases, depending on the distance from the primary tumour. These recurrences occur in about 5 per cent of patients treated for melanoma, with an increasing incidence in thicker and ulcerating primary tumours. Following the occurrence of regional cutaneous metastases 5-year survival rates varying between 27% and 45% are reported. Having seen these data, treatment of local regional recurrent melanoma becomes an important issue both for optimal regional disease control and survival.

Choosing the right therapy for the satellite and in-transit phenomenon, however, is difficult, due to the variety of therapeutic modalities, reflecting the poorly understood pathophysiology and versatile appearance of these metastases. While aiming for a cure is still an option in some patients, palliation is the best that can be achieved in most. Surgical excision is a valuable treatment option in case of a limited number of lesions. Isolated limb perfusion with melphalan is the treatment of choice when multiple in-transit metastases are confined to one extremity. Immunotherapeutical regimens such as intralesional BCG or topical DNCB have been used with variable success rates. Radiotherapy in combination with hyperthermia is used for cutaneous and subcutaneous melanoma metastases with a favourable response rate. Once distant metastases are present, systemic chemotherapy can prove beneficial for only a minority of patients. In recent literature, carbon dioxide (CO₂) laser vaporisation of cutaneous metastases has been presented as an effective and minimally invasive alternative to the above-mentioned procedures.

In this report, the feasibility of the technique, local disease control and patient acceptance were studied prospectively. An attempt is made to compare the various therapeutic options in non-nodal regional recurrent melanoma.

PATIENTS AND METHODS

Patients with lesions < 2 cm and in (contact with) the skin were eligible for CO₂ laser treatment. Between November 1995 and December 1996, 15 patients with a total of 469 in-transit and satellite lesions of cutaneous melanoma, were treated with CO₂ laser vaporisation. Ten were female and five were male, the median age
was 72 years (range: 61-87). In all but one patient, the primary tumour had been previously excised. The primary tumours were located on the leg in 12 patients, on the arm in one patient and on the scalp in two patients. The median Breslow thickness of the primary tumours was 3 mm (range: 1-13). Previous treatments for the in-transit and satellite lesions consisted of 10 isolated limb perfusions in six patients, repeated excisions in eight patients and immuno-chemotherapy in three patients. Therapeutic regional lymph node dissection had been performed earlier in the course of the disease in 12 patients.

The 469 lesions, with a median of 11 lesions per patient (range: 1-184), were vaporised in the course of one to five sessions per patient and at a median rate of five lesions per treatment session (range: 1-184). The lesions were located on the foot and leg in nine patients, in the groin and lower abdomen in three patients, on the scalp and face in two patients and on the arm in one patient. The median diameter of the lesions was 3 mm (range: 1-14), and most were cutaneous.

Three patients were treated under general anaesthesia, one due to a concomitant lymph node dissection and two because of the large number of the lesions. In all other patients infiltration anaesthesia (lidocaine 1% with adrenaline) was used.

The Sharplan 1030 CO$_2$ laser (Laser Industries, distributed by Nova Medica, the Netherlands) was set to a power of 7 - 9 W, delivered continuously in the superpulse mode to minimise tissue damage. For the same purpose, the tissues were cooled with a cold saline solution on a gauze, applied on the lesions before and after treatment. A higher power was used for voluminous lesions, while slightly defocussing the beam. A smoke evacuator ensured clearance of heated air and dust. Because of the poor visibility of some minor and unpigmented metastases, an undyed alcoholic solution was used for disinfection, taking care not to start CO$_2$ laser vaporisation before the skin was dry. At the onset of laser treatment, the target lesion was encircled, including a free margin of one to several mm, the same we are holding to when performing an excision by scalpel of multiple in-transit metastases. This facilitated ablation of small lesions, where borders may be difficult to visualise once the destruction has started. With fast strokes the outlined area was "painted" by the Helium-Neon red target beam until the entire metastasis was destroyed. If necessary, hemostasis was achieved by defocussing. As in local resections of cutaneous metastases, ablation was considered to be complete when the bottom and the edges of the resulting crater
were free of tumour as judged by the naked eye and by palpation. Completeness of the laser treatment was assessed histologically in the first three patients by taking biopsies from treated areas (5x), removing the entire crater (4x) and taking samples from the bottom (1x).

The resulting full thickness burns were covered with vaseline gauze, to be changed at home daily, until a crusta had formed. Patients were followed to evaluate wound healing, local recurrence or occurrence of new lesions and they were asked a set of questions to compare the side effects of the CO₂ laser vaporisation to previous treatments. When suspicion of local recurrence arose, excision was performed to distinguish between scar formation and tumour.

**Results**

CO₂ laser vaporisation under local anaesthesia proved to be a feasible procedure in the majority of the patients. Following previous isolated limb perfusion, however, infiltration anaesthesia was rather painful in these patients, due to fibrosis of the subcutaneous tissues. The very small laser beam spot size enabled highly accurate tissue destruction, inflicting minimal thermal damage to the surrounding skin. A lesion could be dealt with in 10 to 45 seconds, depending on its diameter. Wound healing was painless and wounds were easily cared for at home by all patients, except for one patient with lesions on the medial side of her foot. Most wounds were dry after a few days to one week after treatment. Exceptions to this quick healing were the wounds on legs in patients who had been repeatedly or recently treated by isolated limb perfusion, and those wounds > 10 mm in diameter. Except some delayed wound-healing problems, no other post-operative complications were encountered.

Histologic examination revealed residual melanoma in two of 10 biopsies, despite the fact that the surgeon felt the treatment to be radical. This finding led to more extensive treatment of subsequent lesions, aiming for wider and deeper margins. Notwithstanding this, however, recurrences at the lasered sites were observed in seven of the 15 patients. Two of them had been referred with overwhelming in-transit disease of the thighs and lower abdomen, another three had lesions on leg and foot, one had a scalp lesion, and one a forearm lesion (Table 1). Almost 1 month after CO₂ laser vaporisation, the tissue defects in these patients already were filled again entirely by recurrent tumour. It is remarkable that in two
of them a biopsy of the treated area suggested complete destruction of the lesion. Treatment of the recurrences consisted of excision, further CO₂ laser vaporisation, radiotherapy, isolated limb perfusion or systemic chemotherapy, depending on the extent and localisation of the disease.

Table 1. Details of treated and recurrent lesions of the seven patients with local failure

<table>
<thead>
<tr>
<th>Patient</th>
<th>Primary melanoma</th>
<th>Treated lesions</th>
<th>Local recurrences</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n</td>
<td>Mean size (mm)</td>
</tr>
<tr>
<td>1</td>
<td>leg</td>
<td>80</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>foot</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>scalp</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>forearm</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>leg</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>leg</td>
<td>184</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>leg</td>
<td>7</td>
<td>12</td>
</tr>
</tbody>
</table>

Five patients suffered recurrent in-transit metastases in areas not previously treated. Four of them received further laser therapy in combination with radiotherapy and hyperthermia, excisions or immunotherapy. One underwent isolated limb perfusion followed by immunotherapy. Two patients died of systemic recurrent melanoma, 2 and 9 months after laser palliation of extensive cutaneous metastases.

Patient acceptance of the laser therapy was good. Patients appreciated the outpatient setting, the ease of the aftercare and the acceptable cosmetic appearance in most cases. When asked for, all patients preferred laser treatment over previous therapies.

DISCUSSION

Cure can be offered to only a minority of patients with satellites and in-transit metastases, from which the need for a treatment that combines effectiveness with a low morbidity can be inferred. CO₂ laser vaporisation seems to meet these requirements. Being a quick technique, it is possible to treat up to 10 - 15 lesions under local anaesthesia in one outpatient session. The number of treated lesions is
almost unlimited when the operation is conceived as a day-case procedure under general anaesthesia.

Adverse effects of the CO₂ laser treatment in our study group were rare. Care has to be taken with patients who previously underwent (repeated) isolated limb perfusion, since they are prone to wound healing problems due to the sometimes fragile skin and fibrotic subcutaneous tissues. Scar tissue formation following the CO₂ laser was seldom a problem, in fact, in some patients treated sites were barely visible.

The high incidence of recurrences at lasered sites in our patients was striking and is in contrast with previous reports.¹¹⁻¹³ It showed that, however minimal the tumour burden left after laser ablation with wide safety margins may be, tumour volumes of more than 1 cm³ can arise in a few weeks. The fact that in two patients with recurrences the biopsies did not show any tumour, suggests that, at least in these cases, high local growth factor concentrations in open wounds healing by second intention could play a stimulating role in this surprisingly fast emergence of local recurrences. It has been shown that melanoma cell lines express a broad range of growth factors and corresponding receptors.¹⁹ In contrast to others,¹² we used the superpulsed CO₂ laser, which ideally only vaporises tissues. Manually operating the laser during vaporisation, however, inevitably leads to some tissue charring, minimising the theoretical possibility of leaving behind vital tumour cells due to inadequate heating of the target area.²⁰ Furthermore it has been shown in vitro, that vital bacteria can be transported from a liver surface down to the bottom of a laser-drilled crater.²¹ A similar transport of vital melanoma cells could have taken place in some patients, causing local recurrences.

Local excision has to be considered standard therapy when the number of satellite and in-transit lesions is limited. It is virtually never followed by recurrences in the excisional scar. Local excision is, however, a laborious and time-consuming option in case of numerous recurrences. The use of electrocoagulation and cryotherapy ²² is limited by the extent of destruction of surrounding healthy tissue and is time-consuming due to carbonisation or to repeated freeze-thaw cycles, respectively.

Local immunotherapy through intralesional BCG injections results in response rates of 62%, lasting for 18 - 28 months.²³ Local and systemic side effects are substantial, which makes this method less suitable as a first line treatment. The
A combination of radiotherapy and hyperthermia yields a promising 46 to 77% complete response rate, mainly in small volume (<3 mm) and superficial lesions. Because of its limited availability, this combination therapy has to be reserved for refractory disease. Isolated limb perfusion with melphalan induces in patients with recurrent melanoma a mean complete remission rate of 54% (7 to 90%) with a 5-year limb recurrence-free interval of 52%. This treatment is preferred when the lesions are large in size, are situated in the subcutaneous tissue, are progressive or recurrent and are large in number. A major advantage of isolated limb perfusion is that this method is presumed to sterilise subclinical tumour deposits. It is however a complicated surgical procedure associated with a substantial morbidity. Systemic chemotherapy and immunotherapy or a combination of both is indicated only in case of disseminated disease because of low response rates combined with a rather severe toxicity. Amputation should only be considered as a rescue measure in the occasional individual patient on condition that a reasonable duration of palliation can be offered in exchange for the mutilation. None of these loco-regional or systemic treatments has a proven survival benefit over the other, while on the other hand the burden for the patient can vary considerably in terms of disturbance of daily life, morbidity and even mortality.

In conclusion, we are of the opinion that the precise place of CO₂ laser treatment in the management of cutaneous melanoma recurrences has yet to be defined. Laser vaporisation should not be considered as first-line treatment for limited in-transit disease as long as the issue of local recurrences at the lasered sites is under debate. Local excision with histological proof of completeness thus remains the first-line treatment of small numbers of lesions. For massive or progressive limb disease, isolated limb perfusion is the treatment of choice. In the case of recurrent disease after (repeated) isolated limb perfusion, and when due to numerous recurrences, excision is no longer feasible, CO₂ laser ablation should be considered. In the presence of distant metastases, laser therapy can bring cutaneous relief when used in conjunction with systemic treatment.
REFERENCES


