**Case Report**

**Multifocal Arterial Thrombosis during Thalidomide Therapy: Case Report and Review of the Literature**

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1. **Introduction**

The antiangiogenic properties of thalidomide have brought to its use in the treatment of multiple myeloma (MM) and other neoplastic disease. However, thalidomide has been associated with venous thrombotic events and, more rarely, with arterial thrombosis.

We report a case of multiple arterial thrombosis in a MM patient treated with thalidomide.

2. **Case Presentation**

A 66-years old man had a one-year history of MM treated with chemotherapy and stem cell transplantation followed by a thalidomide plus prednisone regimen (thalidomide 100 mg/day and prednisone 12.5 mg/day). No prophylactic antithrombotic therapy was initiated. After two months of thalidomide plus prednisone therapy, he was admitted to our hospital with acute right arm ischemia, which was emergently treated with thrombectomy of the right brachio-cephalic trunk. On postoperative day one the patient experienced left side weakness with right internal carotid thrombosis documented at duplex scanning and angiography study (Figures 1(a) and 1(b)). The CT scan at 48 hours after neurological symptoms, showed two acute cerebral infarctions in the frontal lobe with no haemorrhage. No cardiovascular risk or procoagulant risk factors were found, and the basic coagulation parameters were normal before surgery. Other embolic sources were excluded by ECG and transthoracic echocardiography.

Thalidomide treatment were the only risk factor associated with arterial thrombosis and therefore was immediately stopped. Enoxiparine (4000 IU twice a day) and acetyl-salicylic acid (ASA-100 mg/die), was administrated for five days, with subsequent administration of warfarin (INR range 2–2.5) and ASA 100 mg/day. With anticoagulation therapy the patient was free of further signs of new ischemic events.

After discharge was initiated a rehabilitative program, with complete regression of arm and leg weakness in 1 month.

3. **Discussion**

Thalidomide is one of the most used drugs in the treatment of newly diagnosed and relapsed/refractory MM and is currently used together with cytotoxic chemotherapy because of its antiangiogenic properties. Continuous low dose of thalidomide and low dose prednisone was part of maintenance program posttransplant [1–3]. The thalidomide's antiangiogenic mechanism is thought to involve blocking (vascular endothelial growth factor) VEGF and fibroblast growth factor activity, resulting in increased MM cell apoptosis [2]. Thalidomide is likely to determine a prothrombotic
Table 1: Arterial complication during Thalidomide administration for MM.

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Localization</th>
<th>Cytotoxic/corticosteroid therapy</th>
<th>TEE* prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowcock 2002 [6]</td>
<td>2</td>
<td>Cerebral</td>
<td>None</td>
<td>none</td>
</tr>
<tr>
<td>Scarpace 2005 [7]</td>
<td>4</td>
<td>Tibial-Cerebral</td>
<td>Cytotoxic and corticosteroid VAD’ protocol</td>
<td>none</td>
</tr>
<tr>
<td>Ortin 2006 [8]</td>
<td>1</td>
<td>Cerebral</td>
<td>Cytotoxic and corticosteroid</td>
<td>none</td>
</tr>
<tr>
<td>Altinas 2007 [10]</td>
<td>2</td>
<td>Femoral-Tibial</td>
<td>VAD’ protocol and corticosteroid</td>
<td>none</td>
</tr>
</tbody>
</table>

* TEE (thrombo-embolic events). VAD protocol (vincristine, adriamycin, dexamethasone)

The highest risk of thrombotic events with the thalidomide use is within the first months of induction therapy, particularly when thalidomide is concomitantly used with high dose cytotoxic agents. A prophylactic antithrombotic therapy by antiplatelet and anticoagulant drugs is mandatory in these cases, however no studies are available to confirm this assumption [13, 14].

4. Conclusion

Thalidomide is one of the most widely used drugs on the treatment of MM because of its antiangiogenic properties. Because of the rare but severe arterial complication, this side effect should be expected when the thalidomide therapy is administered, especially with concomitant cytotoxic chemotherapy or corticosteroid therapy. Until future studies on the mechanism of thalidomide are available, prophylactic therapy with ASA or anticoagulation during thalidomide administration is mandatory.

References


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