Aortic dissection during antiangiogenic therapy with sunitinib. A case report
Dissecção de aorta em terapia anti-angiogênica com sunitinibe. Um relato de caso

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ABSTRACT
CONTEXT: Sunitinib is an antiangiogenic drug that has been approved for treating metastatic renal cancer. Its action as a tyrosine kinase inhibitor of vascular endothelial growth factor receptors (VEGFRs) and other angiogenesis receptors may lead to adverse effects such as hypertension and heart failure. However, reports in the literature on an association between sunitinib therapy and acute aortic dissection are rare.

CASE REPORT: We report the case of a 68-year-old man with metastatic renal carcinoma who developed acute aortic dissection during sunitinib therapy. He had no history of hypertension or any other risk factor for aortic dissection. After aortic dissection had been diagnosed, sunitinib was withdrawn and an aortic endoprosthesis was placed. Afterwards, the patient was treated clinically with antihypertensive drugs and new therapy for renal cancer consisting of temsirolimus, an inhibitor of the mammalian target of rapamycin (mTOR) pathway.

CONCLUSION: Hypertension is a common event when antiangiogenic drugs are used in oncology. However, knowledge of other severe cardiovascular events that may occur in these patients, such as acute aortic dissection, is important. Adequate control over arterial pressure and frequent monitoring of patients during the first days of antiangiogenic therapy is essential for early diagnosis of possible adverse events.


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INTRODUCTION

Sunitinib is a tyrosine kinase inhibitor that targets several vascular endothelial growth factor and platelet-derived growth factor receptors. It is indicated as first-line therapy in metastatic renal cell carcinoma, at a dose of 50 mg given orally once daily for four weeks, in a six-week treatment cycle. The most common adverse effects are fatigue, diarrhea, hand-foot syndrome, skin discoloration and hematological alterations (leukopenia, anemia and thrombocytopenia). The cardiovascular effects observed in these patients are hypertension (all grades 15% to 34%; grade 3: 4% to 13%), peripheral edema (24%), decline in ejection fraction (11% to 16%; grades 3/4: 1% to 3%), heart failure (≤15%) and chest pain (13%). Aortic dissection associated with sunitinib therapy is a rare adverse effect (<1%). Hypertension is the main predisposing factor for aortic dissection but, in the medical literature, there is only one case of aortic dissection relating to sunitinib (Table 1). Here, we discuss the case of a 68-year-old patient with metastatic renal cell cancer who presented aortic dissection without preexisting hypertension, during sunitinib therapy at the usual doses.

CASE REPORT

Our patient was a 68-year-old man with a history of smoking (58 pack-years), who had undergone partial left nephrectomy in January 2006. Anatomopathological analysis showed a 25 mm clear cell carcinoma, of Fuhrman grade 2 and clinical stage T1N0M0. He was followed up with serial imaging studies.

In November 2009, bilateral renal and adrenal nodules were found on computed tomography scans. A biopsy was performed on the adrenal lesion. The result was consistent with metastatic clear cell carcinoma. His Memorial Sloan-Kettering Cancer Center score was low risk (Karnofsky performance score of 90%, with normal values for corrected serum calcium, lactate dehydrogenase and hemoglobin, and metastatic recurrence more than one year after the nephrectomy).

In April 2010, after clinical evaluation showing normal blood pressure levels, he was started on target therapy with sunitinib, at a daily dose of 50 mg (four weeks on and two weeks off). After the first cycle, his clinically evaluated blood pressure was normal. He began the second cycle and 20 days later, when he sought the emergency room with chest pain, his blood pressure was 210 mmHg x 120 mmHg. Electrocardiography did not show ischemic signals but the chest X-ray showed an enlarged mediastinum (Figure 1) and chest CT-angiography revealed Stanford type B aortic dissection from the aortic arch to the abdominal aorta (Figure 2). He received intravenous β-blocker (metoprolol) and sodium nitroprusside, and then the blood pressure dropped to 160 mmHg x 110 mmHg.

The patient was referred to a cardiovascular hospital, and an endoprosthesis was placed. He recovered well and started new therapy with temsirolimus, 25 mg weekly. His hypertension was managed using oral antihypertensives. After 10 weeks of therapy, the

### Table 1. Search strategies used and results from each database

<table>
<thead>
<tr>
<th>Database</th>
<th>Keywords</th>
<th>Results</th>
<th>Relevant findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medline (via PubMed)</td>
<td>(sunitinib) AND (hypertension)</td>
<td>218</td>
<td>Main effects reported are hypertension and left ventricular ejection fraction dysfunction</td>
</tr>
<tr>
<td></td>
<td>(renal cancer) AND (acute aortic dissection)</td>
<td>6</td>
<td>One report of sorafenib associated with acute aortic dissection</td>
</tr>
<tr>
<td></td>
<td>(antiangiogenic) AND (aortic dissection)</td>
<td>7</td>
<td>One report of acute aortic dissection during sunitinib therapy and another report relating to bevacizumab therapy</td>
</tr>
<tr>
<td>Lilacs (via Bireme)</td>
<td>(anti-angiogenic) AND (aortic dissection)</td>
<td>1</td>
<td>One report of acute aortic dissection in a hypertensive patient with prostate cancer treated with bevacizumab</td>
</tr>
<tr>
<td>Embase (via OVID)</td>
<td>(sunitinib) AND (aortic dissection)</td>
<td>8</td>
<td>Only one case of aortic dissection in a patient with metastatic renal carcinoma and preexisting hypertension as a predisposing factor</td>
</tr>
</tbody>
</table>

CONCLUSION
This report emphasizes the need for strict blood pressure control among patients taking antiangiogenic drugs. Blood pressure evaluations should be scheduled more frequently, especially at the beginning of the treatment, so as to enable early recognition and manage hypertension or other side effects.

REFERENCES

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