Intracerebral hemorrhage is a well-known complication resulting from warfarin use; however, warfarin-associated intraspinal hematoma is very rare. Warfarin-associated intraspinal hematoma may exhibit delayed progression, and patients may present with atypical symptoms, occasionally resulting in delayed diagnosis. We report the case of a 65-year-old man who visited our emergency department (ED) with acute urinary retention. He had been previously diagnosed with non-valvular atrial fibrillation, arterial hypertension, and benign prostatic hyperplasia, and he used warfarin for the prevention of systemic embolism. The patient was initially diagnosed with worsening of the prostatic hyperplasia. After 2 days, he revisited the ED with painless paraparesis. Magnetic resonance imaging of the thoracic spine revealed an intraspinal hematoma at Th7–8, and blood coagulation tests indicated a prothrombin time-international normalized ratio of 3.33. Despite attempts to reverse the effects of warfarin with vitamin K administration, the paraparesis progressed to paraplegia, necessitating urgent surgical removal of the hematoma. Partial recovery of motor function was evident after surgery. From the present case, we learned that intraspinal hematoma should be included in the differential diagnosis of patients using warfarin who present with acute urinary retention. Although there are no evidence-based treatment guidelines for warfarin-associated intraspinal hematoma, surgical treatment may be warranted for those who exhibit neurological deterioration.

Keywords: atrial fibrillation, warfarin, intraspinal hematoma, diagnostic delay

Introduction

Warfarin is an oral anti-coagulant that is widely used for the prevention of systemic embolism, including stroke. Although intracerebral hemorrhage (ICH) is a well-known complication resulting from warfarin use, warfarin-associated intraspinal hematoma has rarely been reported in the literature.1 Warfarin-associated ICHs are infamous for their slow progression,2–4 and patients with warfarin-associated intraspinal hematoma may also present with atypical symptoms associated with delayed expansion of the bleeding, resulting in diagnostic delay.1 Herein, we report a case of warfarin-associated intraspinal hematoma in which the diagnosis was delayed because of comorbidity.

Case Report

A 65-year-old man with non-valvular atrial fibrillation (AF), arterial hypertension, and benign prostatic hyperplasia (BPH) visited our ED with acute urinary retention. His regular medication included warfarin (5.5 mg/day for more than 10 years) for AF, and imidafenacin for BPH. The patient had nocturnal polyuria because of BPH, but had not previously experienced acute urinary retention. He was examined by the urologist on call and underwent the insertion of an indwelling urinary catheter, from which more than 1000 mL of cloudy dark-colored urine

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with a pH of 6.5 was evacuated. After the procedure, the patient was discharged home without undergoing a thorough neurological examination. Two days after the first visit, the patient revisited the ED because of numbness and weakness of the lower extremities. A neurological examination revealed mild paraparesis rated as 3/5 on the manual muscle testing scale, diminished position and vibration sense below the umbilicus, and hyporeflexia of the knee and ankle joints. Blood coagulation tests revealed a prothrombin time-international normalized ratio (PT-INR) of 3.33. Brain computed tomography was performed to rule out warfarin-associated ICH and yielded negative results. However, magnetic resonance imaging (MRI) of the thoracic spine revealed an intra-medullary mass at Th7–8. The mass was isointense on T1-weighted images (A) and appeared as a mixed intensity lesion on T2-weighted images (B). Extensive perihematomal edema was also noted on T2-weighted images (B).

the administration of methylprednisolone (500 mg) to attenuate the spinal edema, the paraparesis progressed to paraplegia within 6 h of admission. Sensation to painful stimuli was partially diminished. The patient was taken to the operating theatre for the removal of the hematoma. PT-INR decreased to 1.35 immediately before surgery. After performing laminectomy at Th7–8 and subsequent midline myelotomy, the hematoma was identified and completely removed using an operative microscope (Fig. 2). Under microscopic assessment, vascular anomaly was considered unlikely as the source of bleeding. Because of the small amount of surgical specimen recovered, however, the results of pathological examination were inconclusive. The postoperative course was uneventful, and warfarin was replaced with dabigatran (150 mg bid), administration of which was started 7 days after surgery. The patient was transferred to a rehabilitation facility after 2 months. A follow-up MRI at 6 months showed resolution of the hematoma and edema and subsequent cavity formation, without apparent contrast enhancement (Fig. 3A-C). At 1 year, the patient was able to walk using four-footed canes, and urinary retention was managed by intermittent self-catheterization. Permission for the publication of this Case Report was granted by the patient.

Discussion

Until recently, warfarin was the only oral anti-coagulant approved for the prevention of systemic embolism in patients with AF. Despite its efficacy, warfarin has an inherent risk of bleeding, and ICH is one of the most feared complications resulting from warfarin use. In a recent study involving 404 cases of non-traumatic ICH, 69 (17%) were causally associated with warfarin administration.2 In contrast, warfarin-associated intraspinal hematoma is rare: to date, fewer than 20 cases have been reported in the literature.5–17 Because of its rarity, it is usually difficult to identify warfarin users who are at risk of intraspinal hematoma. Although advanced age and high PT-INR values (> 3.0) are known risk factors for warfarin-associated ICH,3 these factors may not necessarily be associated with intraspinal hematoma. As with warfarin-associated ICH, warfarin-associated intraspinal hematoma may progress slowly. Ideally, early detection and intervention, including the administration of vitamin K and fresh frozen plasma to reverse the effects of warfarin, may minimize the hematoma expansion and subsequent neurologic sequelae. In reality, however, diagnosis is often delayed, resulting in only limited neurological recovery.1 Typically, patients with warfarin-associated intraspinal hematoma present with the triad of back or neck pain, progressive para- or quadriplegia, and acute urinary retention.5 Diagnosis is more likely to be delayed in patients who do not present with back or neck pain.5 In the present case, pre-existing BPH was responsible for the diagnostic delay. The evolution of symptoms, i.e.,

Fig. 1 MRI of the thoracic spine showing an intra-medullary mass at the Th7–8 level. The mass was isointense on T1-weighted images (A) and appeared as a mixed intensity lesion on T2-weighted images (B). Extensive perihematomal edema was also noted on T2-weighted images (B).

Fig. 2 Operative photo showing evacuation of the intramedullary mass at Th7–8 using an operating microscope.

Fig. 3 Follow-up MRI images showing resolution of the hematoma and edema and subsequent cavity formation (A-C).
Fig. 2 Intraoperative photograph after Th7–8 laminectomy and midline myelotomy showing an intraspinal hemorrhage (asterisk).

Fig. 3 MRI images obtained 6 months after surgery. There was no apparent contrast enhancement on T1-weighted images (A, without contrast; B, with contrast). Shrinkage of the hematoma and cavity formation was seen on T2-weighted images (C).
acute urinary retention followed by numbness and paraparesis, suggested that the hematoma originated around the spinal canal, and that it gradually spread outward. Although there were no sequential imaging studies of the spinal cord to provide evidence for delayed growth of the hematoma, the presence of a mixed-intensity lesion on T2-weighted images (Fig. 1B) suggests heterogeneity of the composition and age of the hematoma.

From the present case, we learned that intraspinal hematoma must be included in the differential diagnosis of anti-coagulant users who visit the ED with acute urinary retention. Because of its rarity, there are no evidence-based guidelines for the treatment of warfarin-associated intraspinal hematoma. Conservative management may be justified in patients with mild symptoms without progression. However, surgical treatment may be warranted for those with neurological deterioration. In the present case, postoperative neurological improvement may have resulted from both neural decompression on hematoma removal and resolution of perihematoma edema. After the hemorrhagic event, warfarin was replaced with dabigatran, a novel oral anti-coagulant approved for use in Japan in 2011. Although hemorrhagic complications are less common in patients using dabigatran than in those using warfarin, there is a lack of data on the frequency of dabigatran-associated hemorrhage in patients who have already sustained warfarin-associated hemorrhage, and careful follow-up is warranted.

Regarding the cause of bleeding, we assumed that underlying arterial hypertension may have caused disruption of an arteriole within the spinal cord, and coagulation disturbances associated with warfarin administration may have prompted expansion of the hematoma. Intramedullary tumor is a possible cause of such bleeding; however, there was no contrast enhancement on postoperative MRI (Fig. 3A, B), and a high-grade malignancy such as glioblastoma was unlikely. However, periodical surveillance MRI is required to rule out the presence of low-grade malignancy such as cystic ependymoma.

Conflict of Interest

The authors declare that there is no conflict of interest regarding this manuscript.

References