

# Heterotopic Ossification Induced Autonomic Dysreflexia in Spinal Cord Injury: A Case Report and Review of the Literature

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## ABSTRACT

Spinal cord injury is a devastating neurological condition that results in numerous complications. We present a case of a 17-year-old male who sustained a gunshot wound to the neck, resulting in a complete spinal cord injury at T1 and a left brachial plexopathy. He developed sudden onset of hypertension and facial flushing, consistent with autonomic dysreflexia. Further evaluation suggested that his autonomic dysreflexia was triggered by severe bilateral hip heterotopic ossification (HO). This case report emphasizes the importance of recognizing HO as a trigger for autonomic dysreflexia. Raising awareness about HO and its imaging findings can broaden the differentials for potential triggers of autonomic dysreflexia in individuals with spinal cord injury.

**Keywords:** Spinal cord; Autonomic dysreflexia; Plexopathy; Heterotopic ossification

## Introduction

Spinal cord injury (SCI) is a devastating neurological condition that results in impaired motor and sensory functions at and below the level of injury. Following SCI, numerous medical complications can develop, including heterotopic ossification (HO). HO refers to the pathological formation of bone within muscles and adjacent joints<sup>1</sup>. It is commonly observed as a complication following SCI, traumatic brain injuries, burns, and major orthopaedic surgeries. The incidence of developing HO ranges from 15 to 30% in cases of combined SCI and polytrauma. Clinically significant HO, characterized by restricted ROM that impacting function, occurs in approximately 10-20% of cases, with 5-8% progressing to ankylosis<sup>2</sup>.

HO often presents with painful, swollen joints and limited joint range of motion (ROM). We present a case of thoracic SCI from a gunshot wound that developed autonomic dysreflexia (AD), and later it was found his AD was triggered by HO. This case highlights the importance of awareness and management of complications related to SCI.

## Case Presentation

A 17-year-old male sustained a gunshot wound to the neck resulting in a C6 transverse process fracture, C7 fracture, and retained bullet fragments at T1 to T2, leading to a complete spinal cord injury (SCI) at T1 and a left brachial plexopathy. His

injuries were treated conservatively with a spinal orthosis. He was subsequently transferred to an inpatient rehabilitation unit, remaining paraplegic with no sensory or motor preservation at and below T1.



**Figure 1:** Pelvic X-ray. Evidence of soft tissue calcification/ossification around bilateral hip joints, indicating severe heterotopic ossification (HO).

At two months post-injury during his rehabilitation unit stay, he was noted to have elevated blood pressure (BP) at 200/120mmHg and facial flushing during the passive ranging of his lower extremities. These symptoms were suggestive of autonomic dysreflexia (AD). Common triggers for AD, including bladder distention, urinary tract infection (UTI), or stool impaction, were excluded. Of note, patient was found to have bilateral swollen hip joints with limited passive range of motion (ROM). A pelvic X-ray and pelvic CT were therefore performed (**Figure 1 and Figure 2**). The pelvic X-ray (**Figure 1**) showed evidence of soft tissue calcification/ossification around bilateral hip joints, indicating severe heterotopic ossification (HO). The pelvic CT (**Figure 2**) in coronal view similarly depicted heterotopic ossification involving bilateral hip joints.



**Figure 2:** Pelvic CT. CT in coronal view similarly depicted heterotopic ossification involving bilateral hip joints.

Further laboratory investigations revealed elevated alkaline phosphate (ALP) at 213 units/L (normal range 35-126 units/L) and a mild elevation in C-reactive protein (CRP) at 4.9 mg/dl (normal range:  $\leq 0.5$  mg/dl). Calcium and phosphate levels were within normal limits. ALP levels were regularly monitored, peaking at 3 months post-SCI, and gradually normalizing by 5 months post-SCI. Due to the functional limitations caused by HO

and its association with frequent AD, the patient was referred to Orthopaedic Surgery for consideration of surgical resection.

## Discussion

The underlying mechanisms driving HO formation remain incompletely elucidated. It is generally understood that the process is initiated following a simultaneous central and peripheral injuries, which stimulate bone formation at the site of peripheral injury through endochondral ossification<sup>3</sup>. SCI prompts the release of osteogenic and inflammatory factors. The influx of these factors instigates the differentiation of osteoprogenitor cells (OPCs) into fibroblasts, mediated by fibroblast growth factors (FGFs). This influx also induces angiogenesis, leading to increased oxygen tension, which in turn prompts OPC differentiation into chondrocytes. These chondrocytes undergo hypertrophy and generate a cartilage matrix, providing a structural scaffold for blood vessels formation, osteoblast proliferation and differentiation, and ectopic bone formation<sup>1</sup>.

Joints frequently affected in SCI are the hip, followed by the knee, the shoulder, and the elbow<sup>1,2</sup>. Typically, HO most often develops between 1-6 months post SCI, with peak incidence at 2 months<sup>4</sup>. Risk factors of HO formation include male gender, smoking, complete injury, presence of pneumonia, pressure injuries, urinary tract infections, and severe spasticity<sup>5</sup>. Clinical signs of HO include joint and muscle pain, paraesthesia, tissue swelling in the involved region, fever, and restricted ROM in the affected joints. AD is a common emergency complication of SCI characterized by a sudden increase in blood pressure triggered by peripheral stimulation, such as bladder distention<sup>6</sup>. This case is distinguished by the notable presence of severe bilateral hip HO, emphasizing the importance of recognizing HO as a potential trigger for autonomic dysreflexia (AD).

Plain radiographs are frequently used for detecting HO. The advantages of radiographs include the low cost and relative ease of acquisition. However, they have limitation in visualizing the full extent of ectopic bone deposition, especially in the early stages of the disease<sup>2</sup>. In the initial phases of HO, plain radiographs may yield negative results. Triphasic bone scan offer earlier detection capability, with positive uptake typically observed in the third phase (static bone/ossification phase)<sup>7</sup>. Bone scan is also used as a reliable indicator to determine the maturity of HO<sup>7</sup>. CT scans enhance preoperative planning by providing three-dimensional visualization of HO in relation to important anatomic landmarks<sup>2</sup>. ALP, specifically bone alkaline phosphatase (BAP), is commonly utilized as a bone turnover marker for monitoring HO progression after SCI<sup>8</sup>. Other biomarkers, such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and creatine kinase (CK), are also utilized. However, the above biomarkers lack specificity for HO, and they are not effective for monitoring HO maturity<sup>9</sup>.

Several pharmacological agents have been investigated for their efficacy in managing HO. Previous studies have demonstrated that non-steroidal anti-inflammatory drugs (NSAIDs) can reduce the incidence of HO when administered early after SCI<sup>4,10</sup>, but the side effects of NSAIDs need to be taken into consideration before initiation of the treatment. Bisphosphonates have been tried in several studies but there have been conflicting results with regards to the effectiveness in treating HO<sup>11</sup>. Palovarotene, a retinoic acid receptor (RAR- $\gamma$ ) agonist, has received approval by the US Food and Drug

Administration (FDA) for reducing the volume of new heterotopic ossification in both adult and pediatric patients with fibrodysplasia ossificans progressiva (also known as stone man disease)<sup>1</sup>. Research on the efficacy of palovarotene in treating HO remains limited. Currently, there is no pharmacological treatment available to reverse established HO formation. Surgical excision is considered the most effective treatment approach once HO has developed<sup>1,3</sup>. However, a careful assessment of the risks and benefits of surgery needs to be carried out when managing each individual with this condition.

## Conclusion

In conclusion, this unique case is distinguished by the notable presence of severe bilateral hip HO, emphasizing the importance of recognizing HO in imaging. Raising awareness about this condition can broaden the differentials of potential triggers for AD identification in patients with SCI.

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