Abstract

A 71-year-old woman on warfarin (2.5 mg daily) developed severe low back pain with reduced touch sensation and weakness of the lower limbs that progressed to complete paralysis within 28 to 30 hours. Imaging revealed bleeding at the D4 through D11 level, however the patient refused emergency laminectomy. No recovery was observed and the patient was discharged to a rehabilitation facility. Only few other cases of hematomyelia linked to anticoagulant therapy have been reported. Early diagnosis, appropriate management and immediate intervention are needed to prevent irreversible neurological sequelae. The elusive clinical features at presentation may cause an important diagnostic delay.

Key words: hematomyelia, spinal hemorrhage, warfarin, anticoagulant therapy

Introduction

Hematomyelia is a rare cause of compression myelopathy that is even more rarely linked with the use of anticoagulants (1). The presentation includes non-specific complaints and subtle physical findings that may nevertheless rapidly progress to devastating and irreversible neurological injuries.

Case Report

A 71-year-old woman who had been on warfarin (2.5 mg daily) for more than two years presented with severe low back pain combined with reduced touch sensation and weakness of the lower limbs that progressed to complete paralysis within 28 to 30 hours. Her history included tuberculosis, hypertension, atrial fibrillation and the implantation of a pacemaker (PMK) two years earlier. There was no personal or family history of bleeding or neurological disorders. The patient was also taking metoprolol, flecainide and valsartan and did not report any recent head or back trauma. The arterial pressure was well controlled (130-140 and 80-85 for systolic and diastolic levels, respectively) and the international normalized ratio (INR) remained within the target therapeutic range (2.0-3.0) 67% of the time, above 3.0 for 17% of the time and below 2.0 for 16% of the time during the six previous months; it was 5.6 one week prior to presentation.

A physical examination showed complete paralysis, hypotonia and areflexia of the lower limbs with absent touch, pain and temperature sensation extending to the D4 through D11 segmental level; vibration and position sensation was also impaired. The patient underwent catheterization for urinary retention; her vital signs and the rest of the examination were normal. The INR was 3.16 and other laboratory results were normal. A contrast-enhanced computed tomography (CT) scan revealed signal hyperintensity and swelling of the spinal cord that were deemed to be consistent with bleeding at the D4 through D11 level (Figure). Performing magnetic resonance imaging (MRI) of the spine was precluded by the presence of the PMK.

The patient refused an emergency laminectomy. Therefore we discontinued the warfarin, and fresh frozen plasma and vitamin K were administered. Two weeks later, the results of a clinical examination were unchanged and a CT scan showed an angioma in the right side of the D4 body however no active bleeding into the spinal cord was observed. The patient was ultimately discharged to a rehabilitation facility.

Discussion

In the present patient, spontaneous hematomyelia occurred in the context of exaggerated anticoagulation (at presentation.

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INR was largely outside the therapeutic reference range and led to the development of a devastating compression myelopathy with irreversible paraplegia. This case demonstrates the importance of distinguishing hematomyelia among other more common causes of myelopathy during long-term anticoagulant therapy. The question of a potential role for an unrecognized angiodysplasia as an additional cause of hematomyelia in this patient remains unanswered as angiography and MRI were not performed. A follow-up contrast-enhanced CT scan revealed the presence of an angiomata consistent with active or recent bleeding from the vascular malformation that was not shown on imaging studies performed two weeks earlier however no direct or indirect stigmata consistent with active or recent bleeding from the vascular malformation were observed, which leaves us with exposure to warfarin as the only reasonable cause of the hematomyelia.

Hematomyelia refers to intramedullary bleeding into the spinal cord (1). It is more rare than epidural, subdural or subarachnoid spinal hemorrhages and can be associated with trauma, vascular malformations, tumors, syrinx, infection, radiation and coagulation disorders (1). Patients with hematomyelia classically present with the triad of excruciating local or radicular spinal pain, motor or sensory deficits progressing to complete paralysis over a few hours to days and urinary retention (1).

The diagnosis is often delayed, which contributes to the very poor outcomes observed in most cases. There are no clinical trials to guide the management of hematomyelia and treatment is usually directed toward managing the underlying cause. The initial evaluation requires spinal imaging and consultation with a neurosurgeon as nearly 100% of patients progress to irreversible neurological deficits if they are not urgently treated with immediate surgical decompression. Conservative management may be considered in those with incomplete spinal cord dysfunction and evidence of a neurological recovery occurring within 24 hours of bleeding. Our patient presented more than 24 hours after the onset of symptoms and exhibited extensive bleeding into the thoracic cord, two important clinical features that indicate a high probability of permanent neurological sequelae.

Anticoagulant therapy is a predictable cause of spinal hemorrhage (2). Compared with patients with intracranial hemorrhages due to anticoagulants, patients with spinal hemorrhages are younger, less frequently have hypertension, receive warfarin alone more frequently, more commonly have a therapeutic anticoagulation level and undergo surgical treatment more frequently (2). A meta-analysis of 613 cases of spinal hemorrhage published between 1826 and 1996 demonstrated that treatment with anticoagulants is the second most common cause of the disorder (3). An important point, however, is that exposure to anticoagulants does not by itself trigger the occurrence of a spinal hemorrhage, including hematomyelia, however a secondary event such as the presence of a “locus minoris resistentiae” combined with an increased vertebral venous pressure is required to cause spinal bleeding in the context of anticoagulant therapy irrespective of the achieved anticoagulation level.

Very few cases of atraumatic hematomyelia linked to oral anticoagulant therapy have been reported (4–14). Of note, the patient described by Suzuki and colleagues was receiving combined treatment with warfarin and aspirin (14), which greatly increases the risk of bleeding into the central nervous system including the development of spinal hemorrhage and hematomyelia. Bleeding into the thoracic cord occurred in most of the reported patients with anticoagulant-associated hematomyelia however, whether this finding represents a chance occurrence or rather points to an increased bleeding propensity into the thoracic, as compared to the cervical, cord is unclear (4–14).

A greater anticoagulation intensity is reasonably expected to confer an increased risk of hematomyelia. Our patient and most of the previously reported patients exhibited anticoagulation above the therapeutic reference range. However, anticoagulation was often evaluated using the prothrombin time rather than INR therefore making comparisons is difficult because the prothrombin time may vary greatly between laboratories.

All reported patients underwent surgical evacuation however only two of them experienced a significant improvement with mild residual weakness whereas the remaining patients exhibited no or minimal neurological improvements after surgery and two patients died of sepsis in the postsurgical period. No cases of hematomyelia have thus far been reported among users of the new direct thrombin or factor X inhibitors. We summarized the key clinical features of patients with warfarin-associated hematomyelia in Table. This case illustrates the challenges faced with anticoagulant treatment and underscores the need for a high index of suspicion and a vigorous search for uncommon bleeding sites. Hematomyelia is a rare cause of myelopathy that is likely to become much more common due to the increasing use of long-term potent anticoagulant therapies. Physicians
<table>
<thead>
<tr>
<th>Ref.</th>
<th>Patient Age, y/Sex</th>
<th>Indication for warfarin</th>
<th>Symptoms</th>
<th>Site</th>
<th>PT/INR</th>
<th>Surgery</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.</td>
<td>62,M</td>
<td>Left ventricle thrombus</td>
<td>Neck pain, Brown-Seqaud syndrome, quadriplegia, urinary retention,</td>
<td>Cervical (C3-C6)</td>
<td>INR 4.6</td>
<td>Yes</td>
<td>Mild improvement</td>
</tr>
<tr>
<td>5.</td>
<td>25,M</td>
<td>Prosthetic heart valve</td>
<td>Back pain, paraplegia, urinary retention</td>
<td>Thoracic (T2-T5)</td>
<td>11%</td>
<td>Yes</td>
<td>No improvement</td>
</tr>
<tr>
<td>6.</td>
<td>64,F</td>
<td>Deep vein thrombosis</td>
<td>Back pain, paraparesis, urinary retention</td>
<td>Thoracic (T1-T2)</td>
<td>0%</td>
<td>Yes</td>
<td>Minimal improvement</td>
</tr>
<tr>
<td>7.</td>
<td>59,M</td>
<td>Prosthetic heart valve</td>
<td>Lower limb pain, paraparesis, urinary retention</td>
<td>Thoracic (T12 and conus)</td>
<td>31%</td>
<td>Yes</td>
<td>Mild improvement</td>
</tr>
<tr>
<td>8.</td>
<td>60,M</td>
<td>Deep vein thrombosis</td>
<td>Back pain, paraparesis, urinary retention</td>
<td>Thoracic (T9-T10)</td>
<td>30%</td>
<td>Yes</td>
<td>No improvement</td>
</tr>
<tr>
<td>9.</td>
<td>68,F</td>
<td>Pulmonary embolism</td>
<td>Weakness of right leg, urinary retention</td>
<td>Thoracic (T4-T11)</td>
<td>18%</td>
<td>Yes</td>
<td>Mild improvement</td>
</tr>
<tr>
<td>12.</td>
<td>48,M</td>
<td>Prosthetic heart valve</td>
<td>Neck pain, quadriplegia, urinary retention</td>
<td>Cervical (C1-C7)</td>
<td>Thoracic (T1)</td>
<td>12%</td>
<td>Death for sepsis</td>
</tr>
<tr>
<td>13.</td>
<td>68,M</td>
<td>Atrial fibrillation</td>
<td>Quadriplegia, respiratory failure</td>
<td>Cervical (C1-C3)</td>
<td>INR 7.1</td>
<td>No</td>
<td>Death for pneumonia and fungemia</td>
</tr>
<tr>
<td>Present report</td>
<td>71,F</td>
<td>Atrial fibrillation</td>
<td>Back pain, paraplegia, urinary retention</td>
<td>Thoracic (T4-T11)</td>
<td>3.16</td>
<td>No</td>
<td>No improvement</td>
</tr>
</tbody>
</table>

M: male, F: female, PT: prothrombin time, INR: international normalized ratio

should be aware of the risk of hematomyelia in this setting with respect to providing an early diagnosis, appropriate management and immediate intervention in order to prevent irreversible neurological sequelae.

The authors state that they have no Conflict of Interest (COI).

References

13. Robbins M, Vergheze J. Acute painless progressive quadriplegia