

Giant hemangioma or metastatic disease of malignant gastrointestinal tumor? Diagnoses through 'new-line' therapy

D. Jost[†], C. Stroszczynski[†], G. Gaffke[†], P. Hohenberger[‡] and R. Felix[†]

[†]*Klinik und Poliklinik für Strahlenheilkunde, Universitätsklinikum Charite, Campus-Buch, Robert-Roessle-Klinik im Helios Klinikum, Berlin, Germany*

[‡]*Klinik für Chirurgie und Chirurgische Onkologie, Universitätsklinikum Charite, Campus-Buch, Robert-Roessle-Klinik im Helios Klinikum, Berlin, Germany*

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Abstract

Centripetal enhancement of liver lesions on MRI scanning is an almost specific finding in the diagnosis of benign hemangiomas. The ability of MRI to produce higher temporal resolution of dynamic measurements shows that malignant liver lesions can also demonstrate centripetal enhancement. We report here a case of a malignant gastrointestinal stromal tumor (GIST) with a huge hepatic metastatic lesion of undetermined origin. During therapy with Imatinib (Glivec[®], Novartis, Basel, Switzerland), a highly selective tyrosine kinase inhibitor, the lesion shrank markedly and exhibited changes in contrast enhancement.

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Keywords

GIST; liver; metastatic disease; hemangioma.

Introduction

Gastrointestinal stromal tumors (GIST) are rare, accounting for 1-3% of all neoplasias from the gastrointestinal tract. Primary tumors are most commonly located in the stomach (40-70%), followed by the small bowel, colon/rectum and oesophagus^[1]. The liver is involved in almost 50% of metastatic disease. In spite of the indolent nature of the tumor a high percentage of patients die from recurrent disease^[2]. The mutation of the KIT gene leads to an increased proliferation rate in GIST tumor cells^[3]. The detection of this pathological feature turned out to be an indication for treatment with Imatinib, one of the known targets of which is the receptor tyrosine kinase KIT.

Imatinib (Glivec[®], Novartis, Basel, Switzerland) is an effective drug for the treatment of chronic myeloid leukemia, and is also extremely active against GIST. Clinical studies for testing the effectiveness and dose-dependent activity in patients with advanced disease are in progress.

Case report

A 78-year-old female underwent surgery in 1994 because of an oesophageal mass detected on a routine chest X-ray. The diagnosis of a benign schwannoma was based on histological findings after resection, but the tumor was subsequently found to be a c-kit positive GIST. In July 1999 a local recurrence was found during a pre-operative examination before thyroidectomy for hyperthyroidism. Histological examination revealed a malignant GIST. A computed tomography scan (CT) showed an inoperable pleural metastasis in November 2000.

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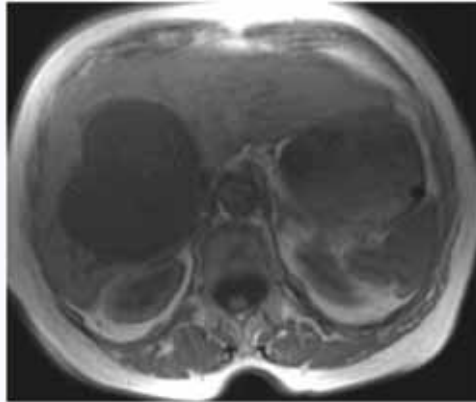


Fig. 1. T1-weighted plain transaxial image of a huge solitary hepatic lesion at the beginning of therapy with Imatinib.

In April 2001 the patient was referred to our hospital and agreed to participate in a phase III clinical trial under the guidance of the EORTC to evaluate the effective dose of Imatinib. Magnetic resonance imaging (MRI) was performed with the commonly available gradient echo (fl2d, TR/TE 105-165 ms/4.5-6.5, flip angle 70-75°, slice 5-10 mm) and turbo spin echo (tse, TR/TE 2200-5600 ms/90-120, slice 5-10 mm) sequences using a breath-holding technique (1.0 T Magnetom Expert; 1.5 T Magnetom Symphony, Siemens, Erlangen, Germany). Dynamic images were acquired for T1-weighted images after administering the paramagnetic contrast medium Magnevist® (Schering, Berlin, Germany) at a dose of 1 mmol/kg/BW, 3 cc per second after 30, 60 and 90 s. The follow-up interval was 2 months.

The abdominal MRI findings demonstrated inconspicuous bowel structures. A huge solitary lesion of 9 × 9 × 6 cm was detected in liver segments 7 and 8. The lesion was oval in shape, sharply delineated, hypointense in T1 (Fig. 1) and hyperintense in T2 with small low-intensity areas in the central portion. Dynamic measurements showed strong

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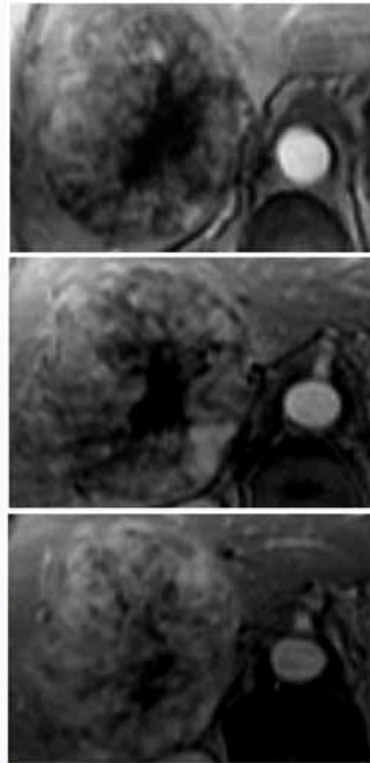


Fig. 2. Dynamic gadolinium enhancement of the solitary lesion demonstrated a centripetal character after 30, 60 and 90 s.

contrast enhancement in the early phase at the rim with centripetal wash-in to persistent enhancement in the late phase (Fig. 2).

Based on the findings, it was not clear whether we were dealing with a metastasis of a GIST or a benign hemangioma. At follow-up, the lesion was slightly reduced in size within the first 4 months of commencement of therapy with Imatinib. There was no convincing change in the pattern of contrast. After 6 months of continuous therapy, there was a marked reduction in tumor size to $5 \times 4 \times 4$ cm together with a change in the pattern of contrast enhancement (Fig. 3). Ninety seconds after contrast injection, the lesion showed a solitary, nodular enhancement in the lower middle portion progressing in the delayed phase (Fig. 3). The hyperintense areas seen in previous T2 images were increased. Because of the reduction in size and decrease in contrast enhancement, together with an increasing signal in T2, we decided that this lesion must have been a GIST metastasis and not a huge benign hemangioma.

Discussion

The development of different MRI sequences, and especially the higher temporal resolution obtained with dynamic images, improves the likelihood of differentiating between focal liver lesions, for example metastases from gastrointestinal tumors and benign lesions such as focal nodular hyperplasia or hemangiomata^[4]. False diagnoses of hemangiomas are uncommon; when this happens they are usually mistaken for metastatic lesions of endocrine tumors^[5].

Hemangioma is the most common benign liver tumor. Most are asymptomatic and are detected incidentally^[6]. These tumors show low intensity in plain T1 MRI, whereas heavily T2-weighted images enhance the ability to differentiate hemangiomas from malignant tumors because of the demonstration of low-intensity areas which are usually associated with fibrosis^[7]. In this case, small low-intensity bands were detected in T2. Transaxial T1 images showed a sharply delineated low-intensity lesion. A peripheral nodular enhancement in the arterial phase with a persistent low intensity centrally is considered to be a specific sign for cavernous hemangioma, whereas smaller hemangiomas present with uniform enhancement progressing centripetally^[5].

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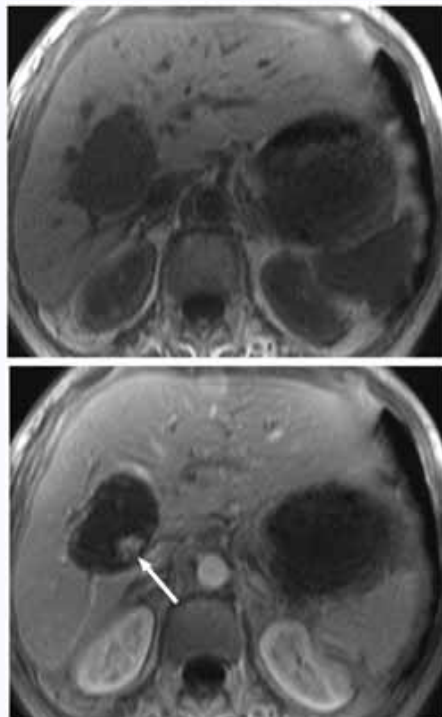


Fig. 3. After 6 months' therapy, Imatinib leads to a reduction in size and reduced tissue enhancement with residual gadolinium flow in the lower middle portion (arrow) after 90 s.

The lesion detected in the liver of the patient showed this enhancement behaviour. Sharp delineation is in keeping with the diagnosis of a benign hemangioma. Needle biopsy of hemangiomas, however, is associated with a high risk of hemorrhage. The patient's consent

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for biopsy could not be obtained during the first 4 months of treatment. After 6 months we decided that the lesion must be a metastasis because of the correlation of decreased size in both manifestations and a biopsy was therefore now unnecessary.

Differentiation between a benign lesion and a malignant metastasis was not a predominantly important problem for staging in this case because of the appearance of the pleural mass. However, in other cases, the detection of liver metastases of GIST is classified as end-stage disease^[2]. To our knowledge, the radiological features of MRI scanning of metastatic GIST tumors have not been widely described in the literature. GIST liver metastases are characterised as round or oval, solitary and sharply delineated lesions with centripetal 'hemangioma-like' enhancement on CT, often resembling the lesions of lymphoma or carcinoid tumors^[8,9]. Our findings in 35 patients with advanced GIST concur with this description. Thus, the intermediate low-intensity character in T1 and the high intensity in T2 are also in common with the diagnosis of hepatic metastatic GIST disease as well as the sharp delineation of the lesion. Chen *et al.* and Johensuu showed that therapy with Imatinib leads to a characteristic progredient cyst-like appearance and reduction in lesion size at CT^[10,11]. The case presented here demonstrated diagnostic difficulties due to the lack of any large necrotic or cystic areas at the first examination despite the size of the detected lesion and our experience with other cases of malignant GIST. Once therapy commenced the lesion changed its appearance to become much more like a typical GIST metastasis undergoing therapy. The finding of highest enhancement at the 90 s interval is also diagnostic of a GIST metastasis; hemangiomas demonstrate the highest CM wash-in at the arterial phase.

Under the influence of 6 months' treatment with Imatinib, the lesion finally responded to treatment, both in size and in contrast-enhanced MRI appearance.

This case demonstrates the current problems in the characterisation of focal liver lesions, where a specific MR finding could lead to a false diagnosis or to inaccurate staging.

Conclusion

The differential diagnosis of liver lesions remains a problem. This case demonstrates that specific MRI findings formerly thought to be diagnostic may actually be misleading

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and that such an error can lead to inaccurate tumor staging and subsequent therapeutic mismanagement.

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