

# Spinal cord infarction during physical exertion due to polycythemia vera and aortoiliac occlusive disease

## A case report

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### Abstract

**Rationale:** Spinal cord infarction is rarely caused by hypercoagulable states. Polycythemia vera (PV) is a myeloproliferative neoplasm that can contribute to thrombotic events due to increased blood viscosity. We report a case of spinal cord infarction due to extensive aortic thrombosis caused by PV.

**Patient concerns:** A 56-year-old man presented with acute paraplegia and urinary retention during heavy physical exertion.

**Diagnoses:** Imaging studies revealed spinal cord infarction at the T9 to T12 levels and aortoiliac occlusive disease. PV was diagnosed during workup for elevated hemoglobin level

**Interventions:** The patient received intravenous hydration and anticoagulation for spinal cord infarction. PV was managed with phlebotomy and hydroxyurea. Courses of inpatient and outpatient rehabilitation programs were also given.

**Outcomes:** The patient became urinary catheter-free 5 months after disease onset, and was able to walk with walker. The American Spinal Injury Association Impairment scale also improved from C at diagnosis to D during last follow-up.

**Lessons:** Etiologic workup is important for patients with spinal cord infarction to direct specific treatment strategies. Physical exertion may act as a trigger for infarction in patients at risk for thrombotic events, and monitoring of neurologic status during and after periods of exercise is warranted.

**Abbreviations:** AIS = American Spinal Injury Association Impairment scale, CT = computed tomography, MRI = magnetic resonance imaging, PV = polycythemia vera.

**Keywords:** aortoiliac occlusive disease, physical exertion, polycythemia vera, spinal cord injury, spinal cord ischemia

## 1. Introduction

Spinal cord infarction is a rare cause of spinal cord injury, with most cases occurring as a result of aortic diseases such as aortic rupture, dissecting aortic aneurysms, thrombosis, atherosclerosis, or iatrogenic injury during aortic aneurysm repairs.<sup>[1]</sup> Polycy-

themia vera (PV) is a myeloproliferative neoplasm characterized by elevated blood hemoglobin and hematocrit levels, and can contribute to thrombotic events due to increased blood viscosity.<sup>[2]</sup> The existing reports<sup>[3-5]</sup> of spinal cord infarction in individuals with PV did not examine the possible contributions of physical exertion to the link between these 2 conditions. We report a case of spinal cord infarction due to extensive aortic thrombosis caused by PV, and explore the potential role that physical exertion plays as a trigger for spinal cord infarction in patients with PV.

## 2. Case report

A 56-year-old previously healthy man with heavy smoking history and sedentary lifestyle presented to the emergency department with acute paraplegia while he was attempting to lift a truck tire weighted about 75 kg off the ground. Accompanying symptoms included urinary retention, severe burning sensation in the low back with radiation to the entire back and anterior torso, and decreased sensation over both legs and the genital region. Physical examination revealed paraplegia, decreased sensation to both pinprick and light touch distal to the T10 dermatome, absent deep tendon reflexes of both lower limbs, and bilaterally non-palpable dorsalis pedis artery pulsations. Proprioception and vibratory sensation were normal. The anal tone was normal, and the deep anal pressure sensation,

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**Table 1****Detailed neurologic examination according to the American Spinal Injury Association Impairment scale and the Medical Research Council Muscle scale.**

Level	At presentation							
	Muscle power		Pinprick			Light touch		
	Right	Left	Level	Right	Left	Level	Right	Left
C5–C8	5	5	C2–C8	2	2	C2–C8	2	2
T1	5	5	T1–T9	2	2	T1–T9	2	2
L2	0	2-	T10	2	2	T10	2	2
L3	0	2-	T11	1	1	T11	1	1
L4	0	2-	T12	1	1	T12	1	1
L5	0	2-	L1–S3	1	1	L1–S3	1	1
S1	0	3-	S4–S5	1	1	S4–S5	1	1
During last follow-up visit, 14 months after disease onset								
C5–C8	5	5	C2–C8	2	2	C2–C8	2	2
T1	5	5	T1–T9	2	2	T1–T9	2	2
L2	4	3+	T10	2	2	T10	2	2
L3	4	3+	T11	1	1	T11	1	1
L4	4	3+	T12	1	1	T12	1	1
L5	4	3+	L1–S3	1	1	L1–S3	1	1
S1	4	3+	S4–S5	1	1	S4–S5	1	1

anocutaneous reflex, bulbocavernosus reflex, and voluntary anal contraction were all present. Detailed neurologic examination according to the American Spinal Injury Association Impairment scale (AIS) is summarized in Table 1. The patient was classified as T10 AIS C incomplete spinal cord injury. Computed tomographic (CT) angiography of the aorta for possible abdominal aortic dissection or ruptured aneurysm showed aortoiliac occlusive disease distal to the subphrenic aorta with prominent collaterals (Fig. 1). Magnetic resonance imaging (MRI) of the spine (Fig. 2) for suspected myelopathy revealed symmetric hyperintensities in the anterior part of spinal cord at the T9 to T12 level on T2-weighted images and diffusion-weighted images, indicative of acute spinal cord infarct. For aortoiliac occlusive disease with spinal cord infarction, intravenous hydration and anticoagulation with heparin were instituted. The patient opted for medical management for aortoiliac occlusive disease after discussion with vascular surgeon considering the high operative risk, prominent collaterals without imaging evidence of compromised perfusion of visceral organs on CT angiography, and the lack of signs of ischemia in the legs such as chronic ulcer. Anticoagulation was later bridged to warfarin, with the international normalized ratio maintained between 2 and 3. For study of aortoiliac occlusive disease, blood tests were reviewed and showed polycythemia, hemoglobin level 19.6 g/dL, hematocrit level 53.5%, and decreased erythropoietin level. The diagnosis of PV was made after the patient was tested positive for Janus kinase 2 V617F mutation. Exhaustive workup for vasculitis, autoimmune, and coagulation disorders were all negative. Phlebotomy and cytoreduction therapy with hydroxyurea were instituted for high-risk PV, targeting a hematocrit level of <45%. Detrusor hypoactivity and increased urethral pressure were disclosed on urodynamic examination for evaluation of neurogenic bladder, which was then managed with clean intermittent catheterization and medications including terazosin and bethanechol. The patient became catheter-free 5 months after disease onset. Neurological condition and function improved after inpatient and outpatient rehabilitation. Fourteen months after disease onset, the patient could ambulate with a walker. Muscle power by the Medical Research Council Muscle scale improved to grade 4 in the right leg and 3+ in the left leg. The AIS also changed from

C to D. No recurrent thrombotic event or deterioration of neurologic function developed during the 14-month period of follow-up. The clinical course is summarized in a timeline (see Table, Supplemental Content, <http://links.lww.com/MD/C450> which summarizes the clinical course).

Informed consent was obtained from the patient. Ethical approval was not necessary for this case report under the regulations of institutional review board of the National Cheng Kung University Hospital.

### 3. Discussion

Spinal cord infarction is rare and far less common than brain infarction. It constitutes <1% of all central nervous system ischemic events<sup>[1]</sup> and comprises about 8% of all myelopathies.<sup>[1]</sup> Compared with patients with cerebral infarction, those patients tends to be younger and more often female.<sup>[1]</sup> Pain and sensory disturbances are often the first symptoms noted by patients with spinal cord infarction.<sup>[1]</sup> The most frequently affected region of the spinal cord is the lower thoracic levels and in the anterior spinal artery territory.<sup>[1]</sup> The most commonly identified etiologies are aortic diseases such as aortic rupture, dissecting aortic aneurysms, thrombosis, atherosclerosis of the aorta, or iatrogenic injury during aortic aneurysm repairs.<sup>[1]</sup> Other possibilities include vertebral artery dissection/occlusion, systemic hypotension, fibrocartilaginous embolism, vasculitis, arterial or cardiac embolism, hypercoagulable state, or radicular artery compression.<sup>[1]</sup> In one-third of patients, the responsible pathology remains unclear.<sup>[1]</sup>

Only 3 cases of spinal cord infarction or ischemia associated with PV have been published in the literature.<sup>[3–5]</sup> The characteristics of those reported cases are summarized in Table 2. All 3 cases presented with acute onset of pain and weakness. Two cases reported sensory abnormalities, and 1 had urinary retention. Although MRI has been reported to be not very sensitive in detecting acute spinal cord infarction,<sup>[1]</sup> spinal MRI of the 2 cases with persistent symptoms at the time of image acquisition showed findings compatible with ischemia.<sup>[3,5]</sup> All 3 cases were treated with antiplatelet agents, with variable uses of cytotoxic agents and phlebotomy. Two cases had complete recovery without recurrent thrombotic events or neurologic deficits.



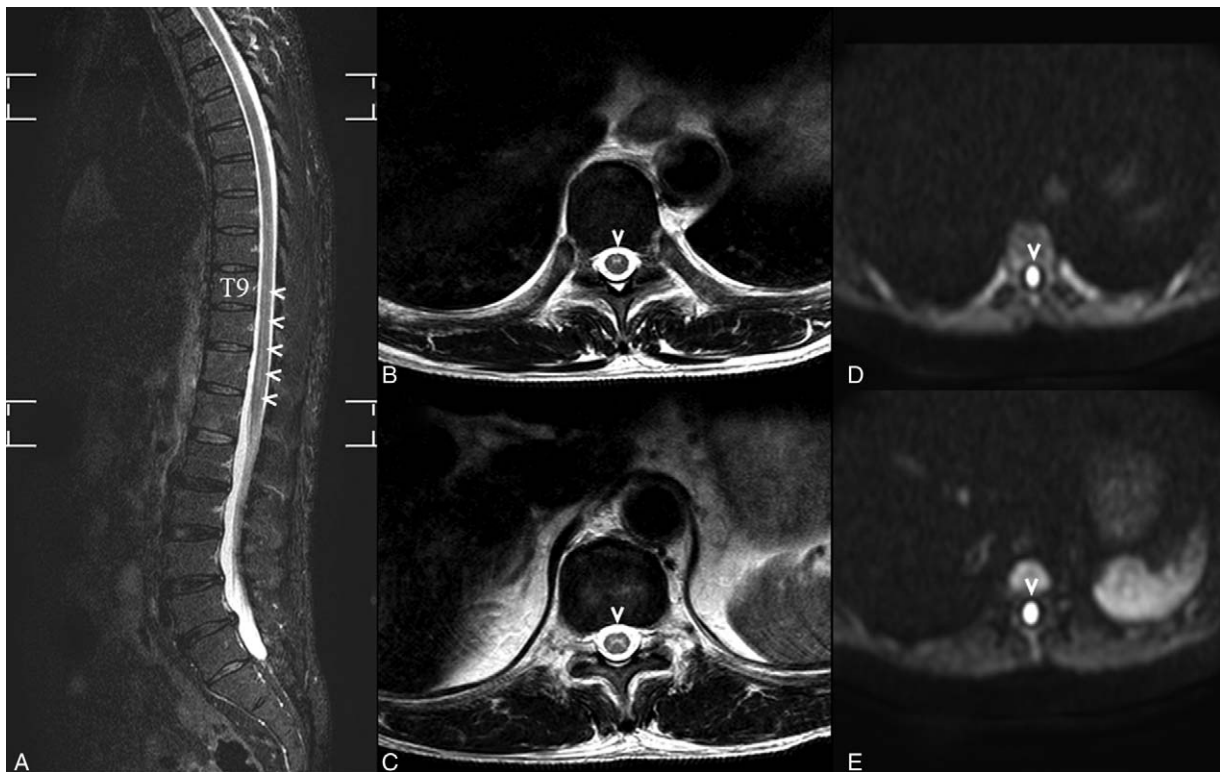
**Figure 1.** Abdominal computed tomography showing aortoiliac occlusive disease with intraluminal thrombosis (arrowheads) distal to the subphrenic aorta.

To date, no guideline on the management of spinal cord infarction has been published. Treatment is thus largely determined by the etiology. General principles include hemodynamic augmentation with fluids and/or vasopressors, and lumbar drains in an attempt to raise the spinal cord perfusion pressure.<sup>[1]</sup> Of note, the support for the use of lumbar drains are based on studies of patients undergoing endovascular thoracic aortic repair only; its role in spinal cord infarction due to other causes have not been evaluated. Risk factor management, antithrombotic therapies with antiplatelet agents or anticoagulants, and pain control should all be considered.<sup>[1]</sup> The use of corticosteroids should be limited to patients with spinal cord ischemia due to vasculitis, as corticosteroids may aggravate myelopathies caused by vascular malformations.<sup>[6]</sup> There is currently no literature available on the timing and patient selection for anticoagulation in patients with spinal cord infarction. The decision to anticoagulate this patient was made in light of the extensive aortic thrombosis that presumably resulted in the spinal cord infarct.

The neurologic examination findings of this patient did not seem to correlate well with the neuroanatomy of spinal cord and the imaging findings on MRI, as the patient had loss of light touch sensation but intact proprioception and vibration sense. There are some possible explanations. The common clinical practice of

examining only the great toe is reported to be less sensitive in demonstrating loss of proprioceptive sense when compared with testing of other digits.<sup>[7]</sup> Similarly, testing vibration sense with tuning fork may yield falsely negative results.<sup>[8]</sup> Hence, some degree of impairments in proprioception and vibration sense may be missed by standard neurologic examinations. In this patient, it is likely that the entire cross-section of the spinal cord sustained ischemic damage but only the anterior cord showed hyperintensities on MRI owing to the limited sensitivity of this imaging modality in detecting acute spinal cord infarction.<sup>[1]</sup>

Smoking and myeloproliferative neoplasms are associated with similar alterations in hemostasis and coagulation parameters, including increased blood viscosity associated with an increased haematocrit and/or plasma viscosity.<sup>[9]</sup> Chronic inflammation and oxidative stress are thought to mediate the clinical, biochemical, and molecular characteristics shared by smoking and myeloproliferative neoplasms. Smoking is known to be associated with accelerated erythropoiesis, leukocytosis, and thrombocytosis, and has also been shown to increase the risk or arterial thrombosis in patients with PV.<sup>[9]</sup> Some epidemiological and experimental evidence support the hypothesis that smoking may even contribute to the development of myeloproliferative neoplasms, through modulation of the transcription factor nuclear factor erythroid-2 and interleukin-8 and activation of



**Figure 2.** MRI of spine. (A) Sagittal imaging T2 STIR showing hyperintensities (arrowheads) in the anterior part of spinal cord. (B) and (C) Axial T2WI showing symmetric hyperintensities (arrowheads) in the anterior part of spinal cord at T9 to T12 level. (D) and (E) Axial DWI showing symmetric hyperintensities (arrowheads) in the anterior part of spinal cord at T9 to T12 level. DWI=diffusion-weighted imaging, MRI=magnetic resonance imaging; STIR=short tau inversion recovery; T2WI=T2 weighted imaging.

the nuclear factor kappa B and Janus kinases (JAK) and Signal Transducer and Activator of Transcription proteins (STAT) pathways.<sup>[9]</sup> These evidence all suggest that smoking cessation is imperative in patients with myeloproliferative neoplasms and thrombotic events.

This patient's symptoms developed during heavy physical exertion. There are studies in the literature examining the potential role of physical exertion as a trigger for cerebral infarction. In the Stroke Onset Study,<sup>[10]</sup> moderate or vigorous bouts of physical activity were associated with a two-fold increased risk of stroke within an hour after each bout of physical activity in individuals who are habitually active.<sup>[10]</sup> The risk increased to 6.8-fold in more sedentary subjects.<sup>[10]</sup> In another study of 200 ischemic stroke patients, Koton et al<sup>[11]</sup> reported a 2.1-fold increased risk of ischemic stroke within 2 hours of physical exertion that did not reach statistical significance. Proposed mechanisms of physical exertion as a trigger for stroke include changes in autonomic nervous control that may result in hemodynamic stress, which in turn causes increased shear stress.<sup>[10]</sup> The increase in shear stress may disrupt vascular endothelial surface which, when combined with increased platelet aggregation and oxygen demand caused by elevated norepinephrine levels during physical exertion, could contribute to increased risk of thrombotic occlusion.<sup>[10]</sup> On the other hand, heavy lifting like what the patient was performing at the onset of his symptoms may alter the levels of intrathoracic pressure resulting from expiratory strain and hence produce a transient elevation in blood pressure.<sup>[10]</sup> The elevation in blood pressure could contribute to the hemodynamic stress that leads to increased shear stress as well.<sup>[10]</sup> Currently there are few reports

investigating the relationship between physical exertion and spinal cord infarction, with the available literature focusing mostly on cases of fibrocartilaginous embolism.<sup>[1]</sup> Reviewing the 3 cases of spinal cord infarction or ischemia associated with PV in the literature, 1 patient also had his symptoms developing after physical effort.<sup>[4]</sup> It is possible that physical exertion acted as a trigger for spinal cord infarction due to the above-mentioned mechanisms.

There are some limitations in this case report. First, smoking is another vascular risk factor the patient has aside from PV. The correlation between spinal cord infarction and PV in this patient is thus arbitrary. Nevertheless, the importance of thorough diagnostic evaluations in this patient population cannot be overemphasized as results of those assessments may alter treatment plans and halt disease progression. Second, the implication that physical exertion may act as a trigger for spinal cord infarction in individuals with PV is based on previous studies for individuals with cerebral infarction.<sup>[10,11]</sup> Further research is necessary before definite causal relationship can be established.

#### 4. Conclusion

This case presentation highlights the importance of comprehensive workup for the etiology in patients with spinal cord infarction, so treatment directed at the specific cause can be initiated timely. Physical exertion may act as a trigger for spinal cord infarction. Clinicians should educate patients at risk to pay attention to symptoms of neurologic deficits both during and

**Table 2****Characteristics of reported cases of spinal cord infarction/ischemia associated with polycythemia vera in the literature.**

References	Age	Gender	Comorbidities	Presentation	Hb and Hct levels at presentation		Imaging	Management	Outcome
					Hb	Hct			
Lee et al <sup>[3]</sup>	66	Female	T12 compression fracture without neurological sequelae	Acute paraparesis, urinary retention, and transient pain and hyperesthesia in both lower leg Transient paraparesis 3 days before hospital visit	Hb: 16.9 g/dL		Spinal MRI: T12–L1 level swelling with T2 high signal intensity in the central portion of the cord. High-signal intensity on DWI with a decreased ADC value Abdominal CT: multifocal wandering thrombi attached to the lumen of the distal aortic arch, descending aorta, abdominal aorta, and right common iliac artery	Antiplatelet and cytotoxic agents	Not reported
Costa et al <sup>[4]</sup>	52	Male	History of transient lower limbs motor deficit without medical investigation	Acute low back pain without radiation, with motor deficits in the lower limbs for 2 times in 24 hours after physical effort with spontaneous recovery One similar episode 5 months later	Hb: 20.1 g/dL Hct: 59.3%		Negative spinal MRI Spinal angiography: artery of Adamkiewicz origin at the T11 level, with no ascending branch	Phlebotomy, hydroxyurea, platelet inhibitor	Spontaneous recovery, no relapses in 2 years
Gul et al <sup>[5]</sup>	40	Male	Nil	Sudden neck and bilateral arm pain, shoulder cramps, bilateral deltoid and biceps weakness, and paresthesia in both hands on getting out of bath	Hb: 21.5 g/dL Hct: 67%		MRI of head: anterior cervical cord ischemia and inflammation secondary to right vertebral artery thrombosis	Phlebotomy, aspirin, interferon alpha	Resolved, no recurrent thrombotic events

ADC = apparent diffusion coefficient, CT = computed tomography, DWI = diffusion-weighted imaging, Hb = hemoglobin, Hct = hematocrit, MRI = magnetic resonance imaging.

after periods of exercise, as these symptoms may herald emerging ischemic events.

### Author contributions

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**Writing – review & editing:** Wei-Pin Lin, Ta-Shen Kuan, Cho-I Lin, Lin-Chieh Hsu, Yu-Ching Lin.

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