

Case Report

Case of heterotopic ossification after carbon monoxide intoxication

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Abstract: Purpose: The aim of this study was to examine gait impairment along with masses in the hip joint caused by heterotopic ossification (HO) after carbon monoxide (CO) intoxication. This present study reports a patient with these symptoms after CO intoxication. Case report: A 36-year-old male geological explorer developed masses in the hip joints and HO after CO intoxication. Plain film, three months after intoxication, indicated HO on the bilateral hip joints. After three months of ineffective rehabilitation, with progressing impairment, an excision of HO was performed. Another plain film, 10 months after the operation, revealed no focal recurrence. Conclusion: HO is a rare complication of CO intoxication accompanied by gait impairment and masses in the hip joints. Excision is an effective option to improve the range of joint motion.

Keywords: Carbon monoxide intoxication, heterotopic ossification, hip joint

Introduction

Carbon monoxide (CO) is a product of the combustion of organic matter under conditions of restricted oxygen supply, preventing complete oxidation to carbon dioxide (CO₂). CO intoxication is typically caused by inhaling too much CO. Large exposure can result in loss of consciousness, arrhythmias, and even death [1]. It can occur accidentally or as a method of suicide. Acute or delayed neurological sequelae may occur in up to 50% of poisoned people within 2 to 40 days [2].

Heterotopic ossification (HO), also known as heterotopic bone formation, is the presence of bone in the soft tissue where bone normally does not exist. It is frequently seen with musculoskeletal trauma, spinal cord injuries, or central nervous system injuries. HO may commonly occur in cases of musculoskeletal trauma. The other common traumatic form of HO, known as posttraumatic neurogenic HO, occurs after nervous system injuries in patients, usually without direct trauma to soft tissue where bone formation will occur. The precise mechanisms

by which the effects of CO are induced upon bodily systems are complex and not yet fully understood [3]. Although it has been hypothesized that switching to anaerobic metabolism may play a crucial role in osteogenic formation, published literature regarding HO after CO intoxication is rare [4]. The current study reports a 36-year-old man with HO around the bilateral hip joints after CO intoxication. Since he had no remarkable medical history prior to CO intoxication, it was suggested that this condition was associated with the development of HO.

Case report

This study reports a 36-year-old male geological explorer that had engaged in independent daily activities before warming himself by burning charcoal in a relatively enclosed tent in Tibet in Western China. Nearly eight hours passed before the patient was discovered unconscious the next morning. He was immediately sent to the local hospital (People's Hospital of Tibet Autonomous Region). At the time of admission, elevated carboxyhemoglobin levels (32.7%), metabolic acidosis (pH = 7.12), oxygen satura-

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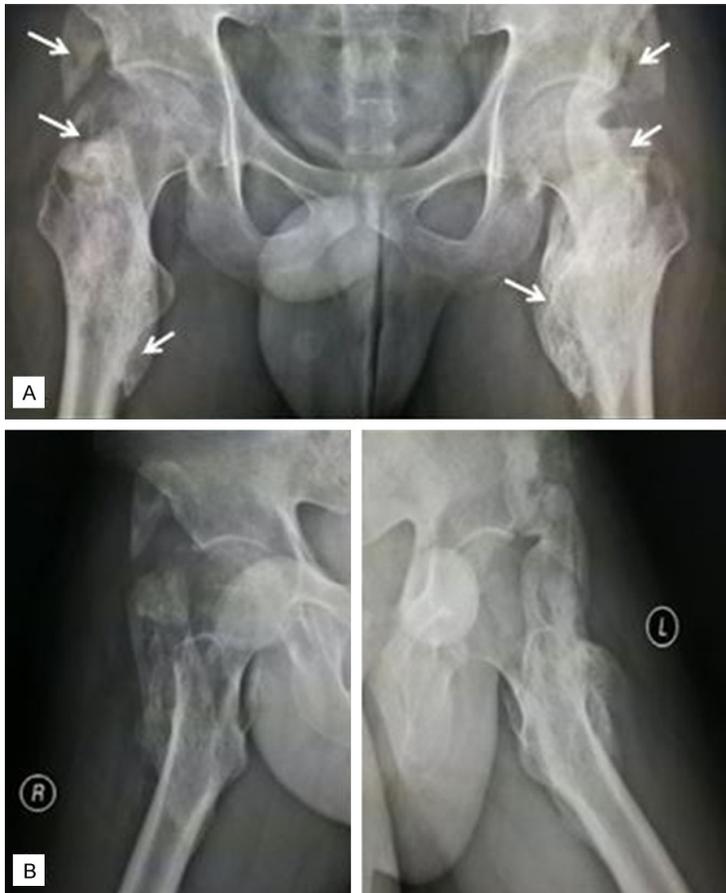


Figure 1. X-ray films obtained three months after CO intoxication demonstrated calcification in both pelvic regions (A, white arrows). Firm bridging from the anterior superior iliac spine to the lesser trochanter of the femur in the left pelvic region and from the anterior inferior iliac spine to the lesser trochanter of the femur on the right side was found (B).

tion (65%), creatine phosphokinase (CPK, 6458 U/L), aspartate aminotransferases (225 IU/L), and alanine transaminase of (102 IU/L) were detected. Follow up serum CPK one day later revealed a level of 4351 U/L. Three days later it was 946 U/L. CO intoxication was diagnosed based on laboratory tests and history. The patient was unconscious in the Intensive Care Unit for 35 days. In the first few days after regaining consciousness, he was unable to move his extremities. Almost 25 days later, he had gradually regained fine coordinate movements in his arms but not the legs.

Three months later, after regaining consciousness, he still experienced limitations in his hip joints and resulting loss of function. Additionally, growing masses were discovered in both sides of the proximal thighs. Cranial nerve examinations were normal. Based on the Medical Re-

search Council (MRC) scale, he had muscle strength of M4 in both upper extremities and M3 in the lower extremities. He was able to flex his hips with a range of motion of 0°~30° on the left side and 0°~45° on the right side. Adduction of the thighs was moderately limited. Muscle tonus was normal in the lower extremities. Sensation to pinprick and joint position sense was normal. Cerebellar function testing was normal except for the heel-to-shin test, he was unable to flex his hip joints as required. Babinski's sign was not elicited. Dystonia, tremors, chorea, and rigidity were not noted. Most laboratory tests were normal, including complete blood counts, fasting blood glucose, serum lactate and pyruvate, erythrocyte sedimentation rate, serum calcium and phosphate, myoglobin, and CPK. Alkaline phosphatase levels were 215 U/L. Repeated x-ray films revealed the development of a Grade C HO based on the classification of Schmidt and Hackenbroch for heterotopic ossification [5] (**Figure 1; Table 1**).

Two days after diagnosis of HO, surgical excision of HO was performed. During the operation, ectopic bones were removed through a conventional Smith-Petersen approach. Firm bridging from the anterior superior iliac spine to the lesser trochanter of the femur and from the anterior inferior iliac spine to the lesser trochanter of the femur was found on the left and right sides, respectively. A small piece of calcification close to the wing of the left ilium was not removed due to excessive bleeding during the operation, with the consideration that it would not theoretically hinder movement of the hip joint (**Figure 2**). Marked passive improvement was immediately obtained after removal. NSAID treatment to prevent the recurrence of HO and improve flexion of the hips began the next day. Upon physical examination on the last follow up ten months later, strength was scored at M4

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Table 1. Classification of Schmidt and Hackenbroch for heterotopic ossification [5]

Region or Grade	Description
Region I	Heterotopic ossifications strictly below the tip of the greater trochanter
Region II	Heterotopic ossifications below and above the tip of the greater trochanter
Region III	Heterotopic ossifications strictly above the tip of the greater trochanter
Grade A	Single or multiple heterotopic ossifications <10 mm in maximal extent without contact with the pelvis or femur
Grade B	Heterotopic ossifications >10 mm without contact with the pelvis but with possible contact with the femur; no bridging from the femur to the proximal part of greater trochanter, with no evidence of ankylosis
Grade C	Ankylosis by means of firm bridging from the femur to the pelvis



Figure 2. Plain radiograph, one day after surgical excision, showed that calcification in the right pelvic region was completely removed. A small piece of calcification close to the wing of the left ilium was not removed (arrow).

while hip residual flexion and external rotation persisted at 30°. The patient was able to walk freely without assistance but still had limitations in flexion, especially on the left side. He confirmed that he was able to ride and swim. Repeated plain films revealed no focal recurrence (**Figure 3**).

Discussion

HO, in the soft tissue, often develops in patients with musculoskeletal trauma, traumatic brain injuries, severe neurologic disorders, severe burns, and spinal cord injuries, most commonly around the hips [6]. Loss of joint mobility and resulting loss of function are principal complications of HO. It is uncommonly seen in patients

with non-traumatic neurological conditions, such as long-term coma or neuromuscular blockade, while the pathogenesis remains poorly understood [7, 8]. HO developed in the patient as a complication of CO intoxication without any of the abovementioned conditions. Motor deficit following HO in the skeletal muscle has been reported in a case, in which the patient attempted suicide by burning charcoal in an enclosed room [4]. The present patient underwent a similar process but endured a much longer period of unconsciousness.

HO is the result of pathologic recruitment of local and distant circulating cellular precursors. Among local microenvironments, oxygen tension is one of the factors impacting bone formation

[9]. It has been reported that HO of the muscles is triggered by ischemia/reperfusion injuries at the time of surgery, suggesting that hypoxia may play an important role in HO formation [10]. A distinctive vascular pattern occurs within HO that coincides with the lesion's ossification and maturation. Angiogenesis and osteogenesis are coupled processes in HO [11]. Previous research has indicated that hypoxia-inducible factor 1-alpha (HIF-1 α) is a key transcriptional regulator of the cellular response to ischemia through stimulation of vascular endothelial cell precursors [12]. Moreover, osteoblasts play a regulatory role in angiogenesis as sensors of hypoxia, likely triggering blood vessel formation in osteogenesis by activating hypoxia-inducible factor alpha (HIF- α) pathways

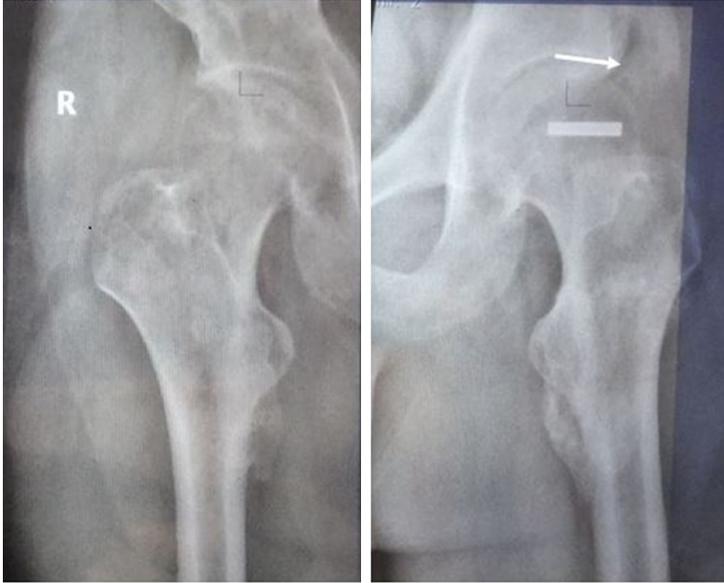


Figure 3. Repeated X-ray film at the last follow up showed no focal recurrence in both pelvic regions, with no expansion of calcification in the left pelvic region (arrow).

[13]. Therefore, in the present patient, it is likely that hypoxia in soft tissues of the hips, caused by CO intoxication, induced angiogenesis, leading to osteogenesis, followed by ossification.

It has been estimated that HO is more likely to develop in areas of high metabolic rates, such as the quadriceps, which are more vulnerable to hypoxia [4]. On the other hand, clinical signs and symptoms of HO may appear as soon as three weeks after musculoskeletal trauma, spinal cord injuries, or other precipitating events. Accordingly, attention must be paid to those that have been unconscious for a long time after CO intoxication to detect the presence of early stage HO. In the present case, HO was not diagnosed in the local hospital until masses in the hips were found by examination. As a result, prophylaxis was not started at an early stage in this patient. There is a consensus that radiation and NSAID therapy are both effective methods of prophylaxis. Hence, it might be helpful to detect HO at an early stage using plain radiographs, which are low cost and relatively easily obtained. Considering patients with positive results as candidates for prophylaxis treatment may decrease subsequent risks of HO.

Although the definition of complete bone maturation has remains inconsistent in the litera-

ture, surgical excision is an effective option for treatment of HO. It should be considered an option for patients with functional deficits resulting from the disorder. In the present patient, the proximal part of HO next to the wing of the left ilium was not removed due to excessive bleeding, with the consideration that it would not hinder movement of the hip joint theoretically during the procedure. In fact, at the last follow up 10 months post-surgery, the maximum degree of the left hip joint was no more than 70°. This study ascribes this restriction to incomplete HO excision around the area. No femoral neck fractures, femoral head osteonecrosis, or expansion or recurrence of HO were found according to follow up plain film. Thus, complete excision or major exci-

sion should be performed in such cases. Furthermore, complete removal of the HO would be preferable.

In summary, this present report recognizes CO intoxication as a rare non-traumatic cause of morbidity after HO. Surgical excision of HO might be an effective option, improving limitations in patients with functional deficits resulting from this disorder.

Disclosure of conflict of interest

None.

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