Unusual response to gemcitabine in a case of peritoneal malignant fibrous histiocytoma

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A 65-year-old woman was diagnosed in April 1996 with a peritoneal malignant fibrous histiocytoma (MFH), presenting as multiple peritoneal implants that were surgically resected. Immunohistochemical staining was positive for vimentine, CD68 and factor XIIIA, and negative for queratine, desmine, S-100 and CD34.

The patient relapsed in March 1999 with unresectable implants in peritoneum and ascites; pathological examination of ascitic fluid was compatible with MFH.

She received six cycles of doxorubicin (50 mg/m^2 every 21 days), without response. Ifosfamide was initiated (3 g/m^2 for 3 days every 21 days) in August 2000; she received three cycles with poor hematologic tolerance and no response. The patient presented refractory ascites and was treated with best supportive care until April 2001, when the disease progressed again and compassionate ET-743 was initiated (1300 μg/m^2 every 21 days); after seven cycles a stabilization of the disease was documented.

In January 2002 the patient presented progressive weight loss and ascites (Fig. 1, left images). c-Kit (CD117) was inmunohistochemically assessed in the initial surgical sample, with negative results. She started gemcitabine (800 mg/m^2 days 1 and 8 every 21 days) and a major response was documented after five cycles. The objective response was accompanied with progressive weight gain and improvement of performance status. At the time of this report, the patient has received 14 cycles with excellent tolerance, no relevant toxicities and a maintenance of the response after 9 months (Fig. 1, right images).

MFH is a tumor of late adulthood with a peak incidence in the seventh decade, although it may occur in younger adults. The most common site are the extremities, followed by the retroperitoneum [1]. Whereas a combined modality approach with surgery and radiotherapy can be curative, the mainstay of management in non-resectable and/or relapsed cases is anthracycline-based chemotherapy.

Gemcitabine is a novel nucleoside analog with activity in a number of malignancies, such as non-small cell lung cancer, pancreatic carcinoma and breast cancer.

The activity of gemcitabine as single agent in advanced soft-tissue sarcomas has been evaluated with disappointing results. A EORTC phase II study in 32 patients with soft tissue and bone sarcoma with gemcitabine as second-line therapy (1250 mg/m^2 days 1 and 8 every 21 days) documented one partial response, with a median time to progression of 45 days [2]. In another phase II trial with weekly gemcitabine in 29 patients with relapsed sarcomas, only one partial response was observed. Grade 3–4 haematological toxicities were observed in 32% of the patients [3]. A phase II trial of the combination of gemcitabine and docetaxel in 34 patients (16 previously untreated) with unresectable leiomyosarcoma reported a 53% response rate [4].

Our case is noteworthy because, to our knowledge, (i) it is the first report of a clinical response with single-agent gemcitabine in a patient with chemotherapy-refractory MFH and (ii) the patient had an excellent tolerance to the treatment. Although studies with gemcitabine in a general sarcoma population have failed to show significant activity, the activity of gemcitabine in some sarcoma subtypes remains undetermined.

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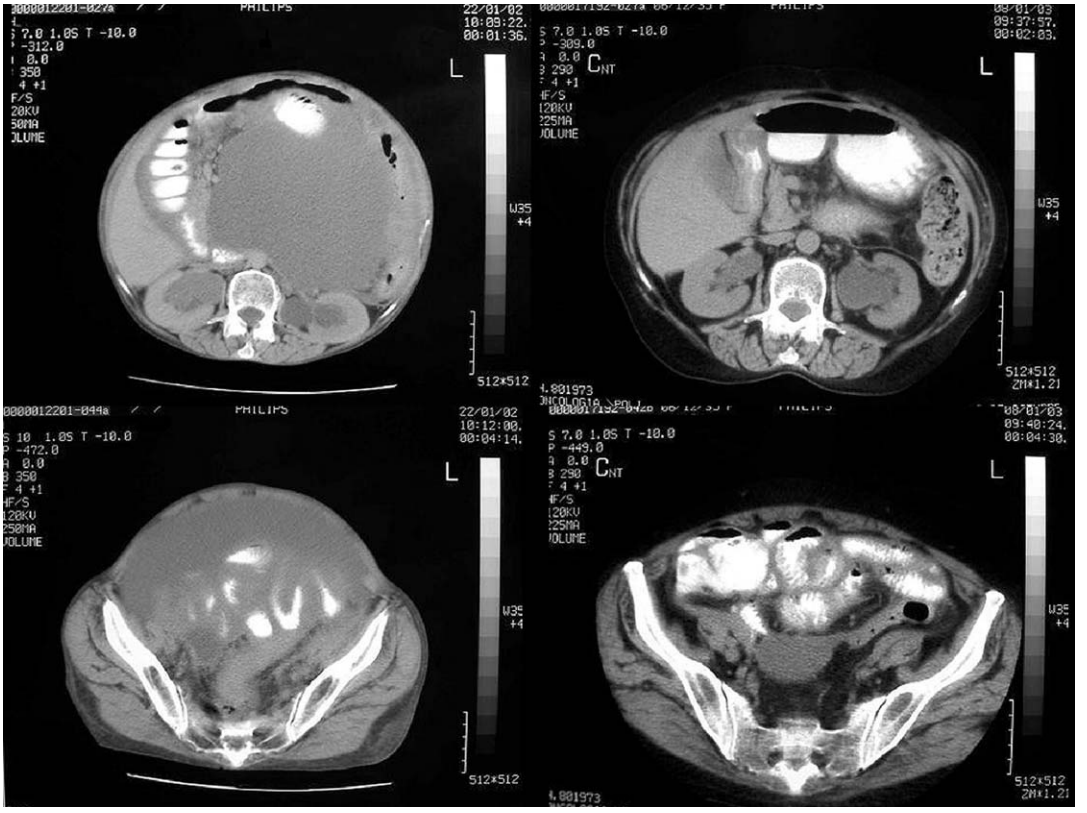
Fig. 1



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