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SHORT COMMUNICATION

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Lack of efficacy of imatinib in a patient with metastatic Leydig cell tumor

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Abstract Imatinib is a tyrosine kinase inhibitor with activity in gastrointestinal stromal tumor and a variety of other solid and hematological malignancies. Studies in vitro and in a mouse model suggested that the imatinib might also be active in malignant Leydig cell tumor. We report on the—to our knowledge—first treatment experiment with imatinib in a patient with metastatic Leydig cell tumor. Unfortunately, the tumor progressed during treatment.

Keywords Imatinib · Leydig cell tumor · Testicular cancer · Metastases · Positron emission tomography

Introduction

Metastatic Leydig cell tumor is an exceedingly rare testicular neoplasm. It is considered to be largely resistant to cytotoxic chemotherapy and radiotherapy. Recent studies in vitro and in a mouse model suggested a possible activity of imatinib (Gleevec®, Novartis, Switzerland) in this neoplasm [1].

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Case report

A 75-year-old man presented with a right-sided testicular tumor with retroperitoneal and left-sided supraclavicular lymphadenopathy. The tumor markers α-fetoprotein and β-chorionic gonadotropin were within normal range. Endocrinologic diagnostics revealed normal values for testosterone and estradiol and elevated values for luteinizing hormone and follicle stimulating hormone. Gynecomastia was absent. A computed tomography-guided biopsy of the retroperitoneal masses revealed a highly necrotic pleomorphic malignancy. Radical orchiectomy was performed. Photomicrographs of the tumor are shown in Fig. 1. The eosinophilic tumor cells were pleomorphic, showed infiltrative growth and a high number of mitoses. Positive immunohistochemical staining for inhibin (Fig. 1b), CD117 (Fig. 1c), melan A (Fig. 1d), vimentin, and focally for cytokeratin was observed, whereas antibodies against placental alkaline phosphatase, α-fetoprotein (Fig. 1e) and β-chorionic gonadotropin (Fig. 1f) displayed no positive reaction. Considering these findings, the tumor was classified as malignant Leydig cell tumor. An ^{18}F-deoxyglucose positron emission tomography (PET) scan revealed pathologic metabolic activity in the abdominal and left-sided supraclavicular metastatic lesions (Fig. 2a). After discussing the treatment options with the patient and obtaining informed consent, imatinib monotherapy (400 mg daily) was given. The medication was well tolerated. A follow-up PET scan 1 month later demonstrated slightly progressive disease with beginning bilateral ureteral obstruction (Fig. 2b). After another month of treatment, a PET scan disclosed further progression of disease (Fig. 2c), 2 weeks later confirmed by abdominal CT scan. The imatinib treatment was discontinued.

Discussion

Imatinib is a selective inhibitor of c-kit and platelet-derived growth factor (PDGF) tyrosine kinases with

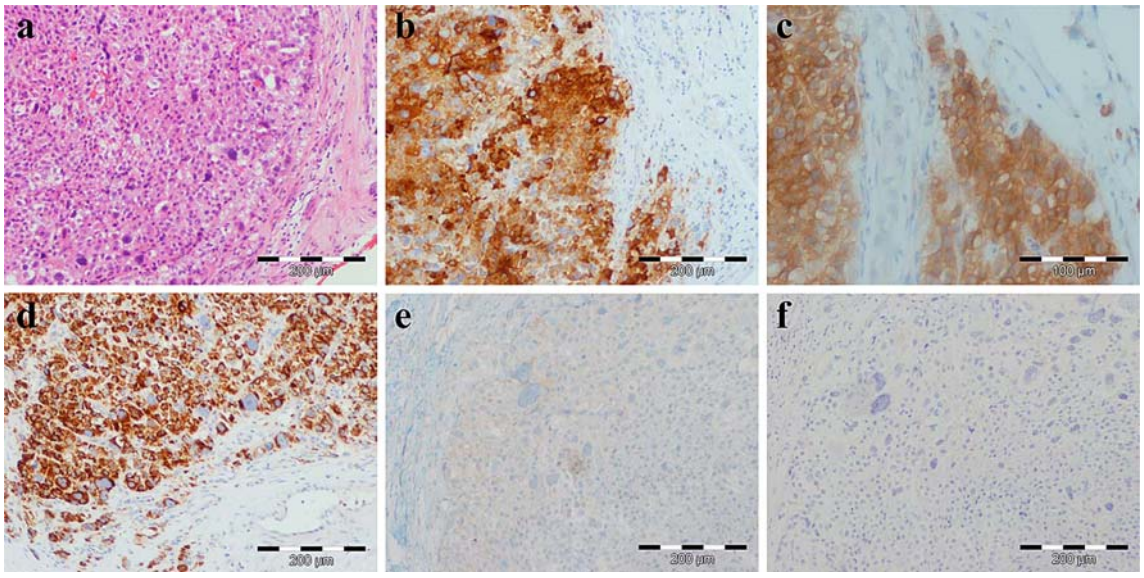

Fig. 1 Photomicrographs of sheets of eosinophilic, pleomorphic tumor cells (**a** H&E), immunohistochemical reaction (brown reaction product) for inhibin (**b**), CD117 (**c**), melan A (**d**), and negative immunoreactivity for α-fetoprotein (**e**) and β-chorionic gonadotropin (**f**)

activity in gastrointestinal stromal tumor and a variety of other solid and hematological malignancies with a favorable side effect profile [1, 3, 4]. Since Leydig cell tumors express PDGF, kit ligand and their receptors, PDGF receptor and c-kit (CD117, Fig. 1c), Brasciani and coworkers investigated the activity of imatinib in rodent Leydig tumor cell lines in vitro and in a mouse model [3]. Based on their promising experimental results, the authors hypothesized that the Leydig cell tumors might be a target for the imatinib treatment [3]. The current case is—to our knowledge—the first reported experience with imatinib treatment of human metastatic Leydig cell tumor. Unfortunately, the lack of response raises questions on the transferability of the cited in vitro and mouse model findings. A single case observation is, however, not sufficient to definitely discourage further studies involving imatinib in malignant Leydig cell tumors. Possibly, with higher doses or a combination with other antineoplastic agents should be considered.

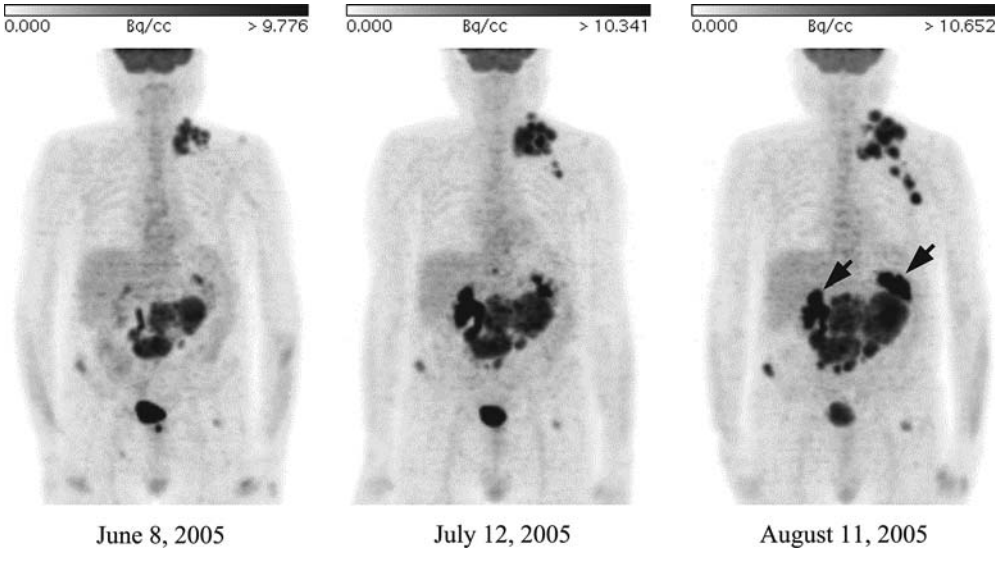

Fig. 2 Three consecutive ^{18}F-deoxyglucose positron emission tomography (PET) scans (maximum intensity projections) prior to (left), after 1 month (center) and after 2 months (right) of treatment with 400 mg imatinib daily demonstrating progressive disease and development of bilateral ureteral obstruction (*arrows*: tracer congestion in both upper urinary tracts). PET was chosen as response monitoring in the analogy to promising experiences reported with this imaging modality in the follow-up of gastrointestinal stromal tumors treated with imatinib [2]

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