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Heterotopic ossification in patients previously hospitalized in an intensive care unit

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Abstract

BACKGROUND: Heterotopic ossification (HO) is a potential complication in patients hospitalized in an intensive care unit (ICU). In this study we examined the association of HO diagnosed with three-phase bone scan (3pBS) in association with various parameters in patients previously hospitalized in ICU.
MATERIAL AND METHODS: We retrieved patient records of the last 12 years subjected to 3pBS and diagnosed with HO from the Department of Nuclear Medicine (2004 up to 2016) and searched for a name match from ICU records.
RESULTS: We found 61 patients that had a positive 3pBS for HO of whom 17 patients were hospitalized in the ICU. Among the 17 patients, twelve fulfilled the study criteria and were included in the study. The mean age was 38 years and 92% were males. HO was unilateral in 7 and bilateral in 5 patients. Patients with unilateral HO had up to 2 joints with HO, while those with bilateral had up to 4 joints. HO was most frequently observed in lower limbs, with hip being the most common joint affected. In the upper limbs, HO occurred predominantly in bilateral joints with elbow being the most frequently involved joint. Patients with longer duration of ICU stay had more joints affected.
CONCLUSION: HO is a potential complication in patients with ICU hospitalization. Since 3pBS is an imaging method for early detection of HO, patients hospitalized in ICU should be screened with 3pBS for appropriate management.

KEY words: heterotopic ossification, bone scan, intensive care unit, head injury management

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Introduction

The term heterotopic ossification (HO) denotes soft tissue bone formation and usually occurs after neurological injuries, such as head or spinal cord injury, and can lead to restriction of patient's mobility. The development of HO presents with the signs of local inflammation [1] that starts approximately 17 days after the neurologic insult [2]. It consists of abnormal ossification in the periarticular areas that spares the periosteum [3], affecting predominantly the neurologically involved extremities [4, 5]. The diagnosis of HO is associated with poor functional outcome. However, it is not clear if it can affect the progress of the neurological disability during rehabilitation [6]. Its pathophysiology is largely unknown [3, 7].

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Nuclear medicine plays an important role in the imaging of several pathological conditions in young and adult patients. Bone scan (BS) is such a study, performed for whole body bone evaluation for various reasons, including HO [8, 9]. The three-phase bone scan (3pBS) in HO patients exhibits increased radionuclide uptake in affected areas and increased vascularity that could precede or follow the formation of the heterotopic bone formation [7]. The test consists of 3 phases: the first phase includes injection of the technetium-99m-MDP followed by serial scans during the first 2 to 5 seconds after the injection; the second phase is obtained 5 minutes after the injection of technetium-99m-MDP and illustrates the inflammation of a lesion; the third phase, obtained 3 hours after the injection, demonstrates the bone turnover within the lesion [3]. Overall, the 3pBS may result in a definite diagnosis of HO within 4 weeks on the average after the insult [2,10] and could be imaged even after 16 years of neurologic injury [11]. The first and second phase verifies the existence of active or mature HO [11,12].

In this retrospective study, we investigated the existence of HO several months post-hospitalization to the ICU. We studied the presence of HO unilaterally or bilaterally and the number of joints affected according to the duration of hospitalization.

Material and methods

In this retrospective study, we retrieved 3pBS studies in patients diagnosed with HO in the Department of Nuclear Medicine and cross-checked them with the archives of patients hospitalized in the ICU at the University Hospital of Ioannina. From this study, we excluded patients with known conditions predisposing to HO prior to their ICU hospitalization, such as movement disorders, paraplegia or tetraplegia.

Characteristics that were recorded for analysis included sex, age, date, and the reason for admission to the ICU and discharge date.

The bone scan performed in the Department of Nuclear Medicine consisted of a 3pBS using 99m-technetium labeled diphosphonate. All these 3pBS studies were performed several months after the ICU hospitalization to assess the extent and the maturity of the suspected HO in order to employ the most appropriate treatment.

The study was approved by the Research Ethics Committee of the University Hospital of Ioannina, Greece.

Study participants

For inclusion of patients for this study, all sixty-one patients who had positive 3-phase 3pBS for HO from 2004 to 2016, were selected initially and cross-checked with the ICU hospitalization records. Among them, 17 patients had been hospitalized in the ICU. Five patients were excluded from the study (1 with a movement disorder and bedridden prior to ICU admission, 1 with prior paraplegia, and 3 additional patients in who their past medical history could not be retrieved). Thus, 12 patients were included in the study.

Patient no 1 was a 29-year-old male who was involved in a fight resulting in severe cerebral injuries requiring bilateral craniectomies to relieve brain edema, and remained in the ICU for 51 days. This patient had 3pBS 3 months later, which was diagnostic of HO. Patient 2 was a 32-year-old female with a head injury resulting in bilateral cranial fractures and traumatic subarachnoid hemorrhages and bilateral craniectomies to relieve diffuse cerebral edema. This patient had BS performed 34 months post-hospitalization, with one HO imaged in the right hip. Patient no 3 was a 22-year-old male with a head injury and multiple cranial bone fractures due to a motorcycle accident. Brain-computer tomography showed intracerebral hematoma in the left hemisphere and multiple hemorrhagic brain contusions in the bilateral frontal and left temporal lobe. The patient was discharged from ICU after 26 days of hospitalization for rehabilitation. One year later, HO was diagnosed with 3pBS bilaterally in the elbows, mostly right.

Patient 4 was a 51-year-old male, transferred from the Neurology inpatient service due to deteriorating clinical status secondary to a recent left middle cerebral artery hemorrhagic stroke. During his 18 days ICU stay his clinical condition improved and was transferred back to the Neurology service with remaining residual moderate aphasia and right-sided hemiparesis. Approximately two years later, HO was diagnosed with 3pBS in the right shoulder and hip. Patient 5, a 35-year-old male pedestrian, was hit by a car and hospitalized in the ICU for 61 days with multiple trauma and bone fractures, including traumatic partial rupture of the aorta, left temporal bone fracture with left subdural hematoma, bilateral tibial fractures, and dislocation of the right elbow. Nine months later, HO was imaged in bilateral elbows, right shoulder and left knee. Patient no 6, a 55-year-old male, hospitalized for 43 days in ICU post-surgical clipping of a ruptured aneurysm. HO was imaged in the left hip after 22 months. Patient 7, a 34-year-old male, was hospitalided for 43 days in ICU with a head injury, rib fractures, lung and myocardial injury after a car accident. 3pBS was performed 25 months later and bilateral HO was imaged in both shoulders and elbows.

Patient 8 was a 32-years-old male hospitalized in the ICU for 88 days after a car accident resulting in head injury and left elbow dislocation. He had residual right hemiparesis and epileptic seizures. Twenty-seven months post hospitalization, BS imaged bilateral HO in hips and knees mostly on the right side. Patient 9 was a 33-year-old man that after a car accident suffered cranial bone, right femur and left forearm fractures. He stayed in the ICU for 30 days and his HO was suggested by x-rays during his hospitalization and re-confirmed 2 years later with a BS. Patient 10, a 57-year-old man, had Hodgkin lymphoma stage IIA and after chemotherapy developed septic shock and multi-organ failure and ARDS. He was hospitalized for 26 days in the ICU and the HO was diagnosed 6 months post hospitalization involving the bilateral knees and hips. Patient 11 was a 32-year-old male hospitalized for 62 days in the ICU for periodontal, neck and mediastinal abscesses and septic shock. He was diagnosed with HO in the left knee 3 months after his ICU hospitalization. Finally, patient 12 was a 48 years old man who was hospitalized in the ICU for 57 days due to spinal injury after a car accident and subsequent paraplegia and acute pulmonary failure Thirteen years post hospitalization, he was subjected to BS for evaluation of suspected HO in the right elbow for treatment options.

Results

The characteristics and medical information of the 12 patients studied are shown in Table 1. Main age was 38.25 (22–57 years old) with the majority of patients being males (92%). The

Table 1. Characteristics of the patients (min-max) and information concerning hospitalization and three-phase bone scan

Characteristics	Patients (Total 12)
Mean age (years)	38.22 (22–57)
Gender	11M (92%) / 1F (8%)
DH-ICU	
days	45.4 (18–88)
DH-3pBS	
months	28.3 (3–153)
< 12 m / > 12 m	5 (42%) / 7 (58%)
Uni/bilateral	7 (58%) / 5 (42%)
No of HO sides	
1/2/3/4	4 (33.3%) / 4 (33.3%) / / 0 (0%) / 4 (33.3%)

M — males; F — females; DH-ICU — duration of hospitalization in intensive care unit measured in months; DH-3pBS — duration of the three-phase bone scan performed after hospitalization in intensive care unit measured in months; HO — heterotopic ossification

Table 2. Cause and duration of ICU hospitalization, time of the three-phase bone scan (3pBS) post hospitalization, and 3pBS findings

Pat No	Cause	DH-ICU (days)	DH-3pBS (months)	3pBS-HO	No HO
1	Cranial head trauma — act of violence	51	3	Unilateral	2
2	Cranial head trauma — car accidence	40	34	Unilateral	1
3	Cranial head trauma — motorcycle accidence	26	12	Bilateral	2
4	Hemorrhagic stroke	18	22	Unilateral	1
5	Multiple trauma — bone fractures — hit by a car	61	9	Bilateral	4
6	Rupture of cranial head aneurysm	43	22	Unilateral	2
7	Cranial head trauma — multiple trauma — bone fractures — car accident	43	25	Bilateral	4
8	Bone fractures — car accident	88	27	Bilateral	4
9	Multiple bone fractures — car accident	30	24	Bilateral	1
10	Septic shock — multiple organ failure	26	6	Unilateral	4
11	Mesothoracic abscess septic shock	62	3	Unilateral	1
12	Car accident — acute pulmonary failure — bone fractures	57	153	Unilateral	2

DH — duration of hospitalization in Intensive care unit, measured in days; DH-3pBS — duration of performed three-phase bone scan post hospitalization in intensive care unit, measured in months; 3pBS-HO — heterotopic ossification in three-phase bone scan seen; NoHO — the total number of heterotopic ossifications

Table 3. Number and anatomic place of heterotopic ossification imaged in three-phase bone scan

No of HO imaged 1HO / 2HO / 3HO / 4HO 4 (1 UL/3 LL) / 4 (4 UL/4 LL) / 0 (0 UL/0 LL) / 4 (7 UL/9 LL)	
Number of total HO	
Upper limbs: 12	Lower limbs: 16
Unilateral: 3	Unilateral: 7
Bilateral: 9	Bilateral:9

HO — heterotopic ossification; UL — upper limbs; LL — lower limbs

Table 4. Duration of ICU hospitalization and number of heterotopic ossifications

Hospitalization (days)	1HO 4 patients	2HO 4 patients	4HO 4 patients
≤ 20	1 (25%)	0 (0%)	0 (0%)
> 20	3 (75%)	4 (100%)	4 (100%)
≤ 30	2 (50%)	1 (25%)	1 (25%)
> 30	2 (50%)	3 (75%)	3 (75%)
≤ 40	**3 (75%)**	1 (25%)	1 (25%)
> 40	**1 (25%)**	3 (75%)	3 (75%)
≤ 50	3 (75%)	2 (25%)	2 (50%)
> 50	1 (25%)	2 (50%)	2 (50%)
≤ 60	3 (75%)	**4 (100%)**	2 (50%)
> 60	1 (25%)	**0 (0%)**	2 (50%)
≤ 70	4 (100%)	4 (100%)	**3 (75%)**
> 70	0 (0%)	0 (0%)	**1 (25%)**

HO — heterotopic ossification

mean hospitalization time in the ICU was 45.4 days (18–88 days). Patient with the longest hospitalization had a head injury (patient no 8 [Table 2]), while the patient with the shortest ICU stay had a hemorrhagic stroke (patient no 4). Half of the patients were subjected to 3pBS within 12 months post hospitalization, while the rest of the patients had 3pBS within two years, except for one patient who was subjected to 3pBS 13 years post hospitalization.

The etiology and duration of hospitalization and length of time between ICU stay and 3pBS testing is shown in Table 2. HO was found only unilaterally in 7 patients and bilaterally in 5 patients. Patients with unilateral HO had up to 2 sites involved, while those with bilateral involvement had up to 4 sites with HO (Table 3). Among all patients, HO was found in 28 joints, 12 located in the upper limbs and 16 in the lower limbs. In addition, 10 HOs had only unilateral and 18 bilateral localization. When upper limbs were involved, the joints affected were mostly bilateral than unilateral (Table 3).

The most frequent site of HO was the hip (8), followed by elbow and knee with (7) HOs and shoulder with 5 HOs. The first and second phases of 3pBS showed active HO in 7 patients and mature HO in 5 patients. In this small cohort of patients,, most of HOs were observed in the lower limbs, with a hip predominance. However, when the upper limbs were involved the most favorite joint was the elbow.

The length of ICU stay was directly related to the number of the affected joints. For example, patients that remained in the ICU for up to 40 days had 1 joint involved with HO, patients stayed for 60 days had up to 2 joints involved, and those that stayed ≥ 70 days had up to 4 joints involved with 4 HO (Table 4).

Discussion

Young people are admitted into the ICU usually as a result of car or motorcycle accidents and brutality, resulting in multiple injuries, coma or paraplegia [5, 13]. In our study, most of the patients were young people with head and other injuries due to motor vehicle accidents. The rest of our patients were a hemorrhagic stroke patient, a victim of brutality and a spinal cord injury patient with paraplegia.

It's been reported that maturation may be seen with other imaging methods such as radiographs, 3 months to 6 years following

the neurological insult, however, 3pBS is more sensitive method because it could reveal the sustained progression of the HO [14]. HO occurs in both hemiplegic and non-hemiplegic extremities [5, 15], however, in non-hemiplegic side of the body it is approximately seen in only 0.5–1.2% of cases [15]. None of our patients had HO only in a non hemiplegic limb.

In our cases, HO was seen in patients with several diagnoses, mostly cranial head trauma. There was an association of the duration of the ICU stay with the number of HO even though the number of patients studied was small for statistical evaluation. However, it appeared that patients with longer ICU hospitalization had more advanced HO compared to those with shorter ICU stay.

Previous studies reported that in patients with burn the most affected joints were the elbows, followed by the shoulders, hips, knees, and forearms [16, 17]. In our cases, HO was seen mostly in lower limbs, with the most affected joint being the hip. Bilateral involvement was seen in 42% of patients. However, in that case the affected extremities included mostly the upper limbs, predominantly the elbows.

In conclusion, the duration of ICU hospitalization seems to correlate positively with the number of joints involved with HO. In addition, HO was seen mostly in lower limbs, predominantly in the hip. It appears that at least in our ICU, the investigation of patients for possible HO is a secondary target because the priority is the preservation of life and the complications of immobility of trauma patients are left for evaluation at a later stage. Our study though indicates that HO is a common, long-lasting disability that needs to be evaluated early during the ICU stay, or at least soon after discharge.

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Conflict of interest

None

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N/A

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