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Case Report

Multiple non-contiguous anticoagulation-related spontaneous acute spinal intradural extramedullary hemorrhages

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ABSTRACT

Background: Spinal intradural extramedullary hemorrhage is a rare and important pathology that may precipitate acute compressive myelopathy. It is most commonly associated with spinal trauma, neoplasia, vasculopathy, and iatrogenesis. In rare circumstances, it occurs spontaneously secondary to anticoagulant and antiplatelet medications without an underlying structural lesion. In these instances, it may be related to vasculopathy and/or cardiovascular disease risk factors. We highlight the salient clinical and radiological features of this pathology, discuss putative mechanisms of its pathogenesis, and describe surgical considerations related to its management.

Case Description: This report describes an elderly gentleman who presented with two discrete spinal hemorrhages associated with separate foci of bleeding, in the context of therapeutic anticoagulation, on a background of significant structural and functional cardiovascular disease with risk factors.

Conclusion: Our report is novel in that there are no other cases, to the best of our knowledge, of multiple non-contiguous anticoagulation-related spontaneous acute spinal intradural extramedullary hemorrhages in the medical literature. This article is written with the purpose of assisting clinicians to recognize and expedite treatment of this rare pathology. Prompt diagnosis followed by urgent decompressive surgery provides the best functional outcomes.

Keywords: Anticoagulation, Extramedullary, Haemorrhage, Intradural, Spine

BACKGROUND

Spinal intradural extramedullary hemorrhage (SIEH) encompasses isolated and mixed, subarachnoid, and subdural bleeding of any cause.[8] The term intradural was coined due to difficulty identifying specific compartmentalization of spinal perileptomeningeal hemorrhage. This is because the subdural and subarachnoid compartments are less clearly radiologically differentiable in the spine as compared with the cranium.[3] Acute SIEH is an important cause of compressive myelopathy and radiculopathy, and manifests clinically as a combination of sudden onset back and/or radicular pain, disturbed sensorium, bowel and/or bladder dysfunction, and weakness.[8] The pattern of symptoms and signs observed is related to the spinal level of cord compressed and the extent and duration of compression. Cranial clinical features of

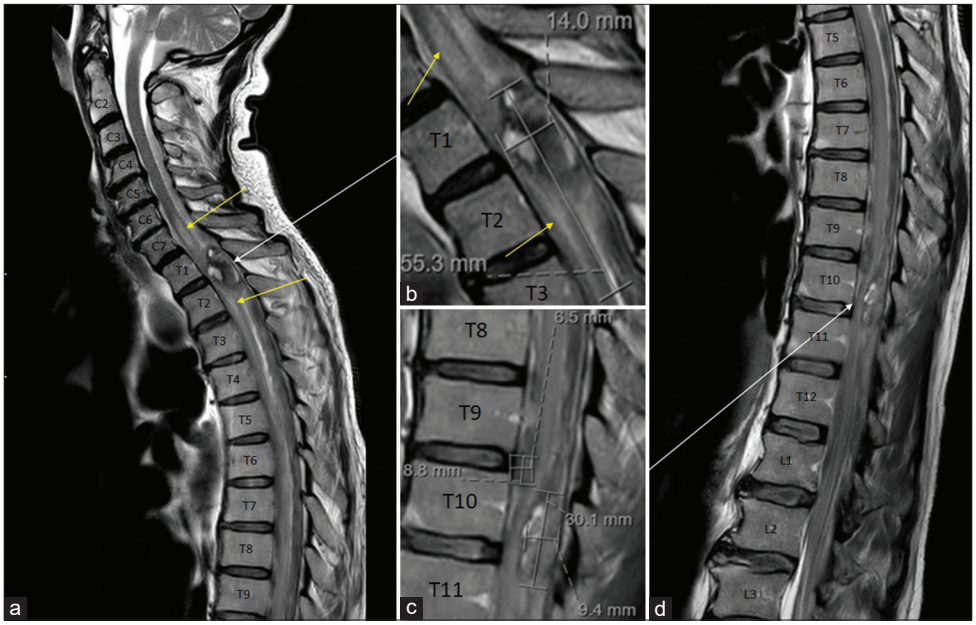

Figure 1: Pre-operative sagittal T2-weighted MRI of the spine. (a) Cervicothoracic image demonstrating SIEH at T1/2. (b) Enlarged field of view (as indicated by the white arrow) over the region of hemorrhage in (a) with dimensions, demonstrating displacement of the cord anteriorly. Note the areas of cord signal change superiorly and inferiorly, indicated by yellow arrows in both (a) and (b). (d) Thoracolumbar image demonstrating SIEH anteriorly at T9/10 and posteriorly at T10/11. (c) Enlarged field of view (as indicated by the white arrow) over the region of hemorrhage in (d) with dimensions. In all panels, the vertebral levels are labeled. Abbreviations: MRI, magnetic resonance imaging; SIEH, spontaneous intradural extramedullary hemorrhage.

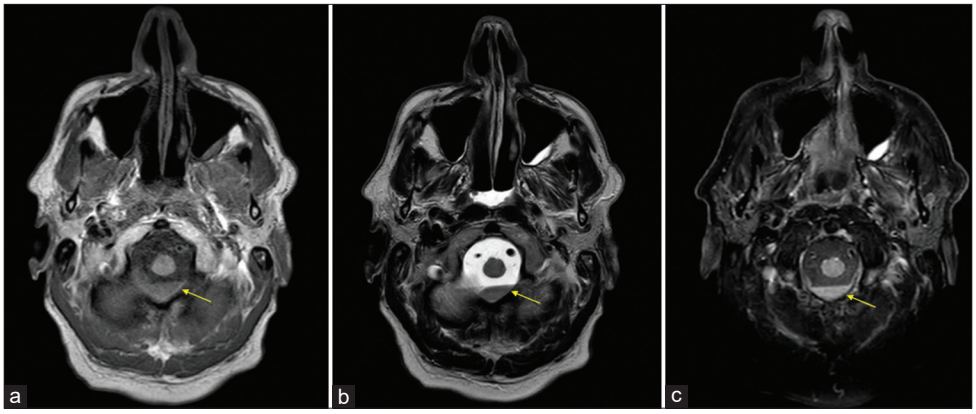

Figure 2: Axial MRI of the foramen magnum showing dependent blood products. (a) T1-weighted imaging. (b) T2-weighted imaging. (c) T2-FLAIR sequenced imaging. The yellow arrows indicate the blood products lying in the spinal canal. This was thought to have migrated from another site of bleeding, during our patient's period of recumbency. MRI: Magnetic resonance imaging, T2-FLAIR: T2-weighted fluid-attenuated inversion recovery.

subarachnoid hemorrhage have been observed in patients with SIEH. Caudocranial hemorrhage extension through the subarachnoid space can predictably cause symptoms including headache, nuchal rigidity, photophobia, nausea, vomiting, and impairment of consciousness. Peñas *et al.* (2011)[10] and Bernsen and Hoogenraad (1992)[1] reported patients with concomitant SIEH and cerebral subarachnoid and intraventricular blood products. The authors posited that cranial migration of blood products from a spinal origin may have occurred due to their patients' long duration of recumbency before presentation, and large volume of hemorrhage.

SIEH can rapidly develop into complete and irreversible paralysis and loss of function.[3] Recognized etiologies of SIEH include trauma, spinal neoplasia, coagulopathy, vasculopathy, and iatrogenesis. Common iatrogenic causes include diagnostic or anesthetic (subarachnoid or extradural) lumbar puncture, and spinal surgery. Rarely,

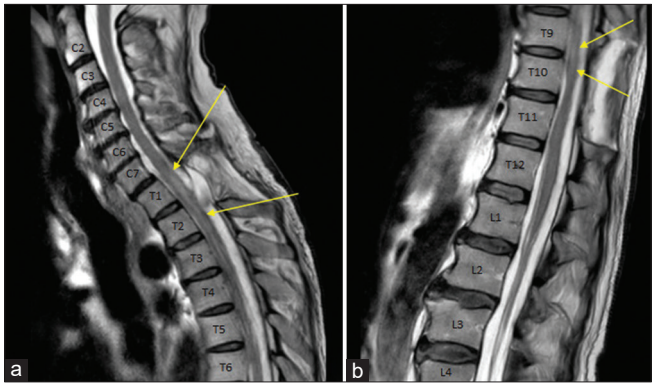

Figure 3: Post-operative sagittal T2-weighted MRI of the spine. (a): Cervicothoracic image showing the decompressed spinal cord at T1/2. (b) Thoracolumbar image showing the decompressed spinal cord from T9-11. In both (a) and (b), note the areas of persistent cord signal change, indicated by the yellow arrows. In both panels, the vertebral levels are labeled. MRI: Magnetic resonance imaging.

anticoagulant and antiplatelet medications are associated with spontaneous SIEH in the absence of an underlying lesion. There are several similar cases in the medical literature with various coagulation-affecting medications implicated.

In the present study, we report a case of a patient who developed acute lower back pain and paraplegia, secondary to a medication-induced coagulopathy. This study aims to raise awareness of a rare but highly morbid pathology, where prognosis is inversely related to the time between the onset of compression and decompressive surgery, and expeditious diagnosis is paramount to preservation of neurological function.

CASE DESCRIPTION

An independent 71-year-old male retiree presented to hospital with chest pain, thoracolumbar back pain, and hypertension (self-measured systolic blood pressure was elevated to 220 mmHg). He was evaluated for possible acute cardiac pathology. His medical history was significant for atrial fibrillation for which he was anticoagulated, and he had recently had an artificial cardiac pacemaker implanted for treatment of sinus node dysfunction. He had known hypercholesterolemia, hypertension, and several benign skin lesions had been excised previously. While in the emergency department, his back pain escalated in severity. He had a headache and was vomiting. He was investigated for possible aortic pathology with computed tomography (CT) and bedside sonography, but there was no evidence of this. He was treated with analgesia.

He subsequently developed numbness and weakness of the right lower limb. This was only detected after several hours had passed, at which time he was re-evaluated for neurological pathology. CT imaging of the brain and circle of Willis revealed no abnormality of note. He was attributed a presumptive diagnosis of a likely anterior or posterior circulation embolic stroke and was admitted to the care of the inpatient cardiology service, with a plan for continuing anticoagulation (rivaroxaban was ceased in favor of enoxaparin), antiplatelet therapy (aspirin), and non-urgent magnetic resonance imaging (MRI). Later that evening, he was reviewed for persisting abdominal and back pain. He had developed allodynia of the lower chest and abdomen and had begun to retain urine, necessitating catheterization.

By day 3 of admission, his right lower limb paresis had progressed to flaccid paralysis and sensory loss. Our patient subsequently developed paresis of his left lower limb and loss of anal tone. He could not feel the tug of his catheter. There were no reflexes in his lower limbs, nor clonus. He could sense punctate stimuli but described the sensation as dull and paresthetic. He was finally referred to the inpatient neurosurgical service for consideration of spinal pathology.

Emergent MRI of the entire spine and brain was performed. Two discrete foci of non-contiguous acute SIEH were discerned, approximately localized behind T1-2 and T10-11. There was associated spinal cord displacement and acute spinal cord edema due to compression, at both sites of hemorrhage. Our patient's pre-operative radiology is depicted in Figure 1. Metastatic disease was suspected as the most likely underlying etiology, due to the multiplicity of the lesions. MRI of the brain showed subarachnoid hemorrhage in the dependent foramen magnum. This was favored to be migratory from a spinal origin. This radiology is depicted in Figure 2. Hematology advice was sought to reverse the effects of enoxaparin, and aspirin. CT pan scan with contrast did not reveal any underlying neoplastic, vascular, or other lesions that might account for the hemorrhages observed. Decompressive surgery was delayed further as enoxaparin had been administered in the morning of the 4th day, and there was concern of unacceptable intraoperative bleeding risk. Surgery was finally performed later that evening, specifically C7-T2 and T9-11 laminectomies. The dura was darkly colored at both foci of hemorrhage. There were no extradural blood products. Durotomy was performed at each site and subdural and subarachnoid clots were discerned. The hematomas were removed in piecemeal fashion until pulsatile neural tissue was observed. No underlying culprit lesions were apparent intraoperatively. Onlay duraplasties with fibrin glue were performed and the wounds were closed in routine fashion.

Immediately post-operatively, there was minimal neurological improvement. Our patient's pain ameliorated but flaccid paraplegia persisted and he was doubly incontinent. His post-operative radiology is depicted in Figure 3. His post-operative course was complicated by a

Table 1: Comparative table of previously reported cases of spontaneous anticoagulation and antiplatelet medication-related spinal intradural extramedullary hemorrhage.

Study	Age/ gender	Medical history	Anticoagulant/ antiplatelet and hematology	Vertebral levels and extension	Symptoms/signs	Treatment	Outcome
[8]	75 M	Unstated	Phenprocoumon (INR 4.1)	T5-L2	Acute lower back and bilateral lower limb pain, headache, nausea and vomiting, right-sided monoplegia and left-sided paresis, and vibration/ proprioceptive sensory loss	T10-12 decompression	Left lower limb paresis resolved. Patient died of a myocardial infarction 5 days following admission.
[8]	34 M	IV illicit drug use and recurrent PE	Phenprocoumon	C2-T6	Headache, nausea, and paraplegia	T1-T3 decompression	Minimal neurological recovery.
[3]	76 M	AF, dyslipidemia, hypertension, and T2DM	Warfarin (INR 6)	L1-4	Acute lower back pain, paraparesis, and urinary retention	T12-L4 decompression	Minimal improvement in neurology after 6 months.
[10]	74 F	AF, hypertension, prosthetic aortic, and mitral valves	Acenocoumarol (INR 4.45)	C2-T10 (and cerebral subarachnoid hemorrhage)	Acute neck pain, confusion, and paraplegia	Conservative treatment with steroids	No improvement in neurology and died within 1 week due to a nosocomial lower respiratory tract infection.
[1]	75 M	AF and DVT	Phenprocoumon (INR 6.1)	T3-L2	Acute lower back pain, confusion, paraplegia with a T8 sensory level, severe headache and vomiting, and urinary retention	T2-L3 decompression	Paraplegia and sensory deficits persisted long-term.
[11]	64 M	MI	Abciximab and unfractionated heparin	T7-12	Acute lower back pain, paraplegia, and urinary retention	Surgical evacuation (unspecified levels)	After 5 months of rehabilitation, could ambulate with a frame, and bowel and bladder function returned.
[2]	50 F	Leg fracture	Unspecified VTE prophylactic anticoagulant	T5-11	Acute upper back pain and paraplegia	T5-6 decompression	No recovery in neurology.
[2]	54 F	Bradycardia-Tachycardia syndrome	Unspecified anti-Vitamin K anticoagulant	T9-L1	Acute lower back pain and anesthesia below knees that developed into paraplegia and urinary retention	T10-L4 decompression	Complete recovery.
[7]	57 F	Recurrent DVT	Warfarin (INR 6.67)	T4-8	Acute diffuse back pain, headache and vomiting, paraplegia, and urinary retention	Surgical evacuation (unspecified levels)	Post-operative course complicated by retrothecal pseudomeningocoele and fistula. Associated medullary edema.

(Contd...)

Table 1: (*Continued*).

Study	Age/ gender	Medical history	Anticoagulant/ antiplatelet and hematology	Vertebral levels and extension	Symptoms/signs	Treatment	Outcome
							Remained paraplegic with bowel and bladder dysfunction after 6 months.
[9]	61 F	AF	Unspecified anti-Vitamin K anticoagulant (INR 3.2)	T8-L2	Acute lower back and bilateral lower limb radicular pain, meningismus, paraplegia with anesthesia below T9, and urinary retention	T8-L2 decompression	Minimal neurological recovery. Persisting Paraparesis and bladder dysfunction after 2 years.
[9]	71 F	AF	Unspecified anti-Vitamin K anticoagulant (INR 3.4)	Conus and cauda equina (levels unspecified)	Acute lower back pain, bowel incontinence, paraplegia with a T12 sensory level, and urinary retention	T12-L4 decompression	No recovery after 1 year.
[9]	47 F	Mechanical heart valve (unstated)	Unspecified anti-Vitamin K anticoagulant (INR 4.1)	T11-S1	Acute lower back and bilateral lower limb radicular pain, paraplegia, and urinary retention	T10-S1 decompression	Walking with assistance and recovery of bladder function after 10 months.
[5]	65 F	AF	Dicoumarol (INR 1)	T7-12	Acute lower back and bilateral lower limb radicular pain, abdominal pain, and bilateral lower limb paresthesia paraplegia	L3-5 decompression	Recovery after 1 year.
[4]	72 F	Laryngeal cancer, MI, and previous spinal radiotherapy	Aspirin 325 mg twice daily, enoxaparin (therapeutic dosing)	T3-6	Paraplegia with a T4 sensory level and urinary retention	T3-5 decompression	Minimal recovery at 18 months.
[6]	61 F	MI	Unspecified oral anticoagulant	L4-5	Acute lower back and bilateral lower limb radicular pain, left ankle weakness, and urinary incontinence	L4-5 decompression	Neurological recovery. Arachnoiditis and pain at 4 months.
[6]	74 F	Coronary artery disease	Aspirin and unspecified oral anticoagulant	At least T2-11	Abdominal pain, acute lower back pain, confusion, meningismus, paraparesis, and urinary retention	T2-11 decompression	Neurological recovery initially. Deterioration in gait and sensation after 6 months due to arachnoiditis.

(Contd...)

Table 1: (*Continued*).

Study	Age/ gender	Medical history	Anticoagulant/ antiplatelet and hematology	Vertebral levels and extension	Symptoms/signs	Treatment	Outcome
[6]	52 F	Angular vein thrombosis and suborbital abscess	Unspecified oral anticoagulant	At least T2-7	Abdominal paresthesia, meningismus, paraparesis, urinary, and fecal incontinence	T2-7 decompression	Almost complete neurological recovery after 5 months.
Present Study	71 M	AF, hypertension, dyslipidemia, and sick sinus syndrome	Rivaroxaban premorbidly, aspirin, and enoxaparin while admitted to hospital	T2 and T10	Acute thoracolumbar back pain, evolving paraparesis, headache, and vomiting	C7-T2 and T9-11 decompression	Persisting paraplegia, bowel, and urinary incontinence after 6 months.

AF: Atrial fibrillation, DVT: Deep venous thrombosis, INR: International normalized ratio, IV: Intravenous, MI: Myocardial infarction, PE: Pulmonary embolism/emboli, T2DM: Type 2 diabetes mellitus, VTE: Venous thromboembolism

hospital-acquired lower respiratory tract infection and a left lower limb deep venous thrombosis. He made modest gains in function with inpatient physiotherapy and occupational therapy and was discharged to a spinal rehabilitation center. At 6-month follow-up, his neurology was unchanged.

DISCUSSION

Spontaneous SIEH associated with anticoagulant and/or antiplatelet medications, in the absence of an underlying lesion, is extremely rare. The gold standard in the assessment of spinal cord or neural compromise due to SIEH is MRI.[3,8] Hyperacute and acute blood products demonstrate signal isointensity to spinal neural elements on T1-weighted MRI.[11] Blood products during the hyperacute phase are signal hyperintense, becoming isointense, then hypointense, after the first 12 hours (the acute phase) on T2-weighted imaging. CT is a useful initial investigation because of its comparably greater accessibility; and its utility in identifying and localizing acute SIEH, and differentiating it from adjacent lower density elements.[2] Intradural hemorrhage, regardless of the compartmentalization of bleeding, may be recognized radiologically by the "inverse Mercedes-Benz sign." This is the tri-star shaped appearance of the descending and exiting neural elements of the spinal cord, limited to the thecal sac, and not extending to the intervertebral foramina, when encased in intradural hemorrhage. Extradural spinal hemorrhage comparatively appears radiologically as a broad-based biconvex lesion that displaces the spinal neural elements.

The pathogenesis of SIEH is not well understood. Previous studies have reported a preponderance of SIEH to occur in the thoracolumbar spine without a gender predominance.[4-7,11] There is a greater incidence among older individuals, especially those with vascular disease-associated risk factors such as atherosclerosis and hypertension.[7,10] This is likely exaggerated by the greater frequency of concomitant anticoagulant and antiplatelet medication usage in advanced age demographics due to age-skewed vasculopathies. [Table 1] lists all reported cases of medication-associated spontaneous intradural hemorrhage. These were primarily older patients with underlying cardiovascular disease. While not exhaustively listed in each report referenced, vascular disease risk factors feature prominently. Bruce-Brand *et al.* (2013)[3] postulated that the vascular spinal subarachnoid space is a potential site for spontaneous blood vessel rupture, perhaps precipitated by sudden rises in intra-abdominal or intra-thoracic pressures. Bleeding would then rupture the subarachnoid mater to involve the subdural compartment. Another theory postulated is that internal dural vessels rupture initially, and bleeding extends to involve the subarachnoid compartment.[9] Seldom is a culprit bleeding vessel identified. Involvement of the subarachnoid compartment may confer a worse prognosis, due to the neurotoxic effects of blood, and the development of arachnoid fibrosis.[3] It is unclear what proportion of these hemorrhages are monocompartmental and multicompartmental.

Surgical and non-surgical treatment strategies have been employed in the treatment of SIEH. The underlying derangement of coagulation should be corrected. Conservative management strategies have been reported in patients with mild or spontaneously improving neurological deficits, although this is uncommon.[9] Watchful waiting with serial radiological and neurological assessments is the cornerstone of a non-surgical approach.[7] Surgical treatment involves decompression with a regional laminectomy, durotomy, and careful evacuation of the hematoma.[2,7] Improvement of neurological deficits post-operatively seems

to be a function of the severity of myelopathy/radiculopathy incurred and the time between symptom onset and decompression. Morandi *et al.* (2001)[9] speculated that follow-up MRI demonstrating spinal cord atrophy and arachnoid fibrosis was associated with poorer functional outcomes.

CONCLUSION

Coagulation-impairing medications rarely cause SIEH. Sudden onset back pain associated with acute neurological deficits may represent compressive hemorrhagic spinal pathology. Vascular disease risk factors including atherosclerosis, and hypertension, may be implicated in its pathogenesis. More research is required to support this assertion. The gold standard of imaging in SIEH is MRI. Urgent decompressive surgery should be considered in patients with neurological deficits. Timely decompression confers a more favorable prognosis. More severe neurology (especially motor deficits) at presentation implies a worse recovery.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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