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LETTER TO EDITOR

CT Scan is not Everything in the Evaluation of a Patient with Gastrointestinal Tumors (GIST) Under Imatinib Therapy

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To the Editor: A number of clinical studies have shown dramatic clinical and radiographic responses to imatinib mesylate in patients with gastrointestinal stromal tumors (GISTs). The degree and pattern of enhancement observed on CT scans are useful for differentiating malignant from benign tumors and identifying posttreatment changes. In contrast to minor tumour shrinkage visualized by imaging modalities, histological examinations demonstrate obviously dormant or apoptotic-like tumour cells embedded in hyaline-degenerated tissue [1].Here we report a patient who received resection after imatinib therapy, in whom the tumor response evaluated through CT scans was in contradiction of the findings of histopathological examination.

In December 2004, a 41-year-old male was referred to our hospital with presence of a submucosal tumor of the stomach by Upper gastrointestinal endoscopy. He underwent a partial proximal gastrectomy combined with a distal pancreaticosplenectomy and partial epinephroectomy, and the tumor was radically resected. The tumor was diagnosed as GIST for been composed of affluent spindle cells (Fig. 1), and positive staining for CD117 and CD34.

The adjuvant treatment with imatinib for 400 mg per day was started one month after the operation. The patient responded to the imatinib therapy well, and there was no tumors recurred through CT scan during the treatment. Ten months later, the administration was discontinued because of economic aspects, possibly due to moderate adverse effects of the imatinib. The patient was followed up through CT scan in outpatient department every three months. In February 2008, a new nodule located between the residual stomach and liver, adhering to the inferior caval vein,about 10 cm in diameter, was detected by CT scan (Fig. 2). We thus restarted the administration of imatinib at that time. Six months after restarting the imatinib treatment, an abdominal CT depicted a smaller nodule with 6 cm in diameter in the same place (Fig. 3), with the same tumor density and tumor vessels as before. Since the recurrent tumor was limited, the patient underwent complete surgical resection in August 2008. Histologically, the GIST cells disappeared in the samples from the second resection, instead of much collagen with hyaline degeneration, among them exist a few small vessles (Fig. 4), thus the recurrent tumor under imatinib therapy was diagnosed as abdominal cavity reactiveness fibropseudoneoplasm. The immunohistochemical examinations revealed the tumor to show negative staining for CD117,CD34. After this operation, the imatinib treatment was discontinued, and the patient was closely followed up by CT scan every six months and there has been no recurrence (for the 16 months, cross out) until now since the second operation.

Imatinib mesylate is a small molecule, which selectively inhibits the enzymatic activity of several tyrosine kinases, and provides a clinical benefit in about 85% of patients with advanced GISTs [2], with 5% of those with a CR

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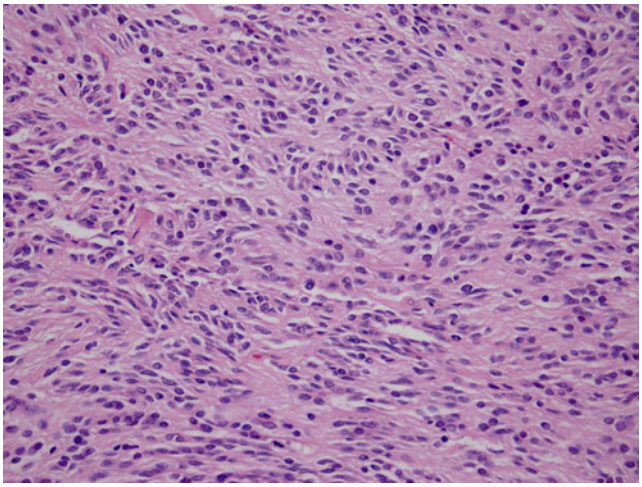

Fig. 1 The tumor cells from the samples of first operation in 2004 composed of affluent spindle cells

demonstrating a clinical response by CT scan [3]. RECIST criteria, a more than 30% decrease in the sum of the maximum diameters of all measurable lesions as partial response, is the current standard in assessing the response of solid tumors to anticancer therapy [4]. Choi and his colleagues found that the RECIST significantly underestimated tumor response to imatinib in patients with metastatic GISTs [5]. Thus, they established Choi response criteria, incorporating tumor density, enhancing intratumoral tumor nodules, and tumor vessels on contrast enhanced CT images, which are more sensitive and more precise than RECIST in assessing the response of GISTs to imatinib. CT assessment is a sensitive and specific method to assess the response of metastatic GISTs to imatinib if evaluated by Choi criteria [6].

In our patient, the recurrent tumor responded to the restart of imatinib therapy and its size decreased significantly, thus the findings at CT suggested that the patient obtained partial remission (PR),regardless evaluated by RECIST or Choi criteria. However, surgical pathology after

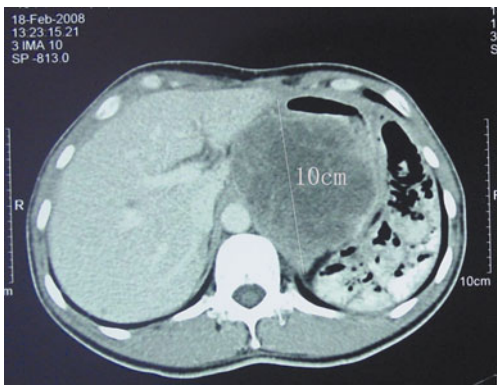

Fig. 2 The recurrent tumor detected before imatinib therapy by CT scan in February 2008, about 10×10×9 cm,which located between residual stomach and liver, adhering to the inferior caval vein

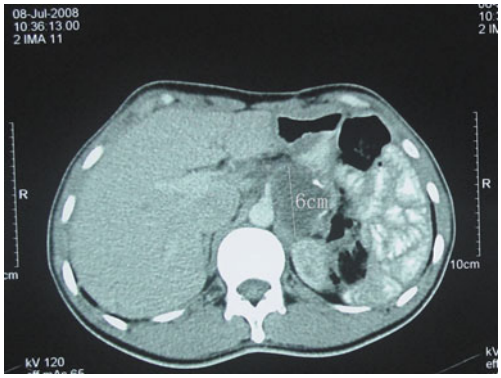

Fig. 3 After been treated by imatinib for about 6 months, the size of the tumor decrease significantly to 6×6×5 cm through CT scan

imatinib treatment is the gold standard reference for evaluation of tumor response. According to the pathologic results of specimen from the second operation, we evaluated the patient as complete remission (CR) after the imatinib therapy for period of six months, although the tumor was still detected by the imaging modality. In theory, although the mechanism of myxoid degeneration is not clearly understood, the reactiveness fibropseudoneoplasm could be secondary to tumor necrosis, hemorrhage, and cystic or myxoid degeneration [7], which may explain the different evaluation of imatinib response between CT scan and pathologic examination. One of the limitations of our study was that the patient had not received PET-CT scan before the second operation, through which we may detect the patient achieved CR.Neverthless, the technical limitations of CT scan were encountered with PET.PET is a sensitive and specific method with which to evaluate tumor

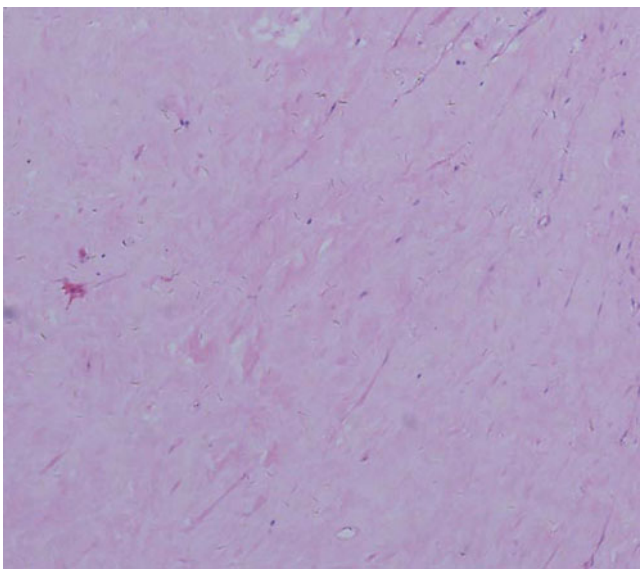

Fig. 4 The GIST cells disappeared completely in the the specimen from the second operation in 2008, instead of much collagen with hyaline degeneration, among the exist a few small vessles

response on the basis of changes in tumor metabolism [8]. Unfortunately the availability and the cost of PET/CT imaging still limits the use of this technique in many countries, therefore it can serve mainly as a reference in clinical trials to compare the results obtained with CT scan. The finding of this study doubted the mainstay of CT scan in the evaluation of imatinib response, and we suggested that CT scan may not be reliable in monitoring the effect of target therapy in some special GIST cases. During the practice of targeted therapy it is of utmost importance to get histological information from masses described as recurrences on morphologic imaging in order to avoid unnecessary treatments or to be able to select more appropriate drugs for further treatments.

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