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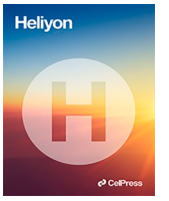

Case report

Spinal subdural hematoma as a complication of tenecteplase treatment for acute ischemic stroke: A case report

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ABSTRACT

Intravenous thrombolysis is an effective treatment for acute ischemic stroke. The ESO recommends that tenecteplase be used for thrombolytic therapy in stroke within 4.5h of onset. However, there are few reports on the complications of intravenous thrombolysis with tenecteplase in stroke, and spinal hematomas are rare. Herein, we report the first case of spinal subdural hematoma secondary to tenecteplase treatment for stroke. A 71-year-old male patient arrived at the stroke center because of left limb weakness that had persisted for 105 min. After intravenous thrombolysis with tenecteplase, the patient experienced unbearable pain in the neck and left shoulder, progressive limb weakness, and sensory disturbance. MRI revealed a spinal subdural hematoma of the cervical vertebrae, and the prognosis was poor after surgical treatment. Once patients develop pain around the spine with intravenous thrombolysis, physicians should be aware of the possibility of a spinal subdural hematoma and promptly perform MRI.

1. Introduction

Currently, the primary drug approved by the regulatory agency for intravenous thrombolysis of stroke is alteplase [1]. Tenecteplase is a thrombolytic drug approved by regulatory authorities for the treatment of ST-segment elevation myocardial infarction. Compared with alteplase, tenecteplase has the advantages of better pharmacodynamics and pharmacokinetics [2]. Recently, a series of studies focused on the use of tenecteplase for stroke treatment; there are few reports on related complications in this treatment. To the best of our knowledge, there have been no reports on the use of tenecteplase in the thrombolysis of stroke patients complicated with spinal hematoma. Herein, we reported a case of spinal subdural hematoma (SSDH) following thrombolysis with tenecteplase, and reviewed the related literature. This case is expected to improve physicians' understanding of this disease in the stroke thrombolysis group.

2. Case report

A 71-year-old male patient presented to the stroke center complaining of left limb weakness for 105 min. His weight was 64 kg, and he denied any history of diseases or specific medications except for hypertension. Neurological examination revealed mild dysarthria, left facial paralysis, and mild left hemiplegia. The fibrinogen level was 3.55 g/L, and other laboratory tests and the brain CT were unremarkable. A stroke was diagnosed. Considering that there were no contraindications for intravenous thrombolysis, tenecteplase 16mg (0.25 mg/kg) IV was administered for thrombolysis. Two hours and 20 min after thrombolysis, the patient complained of

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unbearable pain in the neck and left shoulder. Considering arterial dissection, the D-dimer level was tested at 4.72mg/L. No significant abnormalities were observed on echocardiography. The pain and left limb weakness worsened 2 h and 40 min after thrombolysis. There was no change on brain CT or large-artery stenosis on CTA. The patient's condition progressed rapidly, and he developed quadriplegia and experienced reduced pinprick sensation below the T2 level. MRI of the cervical spine revealed SSDH (Fig. 1a-d); hence, 1.0 g of tranexamic acid was administered intravenously for reverse coagulation; hematoma removal and decompression were recommended as soon as possible. At the request of the patient's family, the patient was transferred to the Third Hospital of Hebei Province for surgical treatment. Twelve hours after the occurrence of neck pain, the patient underwent laminectomy and hematoma clearance; however, we could not obtain the details of the surgery. After the operation, both upper limbs recovered, but the lower limbs remained immobile. Owing to financial constraints, the patient did not undergo follow-up rehabilitation treatment in the Department of Rehabilitation Medicine. At the 2-month follow-up, the patient's condition remained deplorable. He was still paraplegic and had complications, such as venous thrombosis of the bilateral lower limbs.

3. Discussion

Tenecteplase is a thrombolytic drug derived from alteplase via gene recombination. By changing the amino acids at positions T (103), N (117), and KHRR (296–299) of alteplase, thrombolysis of blood clots, resistance to plasminogen activator inhibitor 1, fibrin specificity, and half-life are significantly improved. This allows the drug to remain effective at a relatively low dose with a single

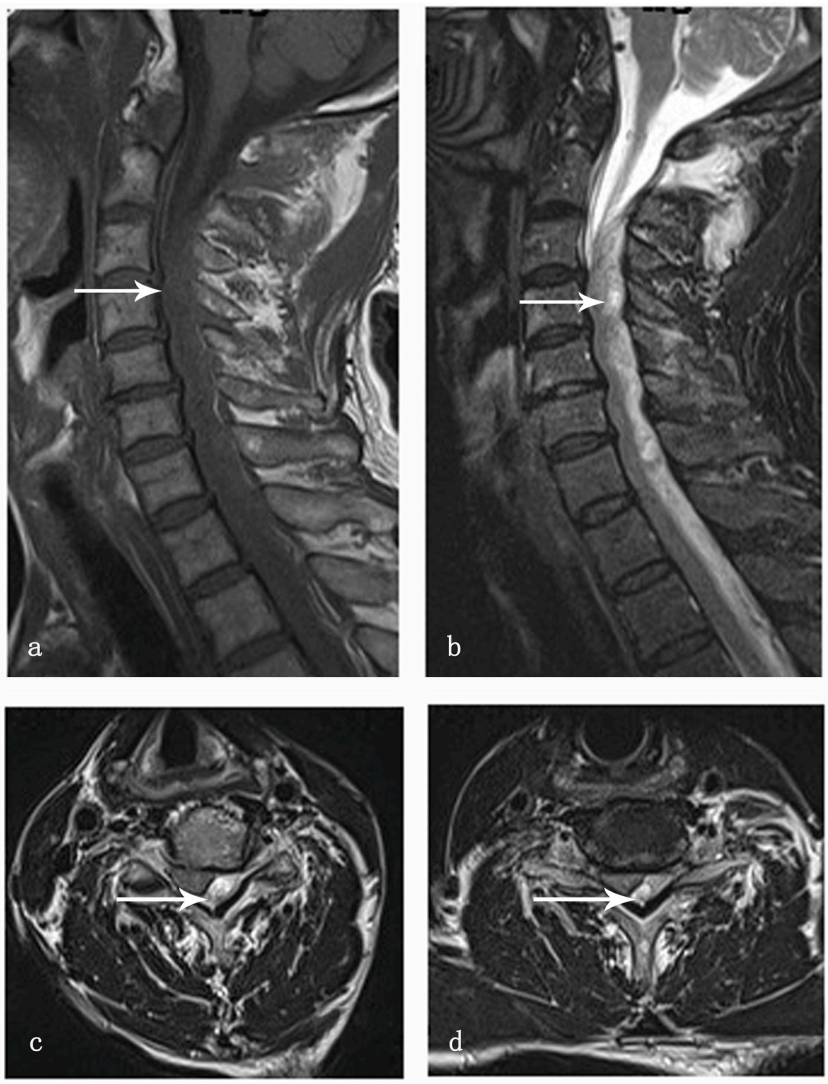

Fig. 1. Magnetic resonance images of the spinal cord. (ab): Sagittal MRI of Cervical spine. (a): the hematoma appears isointense on the T1-weighted image (arrow). (b): the hematoma is hyperintense on the cervical T2-weighted image (arrow); the spinal dura mater is hypointense on T2 imaging, which resembles a dark line. (cd): Axial MRI of the cervical spine; the hematoma exerts a mass effect on the spinal cord (arrows).

intravenous administration [2]. ESO recommends tenecteplase for thrombolytic therapy of stroke less than 4.5 h of onset [3]. Spinal hematoma is a rare complication of thrombolytic therapy. To date, only a few cases of alteplase and one case of tenecteplase complicated by spinal hematomas have been reported, as detailed in Table 1 [4–12]. However, we found no reports of SSDH secondary to tenecteplase use. The spinal epidural space is rich in venous plexus, whereas the subdural space does not contain veins; therefore, SSDH is rarer than spinal epidural hematoma (SEH). To the best of our knowledge, this is the first reported case of SSDH after tenecteplase thrombolysis for ischemic stroke.

The causes of SSDH include coagulation disorders, lumbar puncture, trauma, thrombocytopenia, infection, neoplasms, anticoagulation, vascular malformations antiplatelet therapy, etc [13,14]. No risk factors were identified in this patient, and we speculated that the coagulation mechanism of the patient was affected by the use of tenecteplase, which may have led to hematoma. The MRI of this patient showed a hematoma involving a long spinal cord segment, and the possibility of vascular malformations in the spinal canal could not be excluded; however, the patient did not complete a myelography examination.

Sudden pain in the affected spinal cord is the most common clinical manifestation of SSDH. Additionally, it can radiate along nerve roots. With the increase of hematoma, pain is aggravated. Pain often precedes other symptoms and is followed by varying degrees of spinal cord compression. When the spinal cord is compressed on one side, it can manifest as Brown-Sequard syndrome. Transverse spinal cord injury can also occur when the compression is severe, which may manifest as delayed paralysis of the limbs, sensory loss, and urinary and fecal incontinence. In this case, the patient first experienced tingling pain in the neck and shoulders, which progressed rapidly and led to quadriplegia and sensory disturbance. The sudden onset of pain around the spine may be a warning symptom of SSDH after intravenous thrombolysis, which has not been mentioned in the previous literature.

MRI is the preferred imaging modality for detecting SSDH. Moriarty et al. described the different characteristics of hematomas on MRI due to the changes of hemoglobin during different periods. In the hyperacute phase (<24 h), the hematoma appeared isointense on T1 and hyperintense on T2 weighted imaging. Subsequently, the T1 signal increased and the T2 signal gradually decreased. Finally, hyperintensity was observed at T1 and T2 in the late subacute phase (1–2 weeks). The spinal dura mater was hypointense on T2 imaging, similar to a dark line separating the hematoma from the epidural adipose tissue. The hematoma of SSDH is often covered by epidural adipose tissue, known as the 'Cap' sign, which is the main feature used to distinguish epidural from subdural hematoma. In addition, hematomas often have a mass effect on the spinal cord [15]. This case (Fig. 1a-d) is consistent with the MRI findings of a hematoma in the hyperacute phase.

There are currently no guidelines for the treatment of SSDH after thrombolytic therapy. Vastani et al. [16] found that cervical spinal SSDH, anticoagulation therapy, a high Domenicucci score, and bladder dysfunction were the main factors affecting surgical prognosis. They considered timely surgical treatment to be reasonable for patients with these risk factors. Joubert et al. [17] also supported the recommendation of timely operative treatment for patients with severe neurological impairment, believing that conservative treatment often has a poor prognosis for such patients and that the degree of neurological injury affects the prognosis. This patient had severe neurological deficits and a poor prognosis after surgical treatment, which is consistent with previous reports. Surgical option can be questioned in cases of post-IVT epidural hematomas, while this option is exceptional in intracerebral hematomas; hence, early detection is crucial.

4. Conclusion

We reported a case of SSDH after intravenous thrombolysis with tenecteplase in a patient with ischemic stroke. SSDH progresses rapidly and has a poor prognosis as a rare complication of thrombolysis with tenecteplase. Perispinal pain may be a warning symptom, and MRI is the first choice for examination. Furthermore, the degree of neurological injury affects prognosis.

Ethics statement

Written informed consent was obtained from the patient for participation in this case report and any accompanying images. The protocol was approved by the Ethics Committee of Xingtai Third Hospital. The ethical approval number was 2022-KY-22.

Table 1
Summary of cases of intravenous thrombolysis complicated with spinal hematoma.

Author, Year	Gender, Age	Disease	Drug	Grade	Position	Treatment	Prognosis
Sawin P D,et al., 1995 [4]	Female , 60	MI	Alteplase	Grade III	T8-11 , SEH	Surgery	Good
	Female , 68	MI	Alteplase	Grade III	C2-L2 , SEH	Surgery	Poor
Ron Liebkind et al., 2010 [5]	Male , 80	Stroke	Alteplase	Grade III	C6-T6 , SEH	Surgery	Poor
Cohen JE,et al., 1998 [6]	Male , 69	MI	Alteplase	Grade III	C1-T1 , SEH	Non-surgical	Death
Yeo LL et al., 2009 [7]	Female , 62	Stroke	Alteplase	Grade I	C4-7 , SEH	Non-surgical	Good
Baron EM et al., 1999 [8]	Male , 55	MI	Alteplase	Grade I	C2-6 , SEH	Surgery	Good
So-Hyum Kim et al., 2008 [9]	Female , 49	Stroke	Alteplase	Grade III	C7-T2 , SSDH	Surgery	Poor
Parr CJ et al., 2019 [10]	Female , 78	MI	Tenecteplase	Grade 0	C5-6 , SEH	Non-surgical	Good
Connolly ES et al., 1996 [11]	Male, 69	MI	Alteplase	Grade I	C5-6, SEH	Non-surgical	Good
Zafra Sánchez J,et al., 1997 [12]	Male, 58	MI	Alteplase	Grade I	T12-L3, SEH	Non-surgical	Good

Neurological function grade [13]: Grade 0: asymptomatic; Grade I: back pain, mild sensory, motor, and/or sphincter disorders; Grade II: mild paraplegia; Grade III: paraplegia. Myocardial infarction(MI), Spinal epidural hematoma(SEH), Spinal subdural hematoma (SSDH).

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Data availability statement

All data to support the conclusion have been provided in the article.

CRediT authorship contribution statement

Sisi Zhao: Writing – original draft. **Lingtao Tang:** Writing – review & editing. **Yanpeng Lu:** Investigation. **Yingyi Li:** Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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