Exceptional Case

Biopsy-proven acute interstitial nephritis associated with the tyrosine kinase inhibitor sunitinib: a class effect?

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Abstract
Since their introduction in 2006, the tyrosine kinase inhibitors (TKI) Sunitinib and Sorafenib have become the standard of care for many patients with renal cancer. They are generally well tolerated and have not been significantly implicated in renal toxicity. We report the first biopsy confirmed occurrence of acute interstitial nephritis in a patient receiving treatment with Sunitinib for metastatic renal cell cancer. However, two previous descriptions of interstitial nephritis related to treatment with TKIs, combined with this current report suggest that TKI therapy could be associated with this rare but life-threatening complication.

Keywords: acute interstitial nephritis; renal cell carcinoma; sunitinib; tyrosine kinase inhibitors

Discussion
TKIs are a relatively new class of anti-cancer drug. They rely on blocking signal transduction via various growth factor receptors, thereby interfering with biological outcomes.
as fundamental as cell division, growth and apoptosis. Such anti-proliferative actions have allowed TKIs to act as highly effective anti-cancer agents against a number of malignancies. Indeed Sunitinib, as a multi-tyrosine kinase receptor inhibitor, has found application in the treatment of gastrointestinal stromal tumours and advanced RCC. Interestingly, it is recognized that growth factors and their receptors play a fundamental role in the regeneration and repair of injured renal tubule cells [10] and it might be postulated that TKIs therefore interfere with this process.

Sunitinib shares a side-effect profile that is similar to that of other TKIs with gastrointestinal disturbance, skin toxicity and hypertension being the most frequent observations. Despite the lack of any apparent renal toxicity among the 375 patients receiving Sunitinib during the licensing trial [4], a small number of reports of ARF in the context of this novel class of medications have since been described [5–9]. A review of the literature revealed one case of AIN following administration of Sunitinib [9]. This was in a 69-year-old female with metastatic RCC who developed renal failure, proteinuria, eosinophiluria, and eosinophilia during her first cycle of Sunitinib, which worsened on continuation to a second cycle. Sorafenib was then trialled with a similar outcome. This patient did not have a renal biopsy. A second case is also recorded with the use of Sorafenib in a patient who had recently commenced treatment, after a previous prolonged course of Sunitinib. In this instance, AIN was demonstrated at renal biopsy [8]. Here, we report the first biopsy-proven case of AIN in a patient commencing TKI therapy with Sunitinib for advanced RCC.

AIN is a common cause of renal failure, seen in as many as 15% of renal biopsies performed as part of the work up for ARF. As in this case, there is often a non-specific prodromal phase that can progress to a more severe, generalized hypersensitivity reaction. Aetiological agents include drug-induced phenomena, infection-related processes and immune or neoplastic disease. Drug-induced AIN is by far the most common, accounting for more than 90% of cases with an increasing incidence recognized [1].

In summary, this is the first reported biopsy-proven case of interstitial nephritis shortly after starting Sunitinib. TKIs are proving to be powerful tools in the treatment of various cancers and their application to wider clinical scenarios is already under intense study. This report highlights a possible class adverse reaction profile with TKIs precipitating renal injury, in particular AIN. Supporting this hypothesis is the fact that certain growth factors targeted by these inhibitory drugs are seen to play a role in renal recovery following injury. Whether the acute renal injury described in patients taking TKI such as Sunitinib is precipitated or exacerbated by their inhibitory action on these growth factors remains to be seen. Nonetheless, we advocate appropriate renal surveillance in patients being considered for treatment with such drugs.
Conflict of interest statement. None declared.

References


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