CASE REPORT

Spinal Cord Infarction Following Transarterial Chemoembolization of Hepatocellular Carcinoma with Chest Wall Metastasis: A Case Report and Review of the Literature

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Spinal cord infarction (SCI) is a rare but detrimental complication following transarterial chemoembolization (TACE). The case report presented a case of hepatocellular carcinoma (HCC) involving the lateral chest wall for which the patient underwent TACE, targeted at the right ninth intercostal artery. After the intervention, the patient fully developed complete spinal cord syndrome immediately after TACE. Magnetic resonance images of the spinal cord showed abnormal hyperintense lesions on T2-weighted images involving the anterior and central part of the 9th to 11th thoracic spinal cord, compatible with SCI. Although corticosteroids were not administered, the patient's condition subsequently improved, being capable of walking with a gait aid. SCI after TACE is a possible disabling adverse event. To prevent this complication, the collateral vessels of the spinal arteries, such as the intercostal arteries, should be avoided. Furthermore, monitoring for the symptoms of SCI, especially in the first 24 hours after the intervention, should also be done in all TACE cases.

Keywords: Spinal cord injury; Spinal cord infarction; Transarterial chemoembolization; Hepatocellular carcinoma; Case report

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Hepatocellular carcinoma (HCC) is one of the most common gastrointestinal malignancies. For early stages of HCC, liver transplantation, hepatectomy, and radiofrequency ablation are the mainstay treatments[1]. Transarterial chemoembolization (TACE) is employed as a salvaging treatment for the intermediate stage of HCC and performed according to the Barcelona Clinic Liver Cancer approach[1]. Although, TACE provides great benefits, various complications can occur.

Spinal cord infarction (SCI) is one of the myelopathies caused by the occlusion of the anterior or posterior spinal arteries. The common causes of SCI are dissecting aortic aneurysm or post-aortic surgery[2]. Typically, the patients experience various symptoms of spinal cord syndrome such as back pain, paraparesis, and hypoesthesia of both legs with urinary retention within 12 hours after the culprit event. Given emergency condition, the diagnosis needs prompt clinical suspicion with emergency spinal magnetic resonance imaging (MRI)[3]. The typical MRI finding of SCI shows focal long hyperintensities involving the anterior part of the spinal cord on sagittal T2-weighted images, called 'pencil-like' hyperintensities, in conjunction with spinal cord swelling[2]. Medical revascularization with thrombolysis is the specific treatment for SCI. However, with the typical delay in diagnosis, the patient with SCI is commonly hindered from thrombolysis. Other treatment options for SCI such as lumbar drainage or corticosteroid are suggested but there is still no strong evidence of treatment benefit[3].

SCI is a rare detrimental complication of TACE. The authors reported one case of SCI following TACE and reviewed the previous case reports in the literature regarding this topic. This case report was

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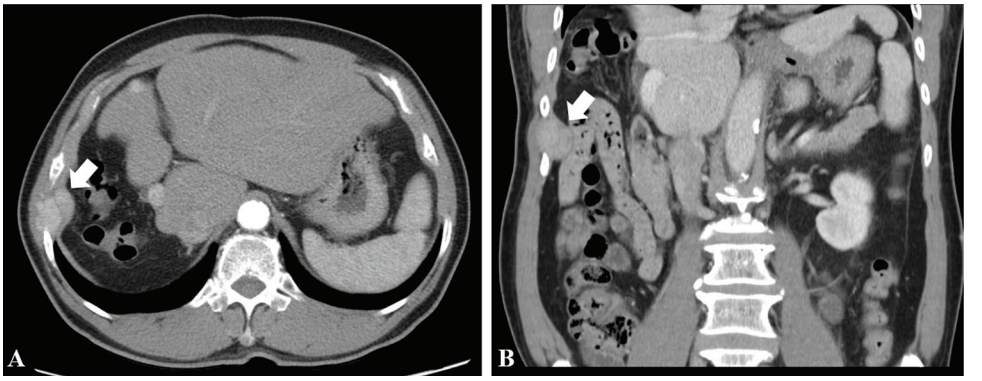

Figure 1. Axial (A) and coronal view (B) of contrast-enhanced CT scan showed an arterial enhancing nodule involving chest wall and peritoneum, sized 2.2 cm.

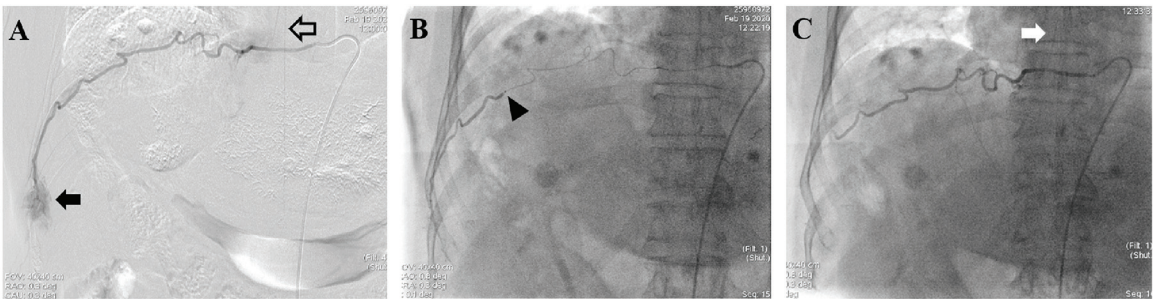

Figure 2. The angiography of the right 9th intercostal artery revealed hypervascular mass at the chest wall (black arrow), corresponding to the mass from CT scan (A). The anterior spinal artery originates from the proximal part of the intercostal artery (open arrow) (A). The tip of the microcatheter was placed at the distal part of the intercostal artery (arrowhead) (B). Post chemo-infusion image showed patent of anterior spinal artery (white arrow) (C).

approved as consent exemption by the Institutional Review Board.

Case Report

History and physical examination

A 63-year-old man with current history of essential hypertension, diabetes mellitus, and chronic hepatitis B infection with Child-Pugh A cirrhosis had developed HCC twelve years ago. The patient underwent right hepatectomy, two courses of radiofrequency ablations, and five times of TACE. He never had any serious complications following those treatments. Two months before the disabling event, a follow-up computed tomography (CT) scan of the abdomen showed two newly developed arterial enhancing nodules with rapid washout in the portovenous phase, about 1 cm each at segments IVb and III of the liver. In addition, a progressively enlarged arterial enhancing mass at the right lateral chest wall at the 10th to 11th intercostal levels was also noted (Figure 1). Diagnosis of recurrent intrahepatic HCC with right lateral chest wall metastasis was given. Consequently, a sixth TACE was scheduled for treatment of this condition.

The patient had no neurological deficit prior to this TACE. The angiographic findings demonstrated the middle and left hepatic arteries that supplied hypervascular masses in segments IVb and III. The other mass at the right lateral chest wall was fed by the right 9th to 10th intercostal arteries (Figure 2). TACE was performed as eight mL of 20-mg mitomycin-C in contrast media and iodized oil (Lipiodol®) was injected to both the middle and left hepatic arteries. After that, the right 9th to 10th intercostal artery was selected. This artery provided vascular supply to the tumor on the chest wall and gave the proximal branch to the anterior spinal artery. While injecting the embolic agent into its distal part, the demonstrated proximal arterial flow slowed down. Therefore, the procedure was halted due to the concern of the risk of SCI. Eventually, post-treatment angiography was performed, and the anterior spinal artery was still noted (Figure 2).

Immediately after the operation, the patient

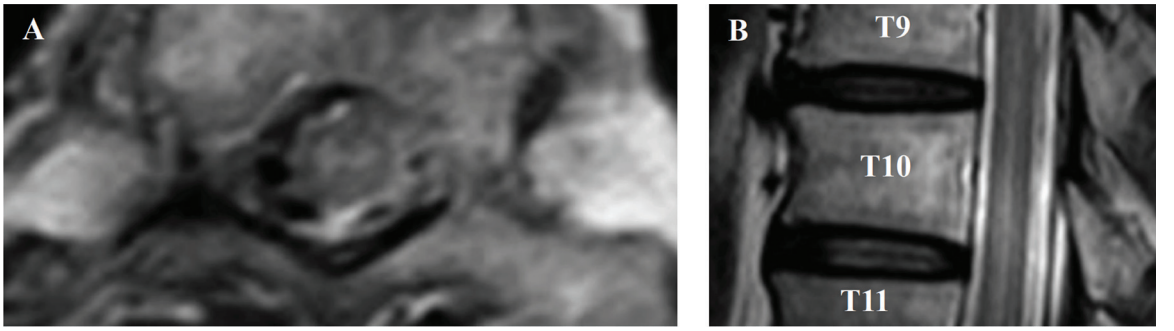

Figure 3. Axial T2-weighted magnetic resonance image of thoracic spine in level of T9 showed focal hyperintense lesion involving anterior and central aspect of spinal cord (A). Figure A showed magnified images of the affected spinal cord (A). Sagittal T2-weighted magnetic resonance image of thoracic spine in the correspondent level also showed linear hyperintense lesion involving anterior aspect of spinal cord resembling 'pencil sign' in T9-T11 level (B).

started noticing a poorly localized back pain with numbness from both legs to the umbilicus. He was incapable to move his legs a few hours later. Six hours after TACE, he experienced acute urinary retention requiring urinary catheterization. Neurological examination revealed hypotonia, hyporeflexia, and paraplegia of both legs. Pinprick and vibratory sensations were totally impaired in both lower extremities up to the umbilicus. Perianal sensation and sphincter tone were also diminished. These symptoms were compatible with SCI involved in T10 level.

Investigations

MRI of the thoracolumbar spine with gadolinium injection was done eight hours after TACE. It depicted a non-enhancing focal hyperintense lesion on T2-weighted at the anterior and central part of the spinal cord from the T9 to T11 level without any restricted diffusion (Figure 3). Due to thrombocytopenia, lumbar puncture was not performed to avoid the risk of spinal cord hematoma.

Differential diagnosis

1. SCI due to oil embolism
2. Transverse myelitis from chemotherapeutic agent
3. Localized vasculitis

Diagnosis

SCI due to oil embolism

Treatment and outcome

After discussing the risks and benefits of intravenous methylprednisolone with the patient, conservative treatment with rehabilitation was employed. Twenty-seven hours after TACE, he could minimally move his left foot. His legs recovered to Medical Research Council grade IV within two weeks, but he still needed a walker due to the persistence of spasticity. He was able to walk with a single cane two months later. However, his sensory deficit and bladder function remained unchanged.

Discussion

The present case report demonstrated SCI after TACE, which presented with a sudden onset of myelopathy following the intervention. The patient presented with complete cord syndrome with evidence of anterior spinal arterial occlusion from the MRI. After being treated solely by extensive rehabilitation without any specific treatment, the patient was capable of walking with a single cane within two months.

The authors conducted a systematic search for case reports or case series of SCI after TACE in the MEDLINE and EMBASE databases from their inception to April 2021. Eight cases from eight articles were included in the present review[4-11].

The extracted information is shown in Table 1. The cases comprised eight men and one woman, with a mean age of 67.6 years, ranging from 45 to 74. The onset of events ranged from immediately after TACE up to eight hours post-TACE. The clinical syndromes could be anterior, posterior, or complete cord syndrome depending on which spinal arteries were involved. Eight patients underwent spine MRI with the findings commonly revealed intramedullary spinal abnormalities.

Etiologies of the myelopathies after TACE were SCI due to oil embolism, localized vasculitis, or transverse myelitis from chemotherapeutic agents[5,7]. SCI due to oil embolism generally presents with hyperacute onset and rapid progression within 24

Table 1. Review of case reports of spinal cord injury after transarterial chemoembolization for hepatocellular carcinoma

Author	Country	Age (years)	Sex	Cirrhosis, CTP, causes	Extrahepatic involvement	Targeted vessel for TACE	Onset of SCI after TACE	Clinical at onset			Cord involvement defined by clinical features	MR findings	Level of involvement	Treatment	Treatment outcome at 1 to 2 months
								Numbness	Weakness (MRC grade)	Bowel/bladder involvement					
Chung et al., 1996	South Korea	50	Male	N/A, N/A	N/A	Right 11th and 12th intercostal arteries	Immediate	Y	Y (N/A)	N/A	Anterior cord	N/A	N/A	N/A	Improved
Kim et al., 2009	South Korea	65	Male	A, alcohol	N/A	Right 11th and 12th intercostal arteries	8 hours	Y	Y (Rt gr II, Lt gr IV)	N/A	Complete cord	HyperSI on T2W at intramedullary spinal cord	T9	Intravenous dexamethasone	Nearly completely improved
	South Korea	55	Male	A, HBV	Left 9th rib	Left 8th and 9th intercostal arteries	6 hours	Y	Y (Rt gr III, Lt gr III)	N/A	Posterolateral cord	HyperSI on T2W at intramedullary right posterolateral spinal cord	T9	Intravenous dexamethasone	Nearly completely improved
Tufail et al., 2010	United States	45	Male	N/A, HCV	N/A	Right inferior phrenic artery and right hepatic artery	8 hours	Y	Y (Rt gr III, Lt gr IV)	Y	Anterior cord	Unremarkable	N/A	Steroid, high dose	Markedly improved
Park et al., 2012	South Korea	57	Male	N/A, HBV	Right 7th rib	Right posterior intercostal artery	Immediate	Y	Y (Rt gr I, Lt gr I)	Y	Complete cord	Unremarkable	T6-T7	Intravenous methylprednisolone (1 g/day)	Improved
Zhang et al., 2013	China	68	Male	N/A, N/A	N/A	Right internal mammary artery	Immediate	Y	Y (Rt gr II, Lt gr V)	Y	N/A	Cord swelling without gadolinium enhancement	T5-T7	Intravenous methylprednisolone (80 mg/day)	Markedly improved
Bazine et al., 2014	Morocco	62	Female	A, HCV	N/A	Hepatic artery proper	Immediate	Y	Y (Rt gr II, Lt gr I)	Y	Anterior cord	HyperSI on T2W at intramedullary spinal cord	T10	Intravenous methylprednisolone (1 g/day)	Nearly completely improved
Hyun et al., 2020	South Korea	65	Male	N/A, N/A	N/A	Right 9th intercostal artery	N/A	N/A	Y (Rt gr 0, Lt gr 0)	N/A	N/A	N/A	N/A	Steroid, high dose	Markedly improved
Lin et al., 2020	Taiwan, China	74	Male	N/A, no	N/A	Right T10 and T11 intercostal artery and right hepatic artery	1 hour	Y	Y (Rt gr 0, Lt gr 0)	Y	Complete cord	Restricted diffusion	T9-T12	Intravenous methylprednisolone (1 g/day)	Unchanged

CTP=Child-Turcotte-Pugh score; gr=grade; HBV=hepatitis B virus; HCV=hepatitis C virus; HyperSI=hyperintense signal; Lt=left; MRC=Medical Research Council's scale; MR=magnetic resonance imaging; N/A=not available; Rt=right; SCI=spinal cord injury; TACE=trans-arterial chemoembolization; T2W=T2-weighted; Y=yes

hours. Spinal cord vasculitis frequently occurs with a more delayed onset of up to several weeks[12]. Lastly, chemotherapy-induced myelitis is also possible. However, the common agents are gemcitabine, cisplatin, and cytarabine, which are not routinely employed in TACE[13]. Since this case presented with a rapid onset and progression of myelopathy after TACE within 24 hours, SCI contributed by oil embolism was considered as the most likely etiology.

The major risk factor of SCI after TACE is performing interventions via intercostal arteries or the collateral vessels of spinal arteries, such as the inferior phrenic artery or internal mammary artery[5,8]. HCC with rib or chest wall metastases, creating vascular collateralization from the feeding arteries of the tumors to the spinal arteries, and a history of multiple prior TACEs are also the risk factors of SCI after TACE[5,9].

Until now, there is no management guideline for post-TACE SCI. Seven of the eight previous case reports of SCI following TACE were prescribed corticosteroids with variable benefit. There was a previously randomized controlled study that showed a favorable neurological improvement in patients with spinal cord injuries from trauma receiving high-dose methylprednisolone compared to patients receiving a placebo[14]. Subsequent meta-analysis study showed that high-dose methylprednisolone in the setting of spinal cord injuries from trauma did not contribute to neurological improvement and had multiple adverse effects such as gastrointestinal bleeding or serious infection[15]. Salvador de la Barrera et al.[16] retrospectively reviewed the prognosis and recovery of patients who suffered from SCI. In the study, the patient did not receive corticosteroid as an adjunctive therapy. They found that the factors associated with favorable outcome were a lower age and lower degrees of motor deficit at the first presentation[16]. Currently, there has been no evidence of high-dose methylprednisolone in a case of SCI from TACE. The improvement of symptoms might be influenced by the level of vascular occlusion, the natural course of SCI, the previous status, and the underlying vascular risk factors in each patient. Yet, high-dose methylprednisolone is likely to bring a beneficial effect in cases where chemotherapeutic agents have led to vasculitis of the spinal arteries or transverse myelitis[3].

The present case report is the first report of the patient with SCI following TACE that regained a favorable neurological outcome without treatment with corticosteroids. There are limitations in this

case report as the authors could not totally exclude SCI caused by vasculitis because lumbar puncture was not performed due to thrombocytopenia. Future studies regarding the role of corticosteroids or other treatments in SCI after TACE should be conducted to be able to provide the appropriate management for this complication.

Conclusion

SCI after TACE is a possible disabling adverse event. To prevent this complication, targeting vessels that connect to spinal arteries, such as intercostal arteries, should be avoided. Monitoring for the symptoms of SCI, especially in the first 24 hours after the operation, should be done in all TACE cases. Finally, until now, there has not been standard management of this condition. Although previous case reports showed an improvement of SCI with corticosteroid administration, the present case demonstrated a marked improvement with only rehabilitation management. Further studies in the management of SCI after TACE should be done to provide a suitable guide for treatment.

What is already known on this topic?

SCI is a rare but severe complication of TACE for HCC. There is no recommendation for treatment or prevention of this complication.

Until now, there is no evidence of benefit of corticosteroid in SCI after TACE. Previous case reports frequently prescribed corticosteroid despite adverse events from this agent.

What does this study add?

SCI following TACE for HCC could be prevented by avoiding collaterals of spinal arteries such as intercostal artery, inferior phrenic artery, or internal mammary artery as targeted vessels. Furthermore, monitoring for symptoms of SCI after TACE should be regularly employed in the first 24 hours after procedure for immediate management.

The present case report showed that although no corticosteroid was added, weakness after SCI following TACE could be improved, questioning the benefit of using corticosteroid in this complication.

Conflicts of interest

The authors declare no conflict of interest.

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