time of nephrectomy for primary RCC is a well-known phenomenon [5]. However, recurrence of RCC in the left ventricle has rarely been reported in the medical literature, our case being the fourth case so far. Those cases including ours had very non-specific symptoms [6]. One earlier case had a presentation with angina with asynergy of left ventricular wall on echocardiography. Hence the high index of suspicion is required to diagnose this uncommon metastasis in the left ventricle. Seeding of the primary tumor is postulated to occur in two ways. Hemogenous spread via inferior vena cava would naturally involve the right side of the heart and lungs. The second mechanism is dissemination via the lymphatic system which would result in more wide-spread organ involvement [7]. The exact mechanism by which the tumor spread in our patient, as well as others reported to have solitary left ventricular involvement, is not entirely clear.

The accepted treatment method for cardiac malignant tumors is wide local excision with histological free margins. In our case this was not feasible for likely damage to the coronary artery and mitral valve apparatus as well as loss of significant myocardium not amenable to repair. Although cytotoxic chemotherapy has proven to be unresponsive in metastatic RCC, improved understanding of the biology of these tumors has provided newer targeted immunotherapy like tyrosine kinase inhibitors [8]. Such targeted immunotherapy may be an alternative management to surgery for unresectable tumors like our case.

References


eComment: Metastatic renal cell carcinoma to heart: cardiac surgery versus cardiotoxicity of kinase inhibitors

Authors: Ioanna Koniali, Department of Cardiotoracic Surgery, University of Patras, School of Medicine, 25500 Patras, Greece; Efstratios Apostolakis, Nikolaos G. Baktoukis
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Your case report concerning cardiac metastasis of renal cell carcinoma (RCC) is of great importance as it constitutes a rare complication with difficult treatment [1]. Indeed, metastatic RCC is highly resistant to cytotoxic agents, hormones, and radiotherapy. However, immunochemotherapy, anti-angiogenesis agents, and molecular targeting have been investigated as alternative treatment in order to improve the outcome in advanced RCC. Specifically, chemotherapy with kinase inhibitors (KIs) provide targeted therapy inhibiting the causal or contributory kinases driving tumor progression, while leaving the function of other kinases intact. This class of therapeutics has had some remarkable successes, as sunitinib and sorafenib have significantly contributed to the management of renal cell carcinoma.

Unfortunately, cardiotoxicity, often manifest as left ventricular dysfunction and/or heart failure, has ensued after the use of KIs in patients. Several mechanisms leading to cardiotoxicity have been proposed. Sunitinib, which was initially developed primarily to inhibit vascular endothelial growth factor receptors (VEGFRs) 1–3, platelet-derived growth factor receptors (PDGFRs) α/β, and c-Kit, has been predicted to inhibit at least 50 kinases [2]. In cultured cardiomyocytes, sunitinib induced loss of mitochondrial membrane potential and energy rundown [3]. Typically, when energy stores drop in the cardiomyocyte, a kinase called AMP-activated protein kinase (AMPK) is activated, leading to increased energy generation and decreased energy utilization. However, AMPK was not activated in the energy-stressed cardiomyocytes. In fact, AMPK activity was reduced in hearts of sunitinib-treated mice and cardiomyocytes in culture, and this was due to potent and direct inhibition of AMPK by sunitinib [2, 3].

Secondly, studies in mouse models have suggested that angiogenesis is key to maintaining cardiac homeostasis in response to pressure overload, which, taken together with the significant hypertension induced by VEGFR inhibitors, might explain, in part, the LV dysfunction seen with sunitinib [4]. More recently, PDGFRα, another target of sunitinib, was also found to be critical for angiogenesis, and deletion of the gene in mice led to heart failure when the mice were exposed to high-pressure loads [5]. Finally, it remains unclear whether LV dysfunction with KIs is attributable to myocyte loss (and therefore largely irreversible) or myocyte dysfunction (potentially reversible). Despite these promising chemotherapeutic approaches, the treatment of metastatic RCC remains ineffective. Surgical resection plays a major role in the palliation of isolated metastatic disease as in your case. While combination therapy that includes surgery and chemotherapy may constitute the best chance of palliation or even cure of this perplexing complication.

References


