Successful Treatment of Metastatic Malignant Melanoma with *Viscum album* Extract (Iscador® M)

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ABSTRACT

**Background:** Recent study results demonstrate possible clinical benefit from adjuvant treatment with a standardized mistletoe (*Viscum album*) extract in patients with malignant melanoma.

**Patient and method:** We present a male patient, currently 68 years of age, with one malignant melanoma at the upper part of the right arm since 1992, and another nodular melanoma at the left shoulder, first diagnosed in 1999. After discovery of the second melanoma and surgical resection, the patient was exclusively treated with standardized mistletoe extract (Iscador®, M; Weleda AG, CH-Arlesheim, Switzerland).

**Course of therapy and results:** In June 1992, histologic analysis confirmed the presence of stage IA superficially spreading malignant melanoma with low infiltration of the papillary dermis in a skin excision sample from the upper part of the right arm. In November 1999, another melanoma was surgically removed at the patient’s right shoulder. In this case, the histologic examination revealed nodular melanoma, stage IIA (pT3, pN0, M0). Therapy with mistletoe extract was introduced shortly afterwards as the sole adjuvant treatment. During the course of the mistletoe therapy, axillary removal of 8 lymph nodes became necessary, 3 of which proved to be metastatic. First signs of a defined solitary liver metastasis in an area next to segments IV and V were detected during an abdominal ultrasound examination in September 2001. This finding was confirmed by further sonographic examinations. The solitary liver metastasis was not resected, nor was classical antitumor treatment (chemotherapy or radiotherapy) initiated. The patient continued subcutaneous treatment with Iscador M after dose adaptation to 2 mg twice weekly (0.2 mL of a 10-mg vial); the treatment is still ongoing to the present. By June 2002, complete remission of the liver metastasis was diagnosed by liver ultrasound examination. There has been no local relapse so far, and the patient has been in stable condition ever since. No further metastases were discovered so far (as of May 2006).

**Conclusions:** The use of low-dose Iscador as the sole postoperative modality for the adjuvant treatment of metastatic melanoma was extremely effective and very well tolerated in this patient. It achieved complete response and absence of all complaints.

INTRODUCTION

Melanoma is a malignant tumor of epidermal melanocytes. In general, four types of melanoma are distinguished based on tumor localization and growth patterns, but only two of them are relevant for this case report and thus will be mentioned. Superficially spreading malignant melanoma (SSM) is characterized by primarily horizontal tumor growth of an intraepidermal population of epitheloidal melanoma cells, showing a lead shot–like dis-
tration (pagetoid growth pattern). Nodular melanoma (NM) shows a basically nodular growth pattern in clinically normal surrounding skin, missing on a tangible phase of radial growth.1

In general, the prognosis depends on the thickness of the tumor. Prognosis depends on the stage at diagnosis and patients with melanoma require close follow-up because they are at risk for recurrence and diagnosis of a second primary tumor.2 Studies show that total survival is inversely correlated to tumor thickness.3 Numerous examples such as spontaneous remissions and extremely aggressive courses in immunocompromised patients confirm the role of immunologic factors for tumor progression in this type of neoplasia.4,5

The use of mistletoe (Viscum album) extracts is currently an important part of complementary tumor therapy. It was observed that extracts from mistletoe show antimetastatic properties in close connection with stimulation of relevant parameters of immunogenicity (e.g., liberation of cytokines). It must be surmised that treatment with standardized extracts from mistletoe should be able to prevent the formation of metastases and the further distribution of malignant cells.6

Recently, an increase in adjusted tumor-dependent survival compared to untreated patients was found by a multicenter comparative epidemiologic cohort study from Germany and Switzerland.7

This case report is about a patient with malignant melanoma who was treated successfully with standardized extract from mistletoe as long-term therapy.

**PATIENT AND METHOD**

**Patient**

We describe the case of a 68-year-old man who had been diagnosed with SSM at the right upper part arm in 1992 when he was 55. A detailed noncancer anamnesis can just be reduced to sport accidents and childhood diseases. Besides benign prostatic hyperplasia with early symptoms of trabeculated bladder, no other comorbidities were present at the time of first diagnosis. Neither comorbidities nor comedication (also noncancer) were reported from the patient.

**Standardized extract of mistletoe**

The drug administered in this patient’s therapy was Iscador® M, a formulation of standardized mistletoe extract manufactured by Weleda AG, CH-Arlesheim, Switzerland.

**Treatment course**

In June 1992, histopathologic findings after skin excision at the upper part of the right arm confirmed a stage IA SSM (with low-grade infiltration of the papillary dermis, Clark level II, pT1, N0, M0, Breslow index 0.375 mm).

In November 1999, another melanoma was surgically resected at the right shoulder. Histology confirmed stage IIA nodular melanoma (pT3, pN0, M0). On August 21, 2001, a sentinel lymph node biopsy was performed on one newly enlarged axillary lymph node. The cytologic results revealed considerable expression of the melanocyte marker S100 but no expression of epithelial marker Lu-5 and lymphocyte marker CD-45 and confirmed the diagnosis of metastatic melanoma with lymph node involvement. Lymphadenectomy at the left axilla was performed on August 29, 2001. The histologic findings on the biopsy revealed a sizeable lymph node metastasis with defined extracapsular tumor extension (maximum diameter 5 cm) and microscopic metastases of the described melanoma in another 2 of the 8 lymph nodes that had been removed. Abdominal ultrasound imaging in August 2001 showed signs of a solitary defined liver metastasis with a maximum diameter of 2 cm in an area adjacent to the liver segments 4 and 5. The patient refused the recommended abdominal computed tomography (CT) examination.

Sonographic examination on October 23, 2001 showed an increase in size compared to the examination that had been done in August. A further follow-up sonography, however, performed on January 7, 2002, established that the size of the still solitary lesion in segment 4 had decreased to a diameter of 10 mm. By June 2002, the lesion had disappeared in the ultrasound images. The findings of a physical examination on December 9, 2002 were as follows: scars unobtrusive, all peripheral lymph nodes clear, heart and lungs unobtrusive on auscultation and percussion, abdominal wall soft, liver and spleen not palpable, unchanged nevi at the rectum. Another liver sonography in January 2003 showed no evidence of malignancy, nor were signs of liver metastasization discernible in January 2004.

Treatment with Iscador (M, Series 0, I, and II) was initiated in November 1999 by the patient’s general practitioner and was continued ever since. From October 2001 until November 2005, the patient received a low dose of 2 mg Iscador M twice weekly by subcutaneous injection (i.e., 0.2 mL of a 1-mL vial containing 10 mg).

Subcutaneous administration of mistletoe extract as the only postoperative treatment was tolerated well by the patient. After the discovery of resectable axillary lymph node metastases and a solitary liver lesion, the dose was adapted and frequent imaging was initiated in order to monitor the size of the lesion. Within a few months after dose adaptation (October 2001 until June 2002), complete remission of the liver metastasis was documented. The patient is still in complete remission as of May 2006.

**DISCUSSION**

In this case presentation of a 68-year-old patient with metastatic melanoma, complete tumor remission was achieved with twice-weekly subcutaneous administration of Iscador M. The remission was established and confirmed by
ultrasound imaging. No other systemic treatments or chemotherapy had been administered before Iscador M.

Considering these circumstances, it stands to reason that the observed complete remission was indeed induced by treatment with Iscador M.

It must be stressed that the observed regression of the liver lesion was achieved using only a low drug dose. The clinical improvement initiated with Iscador M is in accordance with results of our earlier pilot study that observed several cases of tumor regression under low-dose Iscador.9

Obviously, there are data that should be studied carefully and generalization should be avoided.9 On the other hand, there are trials that show benefit.7 The fact that mistletoe is used to a considerable extent implies that much data are available about experience with this extract.10–13

If individual case reports are methodically and systematically correctly documented, however, they can probably provide important knowledge about the effects of a therapy.14–16

One weak aspect in this case report is the type of imaging used to follow the lesion. Although modern ultrasound sonography has become highly sensitive, the power of this method still greatly depends on the experience of the investigator.

Unfortunately, independent confirmation of the complete tumor remission with other imaging methods such as CT or abdominal magnetic resonance imaging was impossible because of the patient’s unwillingness to undergo these tests.

CONCLUSIONS

Regular subcutaneous postoperative treatment with Iscador M has in this case proved to be a very effective, well-tolerated, and successful means in treating metastatic melanoma, leading to complete remission.

This single case report should be encouraging for stimulating further investigation of effectiveness and tolerability of standardized mistletoe extracts for the treatment of malignant melanoma in the framework of carefully designed Good Clinical Practice studies.

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REFERENCES


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