Physical Medicine 1999; 2 (2) : 9-12

PHYSICAL MEDICINE

HETEROTOPIC OSSIFICATION IN TRAUMATIC BRAIN INJURY

TRAVMATİK BEYİN HASARINDA HETEROTOPİK OSSİFİKASYON

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SUMMARY

Heterotopic ossification (HO) is one of the musculoskeletal complications seen in traumatic brain injured (TBI) patients. This prospective study had two main aims; (1) to elucidate the occurrence and distribution of HO in TBI patients and its effect on rehabilitation process, (2) to test the utility of triple-phase bone scans compared with plain-film x-rays in the assessment of HO in TBI patients. HO incidence was found to be 71.9% and the most common location was the hips. Of the 45 joints with HO 26 (57.8%) showed motion restriction. There were no correlation between the presence of HO and age, time since injury, and spasticity. Although it did not reach statistical significance the length of coma was longer in patients with HO. The length of coma in patients with and without HO was 49.6±55.2 and 43.8±38.7 days, respectively. When the effect of HO on the rehabilitation process and functional gains was analyzed, no difference was seen in patients with HO but it was obvious that functional gains decreased with the increasing number of HO in each patient. Our data suggest that HO is an important complication after TBI and the lack of its early diagnosis and treatment increases the progressive motion limitation. Additionally, triple-phase bone scans which is commonly used in the early diagnosis of HO might be used in patients with rather longer time since TBI to assess the distribution of HO.

Key words : Traumatic brain injury, heterotopic ossification

ÖZET

Heterotopik ossifikasyon (HO) travmatik beyin hasarında (TBH) sıklıkla görülen kas-iskelet sistemi komplikasyonlarındandır. Bu çalışmada, kliniğimizde izlediğimiz TBH olgularında HO sıklığını ve yaygınlığını karşılaştırılmalı olarak 3-fazlı tüm vücut kemik sintigrafisi ve direk radyografilerle araştırdık. HO gelişiminde etkili faktörleri ve bu komplikasyonun rehabilitasyon programı üzerine olan etkilerini belirlemeyi amaçladık. Çalışma grubumuzda HO sıklığı %71.9 olarak belirlendi. En sık kalçalarda olmak üzere toplam 45 bölgede HO saptandı. Beş eklem bölgesi dışında kemik sintigrafisi ile HO belirlenen eklemlerin tamamı radyografilerle doğrulandı. HO saptanan 45 bölgenin 26' sında hareket kısıtlılığı olduğu görüldü. HO varlığı ile yaş, hastalık süresi ve spastisite arasında ilişki saptanmadı. Koma süresi, istatistiksel olarak anlamlı olmasa da HO gelişen hastalarda daha uzundu. Koma süresinin ortalaması HO saptanan ve saptanmayan gruplarda sırasıyla 49.6±55.2 ve 43.8±38.7 gün olarak belirlendi. Bu komplikasyonun rehabilitasyon programı ve kazanımları üzerine olan etkileri incelediğinde HO, gelişmiş olan hastalarda anlamlı farklılıklar saptanmadı, ancak her hastada artan HO sayısıyla beraber fonksiyonel kazanımların azaldığı dikkati çekmekteydi.

Heterotopik ossifikasyon TBH olgularında karşılaşılan önemli bir sorundur ve özellikle ağır beyin hasarına uğramış kişilerde daha sık görülebilmektedir. Erken dönemde tanı ve tedavisinin gerçekleştirilmemesi eklem hareket kısıtlılığı riskini artırmaktadır. Çok erken dönemde tanı amacıyla kullanılması önerilen 3-fazlı kemik sintigrafisi, geç dönem olgularında da HO yaygınlığını belirlemede uygun bir yöntem olarak gözükmektedir.

Anahtar sözcükler : Travmatik beyin hasarı, heterotopik ossifikasyon

INTRODUCTION

Advances in trauma care have improved survival from severe traumatic brain injury (TBI) and this has increased the number of survivors. These patients present the rehabilitation physician and the team with problems that are unique in rehabilitation medicine. As the main focus during the immediate management of TBI patients in the acute care facilities is on the life threatening issues, several musculoskeletal problems such as neurogenic heterotopic ossification (HO), skeletal trauma and fractures, or soft tissue trauma might remain undetected. Heterotopic ossification was first described by Dejerine and Ceillier in 1918 in paraplegic patients injured during World War I (1). They referred to the process as paraosteoarthropathy. Since then several terms have been used to describe this condition, including heterotopic ossification,

ectopic ossification, myositis ossificans, and neurogenic ossification (1). HO is the formation of mature lamellar bone in soft tissues. HO formation has been reported in TBI, spinal cord injury, stroke, poliomyelitis, myelodysplasia, carbon monoxide poisoning, spinal cord tumors, tabes dorsalis, syringomyelia, tetanus, and multiple sclerosis. It has also been reported after burns and total hip replacement (2,3). The specific cause and pathophysiology of HO is unclear. It was reported that HO is due to an interaction between local factors (pool of available calcium in adjacent skeleton, soft- tissue edema, vascular stasis, tissue hypoxia, mesenchymal cells with osteoblastic activity) and an unknown systemic factor or factors. The basic defect in HO is the inappropriate differentiation of fibroblasts to bone forming cells. Histologic examination demonstrates that this process differes from soft tissue calcification because it is true osteoblastic activity and bone formation as opposed to deposition of calcium seen in calcific tendinitis (1,4,5).

This prospective study had two main aims; (1) to elucidate the occurrence and distribution of HO in TBI patients and its effect on rehabilitation process, (2) to test the utility of triple-phase bone scans compared with plain-film x-rays in the assessment of HO in TBI patients.

PATIENTS AND METHODS

Thirty-two (4 female, 28 male) consecutive TBI patients admitted to Ankara Physical Medicine & Rehabilitation Center during one year period were studied. The patients were analyzed as to the duration of coma, time since TBI, admission Rancho Level of Cognitive Status (6), duration of rehabilitation stay, presence of spasticity, contracture, and extremity fractures. Functional status of all patients were evaluated by Functional Independence Measure (FIM) (7) both at admission (FIM I) and discharge (FIM II). Total FIM , motor FIM and motor FIM gains (FIM I subtracted from FIM II) results were used in the analysis. Triple-phase bone scans (Tc99mMDP) were done in all subjects within one month of their admission to our center. Increased uptake in the first and second phases of the scan were considered as positive for HO (1). Scan findings were correlated with plain x-rays to rule out fracture and other pathology. X-rays of abnormal areas on scan as well as the x-rays of joints with decreased range of motion (ROM) on clinical examination were taken in each patient.

Correlation analysis, chi-square and t-tests were performed to analyze the data. A statistically significant difference was defined as $p<0.05$.

RESULTS

The mean age of 32 patients was 27.3+10.5. The mean duration of coma was 46.4±50.3 days and the mean time since TBI was 210.1±125 days. Rancho Level of Cognitive Status assessments showed that our patients were at the recovery stages between confused-agitated and purposeful-appropriate. Functional assessments of the patients at the beginning and at the end of the rehabilitation program are presented in Table I. A paired t-test for related samples revealed significant levels of improvement in total and motor FIM sores from admission to discharge. The mean rehabilitation stay was 96.4±54 days.

Table I: Functional improvement between admission and discharge (n:32)

Variables	Minimum	Maximum	Mean	Std.Deviation
Total FIM I	18	126	59.6	28.2
Total FIM II	34	126	76.3	24.8
Motor FIM I	13	91	38.2	20.8
Motor FIM II	12	94	50	20.7
Motor FIM gain	0	65	11.2	14.8

Comparisons were done between total FIM I-II, and motor FIM I-II
Total FIM I-II, $p<0.001$, (t: -4.57, df: 30)
Motor FIM I-II, $p<0.001$, (t: -4.23, df: 30)

Twenty-three (23/32; 71.9%) patients were found to have HO at 45 locations. Of the 45 sites with HO found by scan, X-ray or both; the hips were the most commonly affected (16 of 45, 35.5%), followed by knees (10 of 45, 22.2%), shoulders (10 of 45, 22.2%), and elbows (5 of 45, 11.1%). Figure 1 shows bone scan images of a patient with HO in both hips and left knee. We found limitation in ROM in 26 of 45 (57.8%) sites with HO. Nineteen joints did not show decrease in motion. All patients with documented HO received ROM exercises by physical therapy and etidronate were started in acute or subacute patients. Surgical resection was suggested in one patient. Bone scanning revealed 5 HO sites which were not detectable by radiographs and only one of these 5 joints had limitation of ROM.

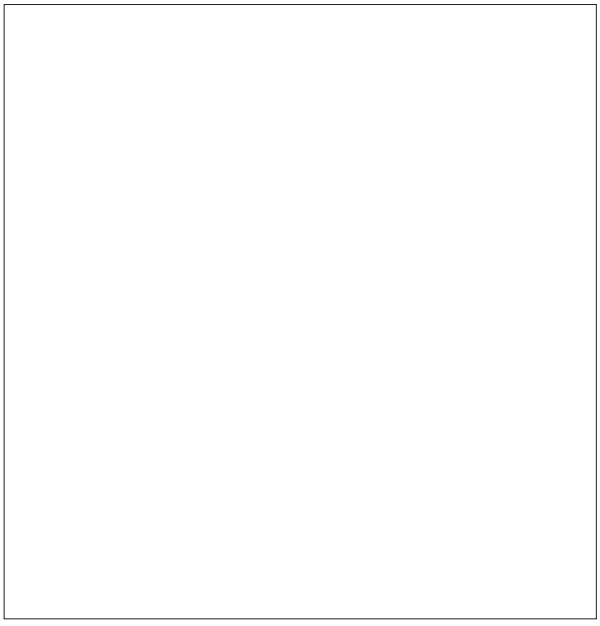

Figure 1. Bone scan showing increased radiotracer uptake in both hips and left knee

There were 14 extremity fractures in the study group but only in four patients coexisting fracture was the major causative factor in the development of HO. There were no significant relationship between the presence of HO and age, time since TBI, or spasticity. Although it did not reach statistically significant difference the length of coma in patients with HO was longer than the patients without HO. The length of coma in patients with and without HO was 49.6±55.2 and 43.8±38.7 days, respectively. Motor FIM and total FIM gains and duration of rehabilitation stays were not found to be significantly different in patients with or without HO. There was a negative correlation between motor FIM gain and the number of HO in each patient ($r= -0.31$, $p>0.05$) Seventy percent of the patients with HO had it at more than one site.

DISCUSSION

The reported incidence of HO in TBI patients varies. Garland stated that in those patients who suffer severe trauma or insult to the central nervous system, 10-20% develop clinically significant HO (8). Mendelson et al. observed HO in 20% of patients with severe brain injury (9). Other authors have reported an incidence in head injured patients ranging from 11% to 76% (1). The wide variations in reports of incidence in these studies most likely result from different criteria for patient selection. Almost 72% of our study group were found to have HO and 57.8% of HO sites were clinically significant demonstrating ROM limitation. In general, only patients who require long-term rehabilitation are referred to our center, so that most of the patients in this study population are severely injured and the mean duration of coma is quite long. Therefore, we suspect that the high incidence of HO in this study represents this condition. Inclusion of patients with minimum deficits might lower the HO incidence. Also most of our patients were found not to have received passive ROM exercises during their acute hospital stay accounting for the relatively high occurrence of progressive contractures at HO sites. Decreased range of motion is reported as the most common complication of HO (1). Non-articular complications of HO include vascular compression, peripheral nerve compression, and lymphedema (10,11). These were not observed in our study group.

The onset of HO usually manifest 4 to 12 weeks after the head injury. Loss of ROM is the earliest sign of HO; other findings include swelling, erythema, heat, and pain on range of motion. Local tenderness and sometimes a palpable mass can be detected in the periarticular area (1,2). During the acute phase radiographs might be normal and triple phase bone scanning detects early increase in vascularity and is a reliable method of diagnosis (1,12). Radiographs may not become positive until 2 weeks after the onset and sometimes it may take as much as 2 to 3 months before there is a delineation of bone from soft tissue (1). Alkaline phosphatase elevates early but is not diagnostic because it can be elevated from other factors such as multiple fractures and hepatotoxicity (13); we did not report alkaline phosphatase levels here. In this study bone scan were done on all patients and all sites of HO were well correlated with plain x-rays. Five sites positive for HO by bone scan were normal in X-rays and only one of them caused motion restriction. These findings might suggest that it may be practical to perform a bone scan survey for screening the distribution of HO in patients even with rather longer time since TBI like our patient group because it seems to be as sensitive as plain x-rays, with less radiation. Additionally, although the usefulness of identifying HO in asymptomatic patients is unclear, early intervention in asymptomatic joints may decrease the progression to a more severe and disabling degree of motion restriction.

Clinical factors effecting the occurrence of HO have been studied before. Sazbon et al. noted that the development of HO is independent of sex and age, as well as, etiology of injury, duration and outcome of coma but report an association with the occurrence of coma (14). Hurvitz suggested a cluster of factors; older age, longer coma, and poorer outcome of TBI, could be associated with the formation of HO in pediatric and adolescent patients (15). He did not identify spasticity as risk factor for HO. In another study spasticity was found as a risk factor based on the greater incidence of HO in patients with spastic tetraparesis, and in the affected extremity with hemiparesis (8). In that study 89% of the involved areas were in the spastic limbs. It was stated that extremity fractures especially which go under open reduction and internal fixation are significantly prone to develop HO (13). Mital and coworkers hypothesized local trauma might be a precipitating factor for HO formation (16). Extended immobility resulting from multiple limb fractures coexisting with TBI, longer lengths of coma, and poorer outcome was emphasized as a primary etiologic factor (1). In our study, coma seemed to be an important confounding variable and prolonged immobilization without physical therapy was present almost in all patients. Only, in four patients, a coexisting fracture seemed to be a major causative factor in the development of HO but we have to note that even fractures distant from HO sites may contribute to the etiology since presence of fractures generate a stimulus for bone repair and formation (15).

Joint deformity from HO could result in significant functional limitations, such as difficulty with hygiene, sitting, or ambulation (13). Our analysis revealed that FIM gains lowered as the number of HO in each patient increased. In clinical practice, we also observed patients with complete ankylosis in their hips or elbows who were not able to sit, walk or feed themselves although they had achieved a good motor and cognitive improvement. Such patients might benefit from surgery.

Overall our data suggest that HO is an important musculoskeletal complication after TBI and the lack of its early diagnosis and treatment increase the morbidity associated with it. We think that such complications might be lowered if TBI patients are evaluated by the rehabilitation team early in the course of their acute care.

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