False-Negative Triple-Phase Bone Scans in Spinal Cord Injury to Detect Clinically Suspect Heterotopic Ossification: A Case Series

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Abstract

Background/Objective: Heterotopic ossification (HO) is a complication seen in patients after spinal cord injury (SCI). Triple-phase nuclear bone scanning is the most sensitive test for the detection of HO. This retrospective study assesses whether patients with clinically suspected HO but negative triple-phase nuclear bone scans develop delayed positive nuclear bone scans.

Methods: Case series: A cohort of patients with SCI and clinically suspected HO who underwent triple phase nuclear bone scans over a period of 2 years was identified from retrospective chart review of an inpatient SCI rehabilitation service. A subgroup of 7 patients with initially negative but subsequently positive triple-phase nuclear bone scans was identified, and the following data were collected: date, mechanism, admission level, and admission completeness of injury as well as date, number, and results of bone scans. Laboratory studies were also collected during the time of imaging.

Results: Over a 2-year period, 343 patients were admitted to the SCI rehabilitation service; 60 patients were suspected of having HO and underwent a total of 85 triple-phase nuclear bone scans. Seven patients were identified with initially negative but subsequently positive bone scans.

Conclusions: In patients with clinically suspicious HO but negative bone scans, follow-up scans are indicated to identify initial false-negative studies.

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Key Words: Spinal cord injuries; Heterotopic ossification; Radionuclide imaging; Bone scan

INTRODUCTION

Heterotopic ossification (HO) is a known complication seen in patients after spinal cord injury (SCI). In 2002, Van Kuijk et al (1) thoroughly reviewed this complication, which is characterized by the formation of ectopic bone in the soft tissue surrounding joints below the level of spinal injury. The incidence of HO in SCI ranges from 1 to 53% (2,3), depending on the study design and

methods of detection. HO most commonly occurs at the hip; other joints often affected include the knee, elbow, and shoulder (4). The onset of HO ranges from 1 to 3 months postinjury, with peak incidence occurring at 2 months (5).

Heterotopic ossification originates in the connective tissue and may be contiguous with the skeleton, but it does not involve the periosteum. It begins in an area of inflammation, where first an exudative cellular infiltration is seen, followed by fibrosis and osteoid formation, and subsequent deposition of bony matrix (6). The mineralization of the soft tissues involves the replacement of calcium phosphate by hydroxyapatite crystals, and the process of bone maturation is normally completed within 6 to 18 months (1). The precise mechanism of HO remains unknown, but it is believed that local, humoral, and neuroimmunological factors are involved. Several possible risk factors to the development of HO have been offered. These risk factors include completeness of SCI, pressure ulcers, spasticity (7), urinary tract infection (1), deep venous thrombosis, and microtrauma (4).

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The clinical variability of HO ranges from incidental findings on radiograph to severe limitation of the range of motion and complete ankylosis of a joint. HO can significantly limit joint function in 10 to 20% of SCI patients (8) and can even develop into ankylosis in 3% of patients with SCI (5). The initial clinical findings of HO are decreased range of motion and soft tissue edema in the area of the joint. Periarticular erythema and warmth may be seen, as well as low-grade fever (9). Pain and spasticity may occur, which can limit sitting tolerance and hinder proper sitting positioning, leading to the formation of pressure sores. This can compromise the ability to perform activities of daily living and reduce quality of life (3).

Although the diagnosis of HO is initially suspected based on clinical signs, the current gold standard of early confirmation is performed by triple-phase nuclear bone scans (8). HO may be detected as early as 2.5 to 4 weeks after SCI with triple-phase bone scanning. Radiography is more specific, but findings on plain radiography can lag up to 2 weeks after a positive triple-phase nuclear bone scan (8). A number of laboratory examinations have also been found to be altered during active ossification, including serum alkaline phosphatase (2,10), calcium, and erythrocyte sedimentation rate (2), but these have often been found to be nonspecific.

The main pharmacologic treatment of HO includes the use of sodium etidronate, a bisphosphonate, which binds to hydroxyapatite and blocks the transformation of calcium phosphate into hydroxyapatite crystals (10). Recent studies have suggested treatment duration of 6 months of oral sodium etidronate after an initial 3-day intravenous loading dose. Nonsteroidal anti-inflammatory drugs may be used in combination with the sodium etidronate to reduce the local inflammatory process (10). In severe cases, surgical resection of the HO may be indicated (10), although regrowth of HO at the site of surgery can also occur. Surgery may be combined with radiation therapy.

The early diagnosis and treatment of HO can reduce both immediate and future medical complications that can have significant impact on functioning and quality of life in people with SCI. Medical complications can include pressure sores, deep venous thrombosis, and joint ankylosis. Early diagnosis permits timely treatment and can halt the progression of HO. This may prevent ankylosing of a joint, which may limit a patient's ability to perform activities of daily living or decrease his/her ability to participate in self-care (eg, assisting with transfers, dressing, bathing). In addition, early diagnosis may reduce the number of days lost due to medical issues during an inpatient rehabilitative stay and decrease costs of future medical care, including wound care, surgical resection, adaptive equipment (eg, wheelchair modifications), and personal attendant care.

By evaluating the number of cases that present with initial negative triple-phase nuclear bone scans in patients

with SCI who have strong clinical findings suggestive of HO, we can heighten awareness of this among clinicians and lay groundwork for more aggressive follow-up in patients with SCI and strong clinical suspicion for HO. A case series of negative bone scans that later become positive can lead to other research questions regarding whether different practices should be adopted for the early detection of HO in patients with SCI.

METHODS

Subjects

A retrospective chart review was performed on all patients admitted to the inpatient SCI rehabilitation service at a level I trauma county teaching hospital from July 2002 through June 2004. Inclusion criteria consisted of a diagnosis of SCI, age of at least 16 years, and no known diagnosis of HO. Patients with a known diagnosis of HO on admission to the SCI service were excluded from the study. The study protocol was approved by the hospital's Institutional Review Board.

Protocol

From the total number of 343 patients with the diagnosis of SCI, a group of 60 patients were identified who underwent triple-phase nuclear bone scans to diagnose clinically suspected HO. The number and results of the nuclear bone scans were noted. Of these total scans, the HO sites discussed in this case series are from a subgroup of those 7 patients in whom the triple-phase nuclear bone scan was initially negative but later positive. Nuclear bone scans were repeated in those patients who had negative plain radiographs but continued to demonstrate a decreasing range of motion and ankylosing joints, which may be consistent with HO. The following laboratory studies were collected, if available, during the time of imaging (within 3 days): alkaline phosphatase, calcium, erythrocyte sedimentation rate, and C-reactive protein levels. In addition, the following information was also obtained: date, mechanism, admission level, admission completeness of injury, and date of bone scans.

RESULTS

Of the 343 patients with SCI admitted to the rehabilitation service during this period, 60 were suspected of having HO and underwent a total of 85 bone scans. No follow-up triple-phase nuclear bone scans were performed on the 283 patients with initially negative nuclear scans in whom HO was no longer clinically suspected. Forty patients had 1 triple-phase nuclear bone scan performed; 20 had 2 or more nuclear scans performed. Thirty-six (60%) of the initial triple-phase scans were positive for HO; 24 (40%) of the initial scans were negative. Of the 24 patients with initially negative triple-phase nuclear bone scans, 13 (54%) had at least one additional triple-phase nuclear bone scan performed due to continued high clinical suspicion for HO and no

Table 1. Demographics of 7 Patients with Initially Negative and Subsequently Positive Nuclear Bone Scans

Patients	Level of Injury	Completeness of Injury	Mechanism of Injury	Number of Days after Injury to First Bone Scan	Number of Days Between First and Second Bone Scan	Total Number of Days after Injury	Location of HO
Patient 1	C2	B	Fall	37	37	74	Right femur
Patient 2	C4	B	Axial load	57	3	60	Left femur
Patient 3	C4	B	Axial load	36	17	53	Bilateral hips
Patient 4	C4	B	Fall	27	21	48	Left hip
Patient 5	C6	A	MVC	33	13	46	Right femur
Patient 6	T8	B	MVC	34	13	47	Bilateral hips
Patient 7	T9	A	MVC	35	9	44	Bilateral femur

MVC, motor vehicle crash.

radiographic evidence of HO on initial or subsequent plain radiographs. Seven of 13 patients (54%) with initially negative triple-phase nuclear bone scans demonstrated evidence of HO on their subsequent bone scans.

Table 1 compares data among these 7 patients. Levels of injury ranged from C2 to T9, with complete and incomplete injuries. These patients had initial triple-phase nuclear bone scans performed an average of 37 days (SD 9.4, range 27–57 days) after injury. The follow-up nuclear bone scans were repeated an average of 16.1 days after the initial bone scan (SD 10.8, range 3–37 days). HO sites occurred at the hip (in 3 patients) and the femur (in 4 patients). Patients were treated with medication after the bone scan became positive. All laboratory values drawn within 3 days of the triple-phase nuclear bone scans were found to be within normal limits, with the exception of 1 case of elevated C-reactive protein (3.3 mg/dl) and 1 case of elevated alkaline phosphatase (137 U/l).

DISCUSSION

We have identified 7 cases in which the triple-phase nuclear bone scan was initially negative but, due to strong clinical suspicion for the presence of HO, was repeated, yielding positive results. No research is available to guide the appropriate course of action for patients in whom a nuclear bone scan is negative while there continues to be a strong suspicion for the presence of HO. No data in the literature were found regarding the treatment of clinically suggestive HO prior to obtaining positive results on triple-phase nuclear bone scans. The timely diagnosis of HO in people with SCI is crucial in preventing possible compromise of functional activity in the future. A delay in the diagnosis of HO can delay treatment and, therefore, result in decreased function in already functionally compromised individuals. Larger scale studies are necessary to investigate the occurrence

of HO in patients with negative nuclear bone scans and how these patients should be managed.

CONCLUSION

For patients in whom HO is strongly suspected clinically but who have negative triple-phase bone scans, additional bone scans should be considered in order to identify those people in whom there is a delay in detection of HO by imaging.

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