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CASE REPORT

Intraspinal Epidural Hematoma in a Warfarinized Patient Presenting with Back Pain: A Case Report

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ABSTRAK

Warfarin adalah ubat mencairkan darah beku yang sering digunakan untuk mencegah daripada pembekuan darah kepada pesakit yang berisiko tinggi untuk mengalami peristiwa thrombo-embolik. Penggunaan warfarin diketahui umum boleh menyebabkan pendarahan kerana kesannya dalam mencairkan darah. Walaupun, bahagian yang paling kerap berlaku pendarahan adalah saluran pencernaan makanan dan saluran kencing, ia juga boleh berlaku di bahagian yang kurang dijangkakan. Kami melaporkan satu kes yang jarang berlaku melibatkan penekanan kepada saraf tunjang disebabkan oleh pendarahan pada bahagian lapisan luar saraf tunjang akibat pencairan darah berlebihan pada seorang pesakit yang pernah menjalani pemindahan hati. Beliau telah menjalani pembedahan serta-merta untuk meringankan kesan tekanan kepada lapisan saraf tunjang dan membuang darah beku setelah kesan pencairan darah cair dibalikkan kepada tahap normal.

Kata kunci: antikoagulan, darah beku, epidural, kord, tulang belakang, warfarin

ABSTRACT

Warfarin is an anticoagulant that is commonly used as thrombo-prophylaxis in patients at risk of thrombo-embolic events. However, the use of warfarin is known to cause hemorrhage due to its anticoagulation effect. Although the common sites of hemorrhage are gastrointestinal and genitourinary tract, it can also occur in the least expected location. We report a rare case of spinal cord compression secondary to intraspinal epidural hematoma as a result of overwarfarinization in a patient who had undergone liver transplant. The patient underwent emergency decompression laminectomy of spinal cord and hematoma evacuation after the

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reversal of overwarfarinization to normal levels.

Keywords: anticoagulant, cord, epidural, haematoma, spinal, warfarin

INTRODUCTION

Warfarin is a vitamin K antagonist that is widely used as a thrombo-prophylaxis in patients with underlying atrial fibrillation or patients who has had heart valve replacement and liver transplant surgeries (Algarni et al. 2015). International Normalized Ration (INR) over 4.5 in patients on warfarin carries an increased risk of hemorrhagic complications where the rate of fatal, major, minor bleeding events were 0.25, 1.1 and 6.2 per 100 patient-years, respectively (Palareti et al. 1996). Although intracranial hemorrhage is a well-known complication in patients with warfarin, intraspinal hemorrhage is rarely reported (Hunderfund & Wijdicks 2009).

Intraspinal epidural hematoma occurs when there is an accumulation of blood in the epidural space that can mechanically compress the spinal cord. Intraspinal haematoma associated with warfarin therapy presents with atypical symptoms due to the delayed expansion of bleeding, hence the delay in the diagnosis and intervention; subsequently leading to serious neurological sequelae (Hunderfund & Wijdicks 2009). It is prudent that doctors in the Emergency Department have a high index of suspicion so that the diagnosis can be made early in patients who present with back pain whilst on anticoagulant therapy. Surgical intervention is often necessary to evacuate the hematoma and minimize risk of permanent neurological damage (Pullarkat & Kalapura 2000).

CASE REPORT

A 34-year-old man with a history of liver transplant secondary to fulminant liver cirrhosis due to Budd-Chiari syndrome presented to Emergency Department (ED) with symptoms of progressive bilateral lower limb weakness and acute urinary retention. A day prior to presentation, he experienced a sudden onset of low back pain upon waking up from sleep which prompted him to immediately seek treatment at another hospital. He was discharged home after given intramuscular pethidine and metoclopramide without a proper neurological examination done. Upon discharge, he was still able to walk slowly with assistance.

He presented to the our hospital's Emergency Department the next day with inability to move both lower limbs and lower abdominal pain secondary to urinary retention. He denied any prior history of fall, trauma, excessive bending or heavy lifting. There was no history of hematuria, hematemesis or passing malaenic stools. His medication history included oral warfarin 3mg once daily, cyclosporine 100mg once daily, prednisolone 5mg

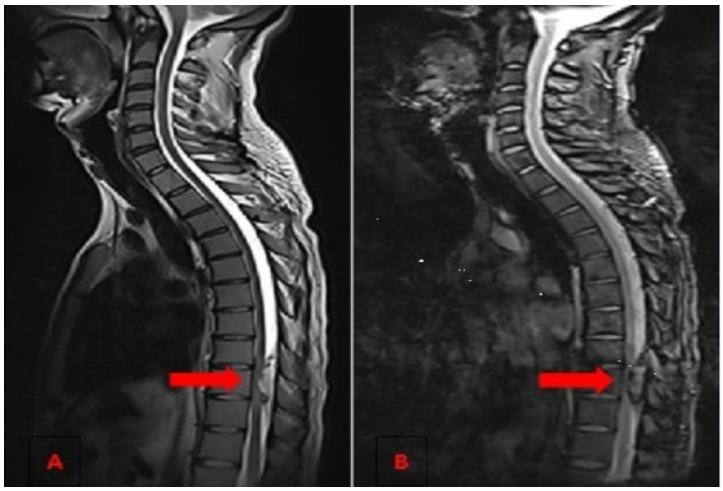

Figure 1: (A) Sagittal view T2 weighted MRI of thoracic shows intraspinal extradural lesion at T8 - T10 level suggestive of hematoma and compressing the cord (red arrow). (B) Sagittal view T2 gradient echo MRI of thoracic shows intraspinal extradural lesion at T8 - T10 level suggestive of hematoma and compressing the cord (red arrow)

once daily and aspirin 75mg once daily.

On general assessment, he was alert and conscious with Glasgow Coma Scale (GCS) of 15/15. He was afebrile and vitals were within normal limits. Cardiovascular system and respiratory system were unremarkable. On abdominal examination, there was a well-healed post liver transplant laparotomy scar and a palpable mass over the suprapubic area suggestive of bladder distension. An immediate per urethral catheterization performed drained 800mls of clear urine.

Peripheral neurological examination revealed motor functionof 0/5 and reduced sensation from level of T10 downward in both lower limbs. The knee and ankle reflexes were also absent. Anal tone was lax but bulbocavernosus reflex was preserved. Bilateral upper limbs neurological examinations were normal.

Blood investigation revealed a deranged coagulation profile with INR of 6.17, prothrombin time (PT) of 54.9 sec and activated partial prothrombin time (PTT) of 68.6 seconds. There was no liver enzyme derangement or electrolytes imbalance. Computed Tomography (CT) scan of the brain showed no evidence of intracranial bleeding or abnormal lesion. Patient then underwent a magnetic resonance imaging (MRI) of the thorax which revealed a well-defined broad based intraspinal epidural mass suggestive of a hematoma at the level of T8 to T10 which cause stenosis of the spinal canal and anterior compression to the spinal cord at the level of T9 as seen by hyperintense signal within T2W1 images (Figure 1 and Figure 2).

Warfarin was withheld and the coagulopathy reversed with transfusion of 4 units fresh frozen plasma (FFP) and Intravenous (IV) vitamin K 10mg. He was referred to Orthopedic and Neurosurgical

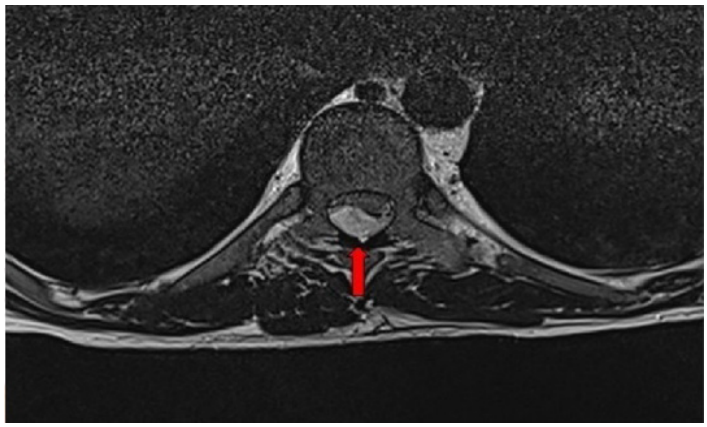

Figure 2: Axial view T2 weighted of MRI thoracic shows intraspinal extradural lesion at T8 - T10 level suggestive of hematoma and compressing the cord (red arrow).

team for definitive surgical plan. He underwent emergency decompressive laminectomy of spinal cord and evacuation of epidural hematoma at level of T8-T10. Intraoperatively, the hematoma was evacuated and a buldging of dura at level T8-T10 was released; followed by laminacteomy at level of T9. There was no evidence of arteriovenous malformation or tumours. IV dexamethasone 4mg was started to reduce edema.

Post-operatively, the motor function of both lower limbs improved to 2/5. He underwent rehabilitation and within a month was ambulating normally. However, he suffered from neurogenic bladder dysfunction that required continuous intermittent urinary catheterization. He was discharged and given follow-up in our center progress monitoring. However, there was no documentation regarding the progress of patient after discharge as patient defaulted follow-up.

DISCUSSION

In post liver transplant patients, the risk of deep venous thrombosis and pulmonary embolism is high due to its rebalanced homeostasis and marked resistance to the inhibitory action of thrombomodulin (Lisman et al. 2010). The level of Antithrombin III and Protein C are reduced and believed to contribute to a hypercoagulability condition that causes vascular thrombosis and possible loss of graft (Stahl et al. 1990). Constant platelet activation and aggregation in post liver transplant patient leads to fibrinogen activation which contribute to arterial thrombosis and graft failure (Patrono & Rocca 2007). Therefore, antiplatelet and anticoagulant agent are required to reduce risk of thrombosis complication (Algarni et al. 2015).

Warfarin is a vitamin K antagonist which produce its anticoagulant effect by interfering with the vitamin K cycle and inhibit protein C and S to prevent anti thrombotic effect (Ageno et al. 2012). Blood coagulation effect is limited due to the absence of coagulation factors (II, VII, IX and X)

and ineffective of vitamin K-epoxide reductase (Ageno et al. 2012).

Warfarin has its well-known and important complication which is increased risk of hemorrhage; hemorrhage can be classified to minor, major and life-threatening or fatal (Palareti et al. 1996). Minor hemorrhage such as hematuria (25.6%), proctorrhagia (20%) uterine bleeding (12.8%) and hematoma (11%); major hemorrhage such as gastrointestinal bleeding (30%), ocular bleeding (21%) and hemoptysis (8%); and fatal cases were due to intracranial bleeding (3%) (Palareti et al. 1996). However, less number of cases regarding intraspinal hematoma secondary to warfarin are reported in the literature (Inamasu et al. 2016).

The INR is used to monitor and modify warfarin dosage. Close monitoring of INR is imperative to achieve desirable effect and reduce risk of side effect. A study shows that risk of bleeding is higher in patients with INR exceeding 4.5 and with arterial disease (Palareti et al. 1996). Another study showed similar result with INR of more than 4 being associated with an increased risk of bleeding (Makris et al. 2010). This patient had an INR of 6.17 upon presentation which may have contributed to the formation of hematoma in the spinal cord's epidural space.

Spontaneous intraspinal hematoma is a rare clinical entity which occurred when it is unrelated to trauma, surgery, arteriovenous malformation, underlying neoplasm, or lumbar puncture (Heppner et al. 2004). This patient presented with sudden onset of back pain progressively leading to complete paralysis with urinary retention without any history of trauma. Anticoagulant therapy and vascular malformations are reported as the pathogenetic factors in the development of spontaneous intraspinal haematoma (Lo et al. 2012; Groen & Ponssen 1990). Other etiologies include vessel anomaly or rupture of spinal epidural vein in venous plexus contributing to increase risk of spontaneous spinal epidural hematoma (Pagano et al. 2012).

Spontaneous intraspinal hematona may occur in all age and at all levels of the spinal epidural spaces; but the most frequent region affected is the thoracic region (Harik et al. 1971; Yu et al. 2016). A patient presenting with acute back pain and neurological deficit may require MRI to identify the cause as it will reveal tumours, arteriovenous malformations or bleeding. MRI also will providea good visualization of the spinal cord and the extension of the abnormalities detected. This patient's MRI revealed that there was epidural hematoma present at the level of T8 - T10 causing spinal cord compression at level of T9.

In reality, diagnosis of intraspinal hematoma are often delayed due to it rarity and varied presentation; resulting in limited recovery. Patient with warfarin-related intraspinal hematoma present with triad of sudden, severe back or neck pain with or without radicular pain, followed by progressive motor and sensory deficit to complete paralysis over a few hours to a day and acute urinary retention (Hunderfund & Wijdicks 2009). In this

case, the initial presentation of back pain without detection of neurological deficit and the slow progression of the neurological deficits were responsible to the delay in diagnosis. A high index of suspicion in diagnosing intraspinal hematoma especially in patients on warfarin or other anticoagulant, presenting with back or neck pain with neurological deficit or urinary retention will minimize this risk.

There are no evidence-based guidelines or clinical trials to guide the acute management of intraspinal hematoma because of it rarity. Conservative management may be justified in patients with mild symptoms without progression (Harik et al. 1971). Warfarin-related intraspinal hematoma may progress slowly; early detection of this complication and early administration of treatment such as transfusion of FFP or administer vitamin K to reverse overwarfarinization may minimize the hematoma expansion and subsequent neurological sequelae (Inamasu et al. 2016). FFP remains the most widely used coagulation factor replacement product for urgent reversal of coumarin anticoagulation (Ageno et al. 2012). This patient was transfused with FFP and given IV Vitamin K to reverse the effect of overwarfarinization.

Surgical evacuation of hematoma is necessary to prevent permanent neurological damage. Patients who underwent surgical intervention within 72 hours of symptoms onset generally provide good prognosis (Pullarkat & Kalapura 2000). A meta-analysis also reported a good outcome in patients with an interval time from incident to operative less than 12 hours (Mukerji & Todd 2013). However, prognosis following surgery is highly dependent on the preoperative neurological status of the patient. Therefore, early detection and diagnosis is important for the initiation of subsequent management which are early reversal of prolonged INR and surgical intervention.

CONCLUSION

Intraspinal haematoma is a neurological emergency that requires prompt diagnosis. The risk of bleeding secondary to warfarin, although infrequent should be recognized and patients presenting with this condition should receive emergent reversal agent to correct the coagulopathy before surgical intervention. Due to the rarity of this pathology, atypical or delayed presentation may lead to missed or delayed diagnosis. Therefore, awareness of the subtle signs of spontaneous spinal epidural hemorrhage in the setting of no clear history of trauma should initiate appropriate imaging and intervention to reduce neurological complication and improve outcomes.

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REFERENCES

Ageno, W., Gallus, A.S., Wittkowsky, A., Crowther, M., Hylek, E.M., Palareti, G. 2012. Oral anticoagulant therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American

College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* **141**(2 Suppl): e44S-e88S.

Algarni, A.A., Mourad, M.M., Bramhall, S.R. 2015. Anticoagulation and antiplatelets as prophylaxis for hepatic artery thrombosis after liver transplantation. *World J Hepatol* **7**(9):1238-43.

Groen, R.J., Ponssen, H. 1990. The spontaneous spinal epidural hematoma: a study of the etiology. *J Neurol Sci* **98**: 121-38.

Harik, S.I., Raichle, M.E., Reis, D.J. 1971. Spontaneously remitting spinal epidural hematoma in a patient on anticoagulants. *N Engl J Med* **284**(24): 1355-7.

Heppner, P.A., Monteith S.J., Law, A.J. 2004. Spontaneous spinal hematomas and low-molecular-weight heparin. Report of four cases and review of the literature. *J Neurosurg Spine* **1**(2): 232-6.

Inamasu, J., Ito, K., Hattori, N., Hirose, Y. 2016. Warfarin-associated intrasponal haematoma. *Keio J Med* **65**(4): 74-7.

Leep Hunderfund, A.N., Wijdicks, E.F. 2009. Intramedullary spinal cord Hemorrhage (Hematomyelia). *Rev Neurol Dis* **6**(2): E54-E61.

Lisman, T., Bakhtiari, K., Pereboom, I.T., Hendriks, H.G., Meijers, J.C., Porte, R.J. 2010. Normal to increased thrombin generation in patients undergoing liver transplantation despite prolonged conventional coagulation tests. *J Hepatol* **52**(3): 355-61.

Lo, C.C., Chen, J.Y., Lo, Y.K., Lai, P.H., Lin, Y.T. 2012. Spontaneous spinal epidural hematoma: a case report and review of the literatures. *Acta Neurol Taiwan* **21**(1): 31-4.

Makris, M., van Veen, J.J., Maclean, R. 2010. Warfarin anticoagulation reversal: management of the asymptomatic and bleeding patient. *J Thromb Thrombolysis* **29**(2): 171-81.

Mukerji, N., Todd, N. 2013. Spinal epidural haematoma; factors influencing outcome. *British J Neurosurg* **27**(6): 712-7.

Pagano, M.B., Chandler, W.L. 2012. Bleeding risks and response to therapy in patients with INR higher than 9. *Am J Clin Pathol* **138**: 546-50.

Palareti, G., Leali, N., Coccheri, S., Poggi, M., Manotti, C., D'Angelo, A., Pengo, V., Erba, N., Moia, M., Ciavarella, N., Devoto, G., Berrettini, M., Musolesi, S. 1996. Bleeding complications of oral anticoagulant treatment : an inception-cohort, prospective collaborative study (ISCOAT). Italian Study on Complications of Oral Anticoagulant Therapy. *Lancet* **348**(9025)**:** 423-8.

Patrono, C., Rocca, B. 2007. Drug Insight: aspirin resistance-fact or fashion ? *Nat Clin Pract Cardiovas Med* **4**(1): 42-50.

Pullarkat, V. A., Kalapura, T., Pincus, M., Baskharoun, R. 2000. Intraspinal hemorrhage complicating oral anticoagulant therapy: an unusual case of cervical hematomyelia and a review of the literature. *Arch Intern Med* **160**(2): 237-40.

Stahl, R.L., Duncan, A., Hooks, M.A., Henderson, J.M., Milikan, J.W., Warren, W.D. 1990. A hypercoagulable state follows orthotopic liver transplantation. *Hepatology* **12**: 553-8.

Yu, J.X., Liu, J., He, C., Sun, L.Y., Xiang, S.S., Ma, Y.J., Bian, L.S., Hong, T.J., Tao, P.Y., Li, J.W., Li G.L., Ling, F., Zhang, H.Q. 2016. Spontaneous spinal epidural hematoma:a study of 55 cases focused on the etiology and treatment strategy. *World Neurosurg* **98**: 546-54.

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