Long-term disease stabilization during second-line gemcitabine in a refractory metastatic haemangioendothelioma

Jan Pintoffl[a], Ines Meisinger[a], Frank Mayer[a], Marius Horger[b,d], Claus von Weyhern[c], Lothar Kanz[a] and Joerg Thomas Hartmann[a,d]

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Departments of [a]Medical Oncology, Hematology, Immunology, Rheumatology, Pulmology, Medical Center II, [b]Diagnostic Radiology, [c]Pathology and [d]Interdisciplinary Sarcoma Center, South West German Cancer Center, Eberhard-Karls-University, Tuebingen, Germany

Correspondence to Professor Dr Jörg Thomas Hartmann, MD, Departments of Medical Oncology, Hematology, Immunology, Rheumatology, Pneumology, South West German Comprehensive Cancer Center, Eberhard-Karls-University, Tuebingen, Tuebingen 72076, Germany
Tel: +49 7071 29 82127; fax: +49 7071 29 4399;
e-mail: joerg.hartmann@med.uni-tuebingen.de

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Epithelioid haemangioendothelioma (EHE) is an uncommon vascular neoplasm that has an unpredictable clinical behaviour. It is characterized by round or spindle-shaped endothelial cells with cytoplasmic vacuolation. Most often, EHE arises from the soft tissues of the upper and lower extremities. In the recent WHO classification, the category of haemangioendotheliomas includes spindle cell haemangioendothelioma, EHE and Dabska's tumour (rare malignant endovascular papillary angioendothelioma), which are defined as vascular tumours of 'intermediate' or 'borderline' malignancy.

Current treatment options for EHE are very limited, as its responsiveness to chemotherapy seems to be low.

All these factors considered, for patients who cannot undergo surgery because of their performance or metastatic spread of the disease, the best strategy for palliation is unknown.

Several trials found a moderate activity level of gemcitabine in refractory adult soft tissue sarcomas [1–5]. For example, the MD Anderson Cancer Center (Houston, Texas, USA) demonstrated a remission rate of 18% with a median duration of 3.5 months in patients with soft tissue sarcoma other than gastrointestinal stromal tumors using a flat dose rate infusion [4].

We report on a 32-year-old patient who was diagnosed with an EHE with intermediate malignancy of the right scapula in December 2000 (Fig. 1). The tumour was primarily resected using a Tickhoff–Linberg resection type B technique of the right scapula with a curative intent (R0-resection). The extent of the tumour was classified as pT2 pN0 cM0, the American Joint Committee on Cancer stage III and histological grading II according to Fédération Nationale des Centres de Lutte Contre le Cancer.

Twenty months later, the patient presented with hepatic and pulmonary masses and multiple osteolytic metastases. A hepatic biopsy confirmed the recurrence of the EHE. A combination chemotherapy with doxorubicin and ifosfamide was initiated. After four cycles, the tumour showed progression. Second-line chemotherapy with gemcitabine at a dose of 1.000 mg/m^2, on days 1, 8, 15, restart on day 29, was initiated in February 2002 within an open label phase II trial. After four cycles, the patient perceived an increase in his performance status. A computed tomographic scan showed disease stabilization. In addition to flu-like symptoms after the application of gemcitabine, no significant therapy-associated toxicity was observed. The patient remained clinically stable, and upon multiple reevaluations the tumour did not show any further growth.

After 62 cycles of gemcitabine (72 months on treatment), a PET scan and a hepatic fine-needle biopsy were performed in order to make a decision about the continuation of therapy. The PET scan only showed fluorodeoxyglucose uptake in the left lung, which was attributed to a pulmonary infection and disappeared during antibiotic therapy. Histopathological examination of the liver biopsy revealed evidence of EHE with regressive changes and fibrosis. Thus, we decided to further treat the patient with gemcitabine. Up to now, the patient has received a cumulative dose of 183.000 mg/m^2, his performance status is 0 (according WHO) and he is working full time.

The approach with gemcitabine is impressively effective in our patient and there are no occurrences of cumulative adverse events. However, given the rare occurrence of EHE and the continuous spectrum of differentiation ranging from borderline to highly malignant tumours, clinical studies of sufficient size will be difficult to implement.

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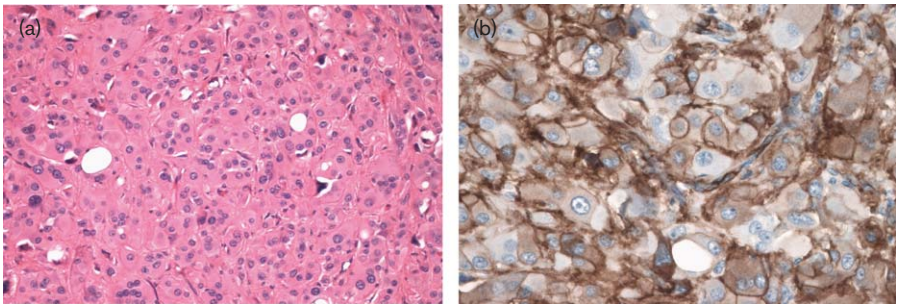
Fig. 1



Sample of the resected tumour showing monomorphic histiocytoid and epitheloid-like cells presenting intraplasmatic vacuolization that 'blister' the cells and form small capillary-type vessels (a, haematoxylin and eosin stain; ×200). Immunohistochemical staining with CD31, a common endothelial marker, reveals a strong membrane-bound staining pattern also staining the intracytoplasmatic vacuols. (b, ×400).

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Conflicts of interest: none declared.

Reference

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