Radiological changes of xp11.2 translocation renal cell carcinoma in response to sunitinib

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Introduction

Xp11.2 translocation renal cell carcinoma (RCC) is a recently recognized rare subtype of RCC[1], that typically affects children and adolescent patients where there is a high female predominance; few cases are reported in adults[2]. This subtype is characterized by various translocations involving chromosome Xp11.2, all resulting in gene fusions involving the transcription factor E3 (TFE3) gene[3].

Sunitinib malate is an oral multi-targeted receptor tyrosine kinase inhibitor that has anti-angiogenic and anti-tumor activities, and is indicated as a first-line therapy for patients with advanced and/or metastatic RCC[4, 5]. Sunitinib is generally well-tolerated by patients, but there have been occasional reports of hemorrhage associated with its use[6–8].

This case report describes the radiological changes associated with sunitinib treatment in a young female patient with Xp11.2 translocation RCC.

Case report

A 16-year-old woman presented in September 2010 with intermittent hematuria and a loin mass. A baseline CT scan showed a large partially cystic mass (17.4 cm) replacing the right kidney (Figure 1). Histological examination of the biopsy specimen showed that microscopically, the tumor was composed of nests of epitheliod cells with moderate eosinophilic cytoplasm, which was focally clear. The nuclei were round centrally and eccentrically located with prominent nucleoli. The stroma was fibrotic, with delicate vasculature. Immunohistochemistry showed the tumor cells to be positive for CD10 and RCC and there was focal staining for CK8/18. However, the tumor cells were negative for pan-keratin, vimentin and CK7. The findings are suggestive of Xp11.2 translocation RCC. The tumor was considered unresectable.

Treatment and clinical course

Treatment with sunitinib (50 mg/day, 4 weeks on/2 weeks off) was initiated in November 2010. During treatment, the patient developed persistent hematuria and her hemoglobin level fell dramatically (Figure 2). As a result of this, the patient received repeated blood transfusions.

In January 2011, a CT scan showed a minimal increase in tumor size. However, the tumor and lymph nodes had undergone significant cystic change towards a more fluid density (Figure 3a and b).

In February 2011, the patient decided to stop sunitinib treatment against medical advice. Hematuria ceased and hemoglobin levels recovered (Figure 2). In March 2011, and while the patient was off therapy, a CT scan was performed. Previously identified cystic changes had reversed, with a significant solid component observed peripherally. The mesenteric nodes also appeared more solid (Figure 4a) and MRI revealed blood products in the cystic component consistent with hemorrhage (Figure 4b).

Discussion

Advances in available therapeutic options have revolutionized treatment for metastatic RCC tumors[9] but most clinical trials have focused on clear cell RCC. Xp11.2 translocation RCC is a recently recognized distinct subtype often found in children. Additionally, there are several reports of adults with Xp11.2 translocation RCC having an aggressive clinical course[10, 11]. Whilst sunitinib is recommended as first-line therapy for patients with advanced or metastatic RCC[4], there are no established effective therapies for the Xp11.2 translocation RCC subtype. However, there are several single case reports of a response to sunitinib in patients with Xp11.2 translocation RCC in the literature[12–14].

In this communication, we describe a case of Xp11.2 translocation RCC in a 16-year-old female. Histological diagnosis was made on microscopic appearance and immunohistochemical staining. Negative staining for pan-keratin and vimentin supported the histological diagnosis of Xp11.2, rather than classic clear cell carcinoma. Young age of presentation was also a supportive factor for this diagnosis. Confirmation of diagnosis of Xp11.2 RCC requires staining for TFE3 protein or gene fusion study. However, these tests were not available at our center.

Radiological or clinical reduction in tumor size is the standard criterion of response

to cytotoxic chemotherapy. It is possible that response to targeted therapies such as sunitinib may be associated with different radiological changes. In our case, the tumor did not decrease in size, but underwent cystic changes during treatment with sunitinib. This has been interpreted as evidence of radiological response to sunitinib. Cessation of therapy led to a return of the enhancing component of the tumor and lymph nodes, giving a more solid appearance, which is likely to represent disease progression. Sunitinib is associated with hemorrhage in a few cases[6–8] and in this patient, MRI revealed blood products in the cystic component. This was associated with persistent hematuria and anemia and may be consistent with sunitinib-induced hemorrhage.

The observations in this case report suggest that this sub-type of RCC may respond to sunitinib as detailed in the literature. However, cystic changes to tumors may occur in response to sunitinib treatment and the tumor response may not necessarily meet standard Response Evaluation Criteria in Solid Tumors (RECIST) criteria; the tumor may even show a slight increase in size accompanied by a decrease in density (measured in Hounsfield Units [HU]). Subsequent changes where the tumor becomes more solid and HU values rise, for example following cessation of therapy, may be associated with, or indicate disease progression.

Our observations are consistent with the report of Smith et al who concluded that use of tumor size and attenuation on contrast-enhanced CT scan improves response assessment in patients treated with anti-angiogenic agents[15]; they showed that decreased attenuation (≥40 HU) was associated with longer progression-free survival. In a subsequent report, they showed that the combination of mass, attenuation, size and structure provided a more accurate assessment of response to targeted therapy than RECIST or modified Choi criteria[16].

Conclusions

Sunitinib treatment of xp11.2 translocation RCC is associated with radiological cystic changes. These changes probably indicate response to sunitinib treament.

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Figures

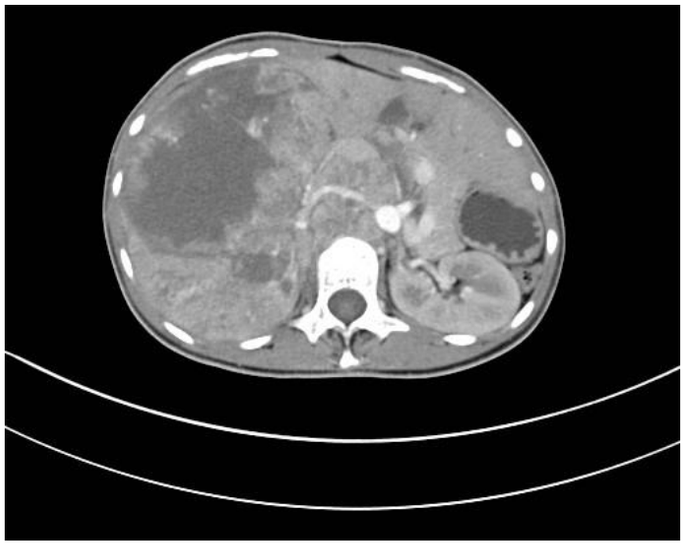


Fig1: Baseline CT scan showing large partially cystic mass replacing right kidney

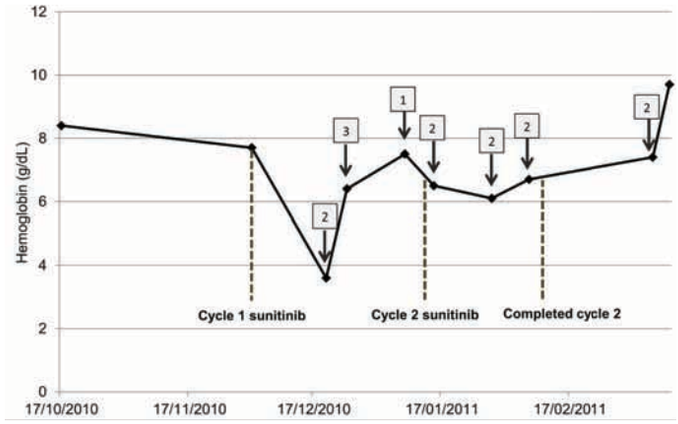
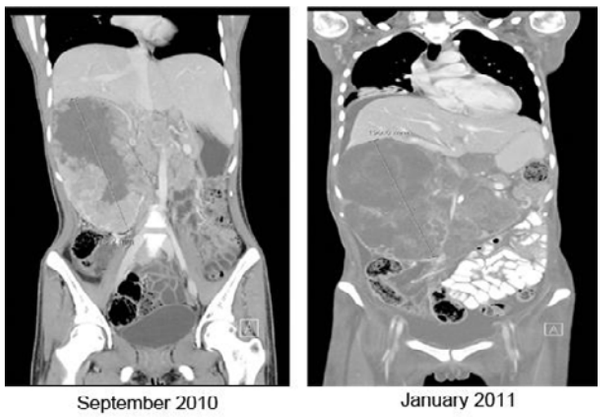


Fig2: Hemoglobin levels before, during and after sunitinib treatment. Arrowed numbers represent units of blood transfused.

(a)



(b)

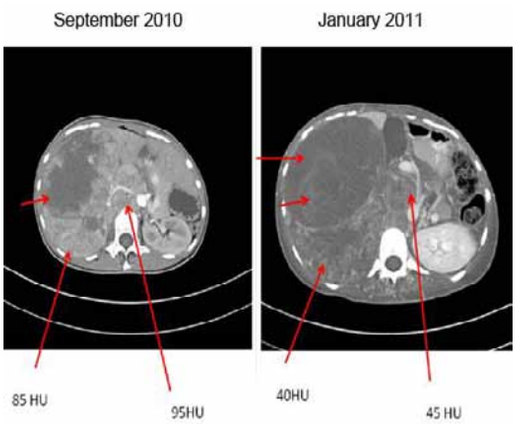
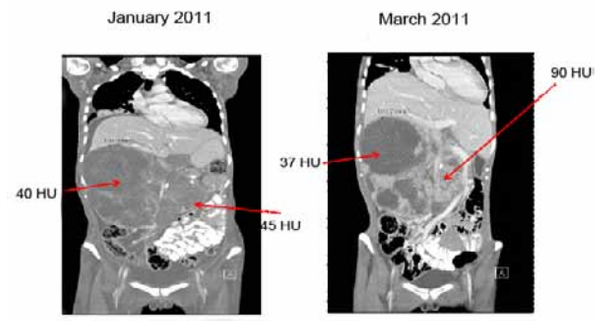


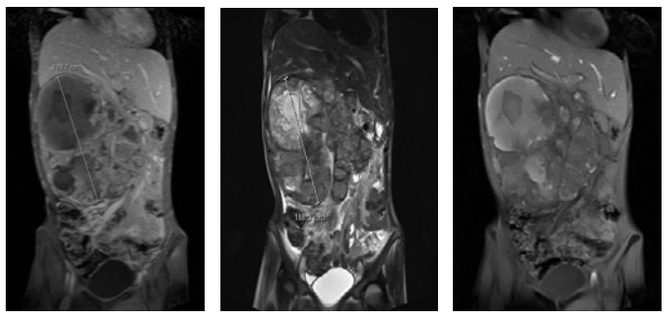
Fig3: (a and b) CT scan at baseline and after 2 cycles of sunitinib showing change to more cystic components (fluid density=0 HU; lower density=cystic component)

(a)



(b)

March 2011



MRI –T21 WI Post-gadolinium | MRI –T2 WI | MRI –T1 WI

Fig4: (a) CT scans showing progress of changes between January and March 2011, once therapy had ceased; (b) MRI scans in March 2011 after cessation of Sunitinib demonstrate central high signal on T2 weighted series likely representing cystic changes and peripheral high signal changes on T1 weighted series in keeping with recent haemorrhage.