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Case Report

Acute carbon monoxide poisoning resulted in isolated cerebellar damage and secondary cerebellar atrophy

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Abstract: During the procedure of carbon monoxide (CO) poisoning, the craniocerebral injury mainly locates in the bilateral cerebral subcortical white matter, globus pallidus, or internal capsule; therefore, CO poisoning-resulted isolated large-area cerebellar damage and secondary extensive cerebellar atrophy is extremely rare. This study reported the clinical symptoms, signs, imaging features, diagnosis and treatment processes, and prognosis of one case of acute CO poisoning-resulted specific cerebellar damage.

Keywords: CO, poisoning, cerebellar atrophy, CT, hyperbaric oxygen

Introduction

Carbon monoxide (CO) is mainly released by the incomplete combustion of carbon-containing materials and has high toxicity; the brain tissues are extremely sensitive to the CO toxicity; during the procedure of CO poisoning, the brain tissues might occur extremely serious damage effects. The vast majority of the patients with CO poisoning would show abnormalities in the bilateral basal ganglia and cerebral cortex [1], and the typical common neuropathological changes mainly included the spotty bleeding in the white matter, degeneration and necrosis of the bilateral globus pallidus, ventriculomegaly, cortical sulcus broadening, or progressive demyelination in the cerebral cortex, hypothalamus, and hippocampus, etc. [2], which thus showed different abnormal imaging features in computed tomography (CT) or magnetic resonance (MR). However, CO poisoning can also cause the cerebellar lesions, although this is extremely rare [3-10]. This will bring great difficulties in differentiation and diagnosis of disease. In this study, we focused on introducing and analyzing the imaging features, clinical signs and symptoms, diagnosis and treatment processes, and prognosis of acute CO poisoning-induced isolated cerebellar damage and secondary cerebellar atrophy. The objective is to provide a reference for differentiation and diagnosis of this disease.

Case description

Patient: male, 49 years old, had no previous history of hypertension, diabetes, or cerebral infarction while had a long history of smoking. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of the Third Military Medical University. Written informed consent was obtained from participants.

On May 20, 2011, he inhaled a lot of smoke when repairing one machine in one smelting factory and then felt dizziness, headache, and malaise; he then independently relied on the corner for the rest; though he could not control his body, he had no coma, nausea, vomiting, convulsions, or blurred vision. About 40 minutes, his colleagues sent him a local hospital, physical examination: systolic blood pressure 190 mmHg, diagnosed as “acute CO poisoning and hypertension”. Therefore, he was performed atmospheric oxygen inhalation, blood pressure releasing, and symptomatic and supportive treatments (reported orally by his families while the details were not clear); the symptoms were not significantly relieved. On May 23,

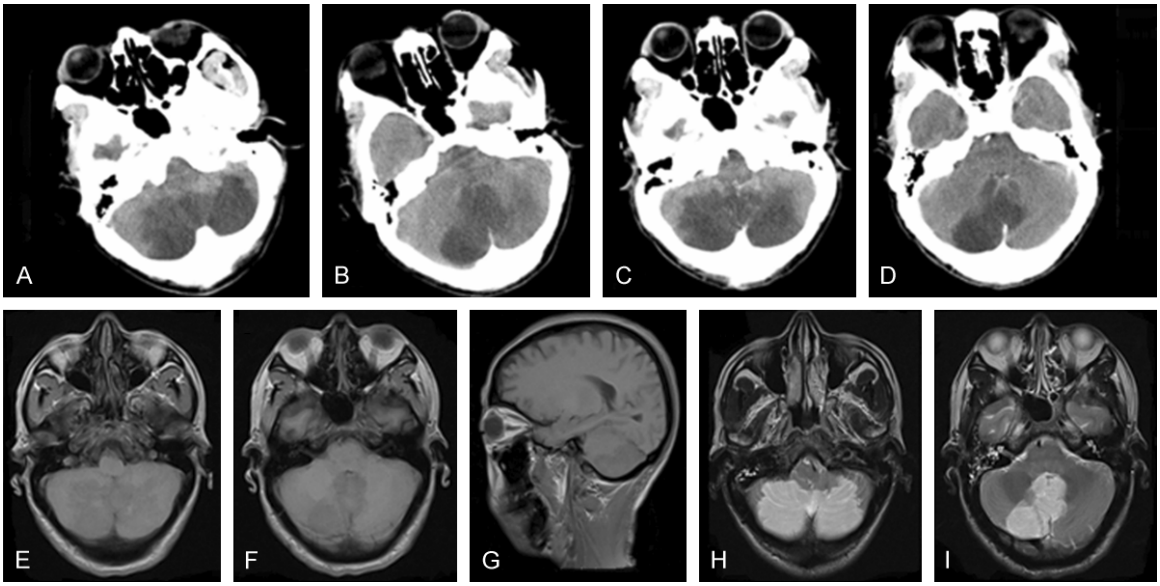

Figure 1. Cranial CT and MRI scannings for the first time after admission. Upper: (A, B) CT routine scanning, (C, D) Enhanced CT scanning: large sheet-like low density shadow in the cerebellar vermis and bilateral cerebellar hemispheres, the lesions' border were unclear, and the space-occupying effects were not obvious. The enhanced scanning showed no significant enhancement of the lesions. Lower: (E-I) Cranial MRI routine scanning: large sheet-like isometric T1 and T2 signals in the cerebellar vermis and bilateral cerebellar hemispheres, the lesions' border were unclear, and the space-occupying effects were not obvious.

2011, the conditions of this patient aggravated: his emotions were exciting, irritably, his judgment was reduced, and he could not stand independently, so he was transferred to our hospital. Physical examination on his admission (at 21:45 on May 23) revealed: T 36.7°C, P 87 beats/min, R 20 beats/min, BP 160/94 mmHg, bilateral pupils were of equal size and round, 3 mm in diameter, dull light reflex, excited, hyperphasia, with positive results of nose-pointing and rotation test; his abilities of disorientation, memory, calculation, and judgment were all decreased; the muscle tension of the right limb was slightly increased, and the rest neurological examinations exhibited negative results; the GCS score was 13 points. After admitted, the blood carboxyhemoglobin (COHb) concentration was tested immediately (at 21:55 on May 23), which showed "10.8%"; the cranial CT routine + enhanced scanning (at 23:35 on May 23) showed that "a large sheet-like low density shadow was seen in the cerebellar vermis and bilateral cerebellar hemispheres, the lesions' borders were unclear, the space-occupying effects were not obvious, and no significant enhancement could be seen in the enhanced scanning; combined with the disease history, this patient was considered as ischemia-hypoxia" (**Figure 1**, upper). The patient was immediately treated by continued middle- and high-flow oxygen inhalation, lowering intracranial pressure, nourishing nerves, promoting brain cell metabolism, controlling blood pressure and other symptom related methods. On May 24, the patient's was performed the hyperbaric oxygen (HBO) therapy [11, 12] (2ATA, once/d, 10 days/course for a total of two courses). On May 25, the patient's mental state was significantly improved, his headache was relieved, and the symptoms of excitement and hyperphasia disappeared. At 12:50 on May 25, the CT cranial angiography showed that: "the intracranial segments of the bilateral carotid arteries, vertebral artery, and basilar artery showed no obvious abnormality". The treatment was the same with before. At 08:01 on May 26, the cranial MR scanning showed "large sheet-like and isometric T1 and T2 signals in the cerebellar vermis and bilateral cerebellar hemispheres; the lesions' borders were less clear, and the space-occupying effects were not obvious; combining his disease history, the above results were consistent with the performance of ischemia-hypoxia" (**Figure 1**, lower); at 10:50, the color Doppler ultrasound of neck vessels showed "the blood resistance index of the right vertebral artery was increased while the rest showed no abnor-

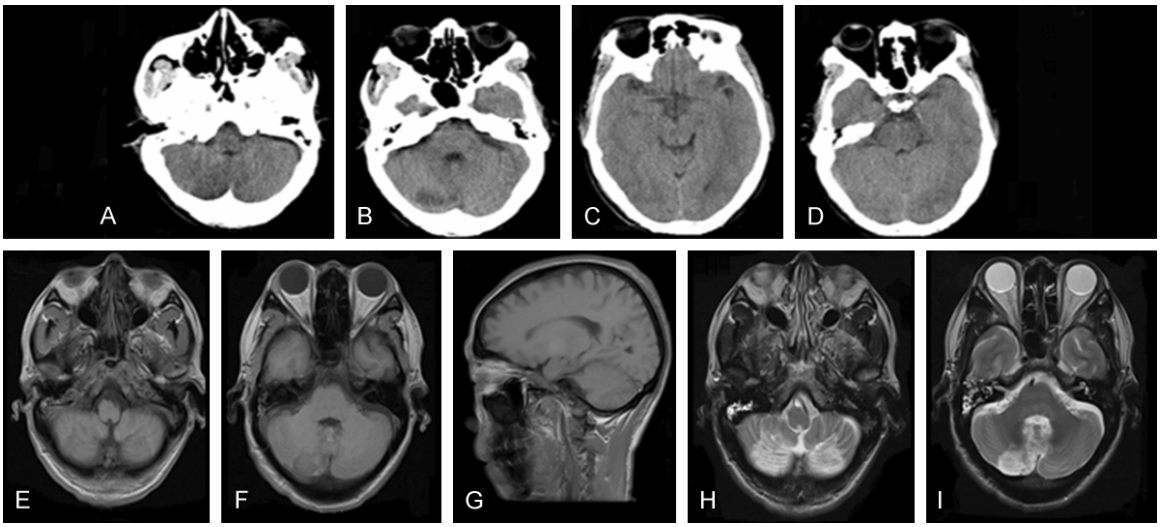

Figure 2. Cranial CT and MRI scannings for the second time after admission. Upper: (A-D) Cranial CT routine scanning: no significant abnormality. Lower: (E-I) Cranial MRI routine scanning: sheet-like isometric T1 and long T2 signals in the cerebellar vermis and bilateral hemispheres, while the ranges were narrowed than before.

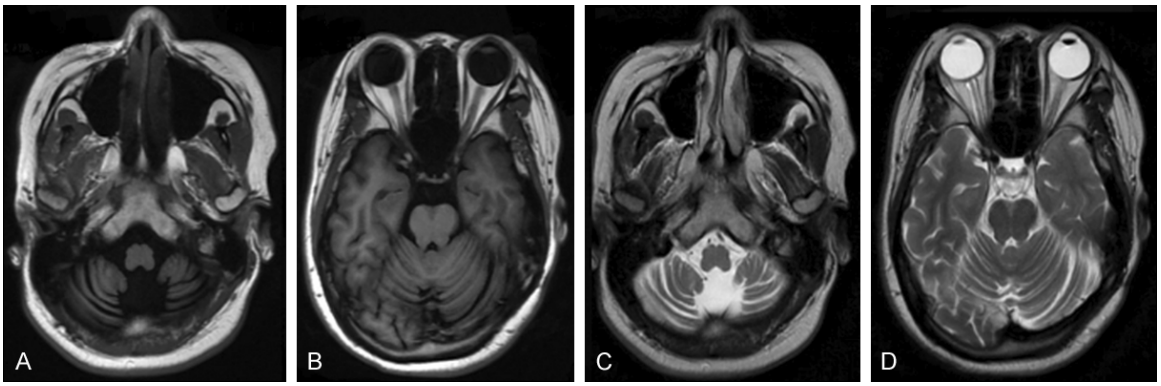

Figure 3. Reexamination of cranial MRI scanning 1 year after hospital discharge. (A-D) Brain MRI routine scanning: cerebellar atrophy, and the rest parts showed no obvious abnormality.

mality"; at 10:58, electrocardiogram (ECG) and cardiac function examination revealed that "mild regurgitation at the bicuspid valve and tricuspid valve, and the rest showed no abnormality"; at 11:15, the transcranial Doppler (TCD) showed " normal cerebral blood flow"; at 14:40, electroencephalograph (EEG) indicated "the a wave was suppressed, and EEG was mildly abnormal", so the original treatments were maintained, and the patient's conditions were gradually improved. At 12:44 on June 6, the cranial CT routine scanning showed "no obvious abnormality" (**Figure 2**, upper); at 08:48 on June 14, the cranial MR showed "sheet-like isometric T1 and long T2 signals in the cerebellar vermis and bilateral cerebellar hemispheres, and the ranges were narrower than the previous" (**Figure 2**, lower). After the treatment, the patient regained consciousness, did not complain special discomfort, had blood pressure fluctuations ranging 136~148/79-94 mmHg and negative nerve examination results; the GCS score was 15 points, and the patient could independently ambulate, but the steps were small, unsteady, and shuffling, exhibiting the performance of lower limb ataxia. On June 15, this patient was discharged. After that, he performed the functional recovery training step by step according to the medical order, with immediate follow-up for any discomfort. Our department continued the follow-up for 1 month after this patient was discharged and learned that, he had good compliance, and could persist the functional recovery training. However, the

recovery of the lower limb ataxia was not obvious. Therefore, this patient was suggested to review cranial MR once, which showed "cerebellar atrophy while no abnormality in the rest parts" (**Figure 3**). Due to certain objective factors, the follow-up was lost in the 20th month after the discharging, and the final follow-up showed that the lower limb ataxia was still not significantly improved, but the rest body parts had no special discomfort.

Diagnosis of CO poisoning

Combined with this patient's disease history, symptoms and signs, blood COHb concentration, and imaging features, he was preliminarily diagnosed as "acute CO poisoning and acute hypoxic ischemic encephalopathy", but CO poisoning-caused brain damages usually located in the bilateral brain cortical white matter symmetrically, globus pallidus, or internal capsule [11], and this rare patient only showed large cerebellar lesions; because he was old and had long smoking history, his blood pressure tested in the first-visit the hospital and our hospital was high, so it could not exclude the possibility of cerebral infarction. Therefore, the differentiation and diagnosis of this case should be started from the special imaging features, so we performed cranial MR and CT angiography so as to understand the situations of cerebral infarction and related vascular diseases. In addition, acute CO poisoning should also be identified from concussion, meningitis, diabetic ketoacidosis, hypoglycemia, anemia, Aspen syndrome, or other poisoning caused coma. Through blood routine assay, blood biochemistry, ECG, TCD, cranial CT angiography, and other tests and inspections showed no signs of the relevant organic diseases including cerebral infarction; furthermore, EEG and cranial MRI features supported the diagnosis of CO poisoning caused brain damage, so "acute CO poisoning caused hypoxic-ischemic encephalopathy" could be clearly diagnosed.

Significance of COHb

The detection of blood COHb is one valuable diagnostic indicator, especially in the acute phase of CO poisoning, which could provide the most direct evidence for the diagnosis and classify the severity grade. However, the blood specimen should be sampled in time because the blood COHb could be reduced to the normal level when separated from CO exposure for more than 8 hours, and it might display non-parallel relationship with the clinical symptoms [12]. Since the first-visit hospital of this patient lacked the related testing equipment, this patient's blood COHb could not be detected in time, and it had dropped close to the normal range (3%-10%) [12] when transferred to our hospital, so an important reference index was lost.

Comparison of CT and MR sensitivity

After the treatment, this patient's cranial CT and cranial MR were reviewed in our department during his hospitalization period; however, the features of these two inspections were totally different: CT showed no obvious abnormality while MR still exhibited obvious lesions, although the range was significantly reduced than before, it once again proved that the MR sensitivity was higher than CT in diagnosing CO poisoning caused encephalopathy [11].

Treatment of acute CO poisoning

When acute CO poisoning-caused neurological damages appeared, the as-early-as-possible HBO therapy was recommended in the guidelines [11, 12]. However, despite that HBO had been used for acute CO poisoning for several decades, there still existed controversies currently, and whether the patient with CO poisoning should be given the HBO treatment and what was the best HBO protocol had not reached common understanding [13]. Regarding the patient in this study, because of the limited conditions in the patient's first-visit hospital, no HBO treatment was performed in time, so the HBO treatment was delayed for nearly four days; even though, when the patients received the HBO treatment, the symptoms were still improved significantly. Clinical evidence suggests that the HBO therapy could prevent the CO-induced cerebral lipid peroxidation, and through confronting the adhesion of leukocytes inside the microcirculation, it could improve ischemia-reperfusion injury [14, 15]. Therefore, we thought that such patients should be implemented the HBO therapy as early as possible, but it could not give up the HBO treatment because the treatment time was delayed. The patient exhibited significant clinical improvements after the aforementioned treatment. So, no hormone therapy was administrat-

ed like most other literatures, and the hormone therapy was not recommended as the regular use either in Chinese guideline or in the American guideline [12].

Prognosis-secondary cerebellar atrophy

After the patient's conditions were significantly improved and the patient was discharged, considering that the secondary encephalopathy might occur during the false-cure period, which was normally within 2-60 days after successfully rescued and resuscitated, in approximately 3-30% of the patients with CO poisoning caused consciousness disorders [16], this patient was still maintained the telephone follow-up after his discharging. Throughout the whole follow-up course, the patient did not appear the secondary encephalopathy, and his conditions were continuously improved; however, the symptoms of lower limb ataxia showed no significant relief, and we analyzed that it might be caused by the post-CO poisoning secondary extensive cerebellar atrophy. Such secondary cerebellar atrophy after CO poisoning was extremely rare, Yang and Jeon once reported the similar case [3], but partial clinical data were lost. Whether the occurrence of the secondary cerebellar atrophy in this patient was related with the delayed HBO therapy still remained to be further studied.

Discussion

CO is colorless, odorless, and highly toxic, and its affinity with the hemoglobin is 200-300 times bigger than O_2; after inhaled, it would immediately bind with the hemoglobin and form COHb; however, the dissociation rate of COHb is only 1/3600 of oxyhemoglobin. COHb not only could not carry oxygen but also would affect the dissociation of HbO_2 and hinder the release and transmission of O_2, thus resulting in severe hypoxemia [4], but this is not the only mechanism of CO poisoning. In recent decades, the mechanisms of CO poisoning have been continuously improved, and lots of theories such as lipid peroxidation, cellular toxicity, oxygen free radical injury, immune-mediated damage, or secondary inflammation have been proposed, which explained the occurrence and development processes of CO poisoning from different angles; nowadays, the generally accepted theory is that the damaging effects of CO poisoning were the co-results of tissue hypoxia, ischemia-reperfusion injury, and CO direct interaction-mediated toxicity [5]. Because the brain tissues are most sensitive to CO poisoning damage, especially the hypoxia, the brain tissues would be the first affected and the most seriously damaged [6]. Typically, the most common site involved was the basal ganglia nuclei, and it was considered to be related with that this area was mainly supplied the blood by the perforating branch artery and the collateral circulation was not rich [7]. In the case of this study, the patient exhibited isolated extensive cerebellar damage and secondary diffuse cerebellar atrophy, which was extremely rare in clinics. Some scholars believed that CO poisoning caused cerebellar lesions were mainly the hypoxic injuries, and the vulnerable parts mainly located at the edge of the regions blood-supplied by the anteroinferior cerebellar artery and posteroinferior cerebellar artery. It was once reported that when CO poisoning caused cerebellar lesions, it might be accompanied with the damages in many other brain parts, especially on the superior cerebral tentorium [8, 9], but in this case, the patient showed the isolated cerebellar diffuse lesions, and the structures on the superior cerebral tentorium did not show any abnormal radiographic change from the beginning to the end, nor did the corresponding clinical symptoms and signs appear. Stephen et al. [10] once reported the case with CO poisoning caused isolated cerebellar damage, but no long-term follow-up was performed towards the prognostic situations, nor were the changes of the secondary cerebellar atrophy observed. Yang and Jeon [3] once reported the case of CO poisoning caused cerebellar atrophy, but most clinical data was lost; meanwhile, he thought [3] that CO caused isolated cerebellar damage was normally seen in chronic poisoning process, but this case was a case with acute poisoning and acute onset. Velioglu [9] thought that the patients with CO poisoning caused cerebellar injury had much more severe illness, but the patient in this study only showed mild consciousness disorder in the early stage of acute poisoning; after a standardized comprehensive treatment (even it had already been delayed for nearly four days), the patient's symptoms were obviously improved, and he recovered faster; despite the emergence of secondary cerebellar atrophy, no delayed encephalopathy occurred; except for the slow improvement of the symptoms of lower limb ataxia, other symptoms and signs basically returned to the normal, and the prognosis was acceptable.

Conclusions

The patient with acute CO poisoning caused isolated cerebellar injury mainly exhibited the lesions in the cerebellar vermis and large areas in bilateral cerebellar hemispheres, but the lesions were not limited in the cortex; after the treatment, the secondary cerebellar atrophy occurred. Because CO poisoning caused cerebellar damage was extremely rare, only relying on the existed clinical researches would be difficult to predict under what conditions could CO cause cerebellar injury or isolated injury, and it would also be temporarily difficult to know the susceptible factors. The CO poisoning caused symptoms and signs were uncertain and nonspecific, so their accompanied imaging features were also diverse; when facing the similar case in this study, we should perform comprehensive analysis and take the possibility of CO poisoning into account for the differentiation and diagnosis so as to avoid misdiagnosis. CT and MR were important imaging means, and the MR sensitivity was higher than CT, thus it could be helpful for the prognosis and follow-up observation. Meanwhile, it should also be emphasized that the HBO therapy might not reverse the nerve damages, but it did relieve the clinical symptoms quickly and efficiently. The pathogenesis of CO poisoning caused secondary cerebellar atrophy was still not entirely clear, and there had been no clear evidence-based preventive measure. So, how to better prevent and treat CO poisoning caused secondary brain atrophy still remained to be discussed through thorough clinical and basic researches.

Disclosure of conflict of interest

None.

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