

HETEROTOPIC OSSIFICATION AFTER SPINAL CORD INJURY

EPIDEMIOLOGY AND RISK FACTORS

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From 1981 to 1986 we treated 413 patients for acute spinal-cord injuries. We reviewed 356 patients followed for a minimum of two years of whom 71 (20%) developed heterotopic ossification around one or more joints.

Heterotopic ossification occurred more often in male patients (23%) than in female (10%), and was most frequent in the 20- to 30-year age group. It was also more common after injuries of the lower cervical or thoracic spine than after those of the lumbar spine. Patients with severe neurological deficits (Frankel grades A and B) showed significantly more heterotopic ossification but there was no correlation with the number or severity of associated head and limb injuries. Serum calcium levels did not change significantly in either group for 30 weeks after injury, but the erythrocyte sedimentation rate and the alkaline phosphatase level were significantly increased at six weeks in patients with heterotopic ossification.

Heterotopic ossification is an important complication of head and spinal-cord injuries, producing metaplastic formation of new bone in connective tissues and muscles surrounding joints (Heller and Ringe 1979). Its reported incidence varies from 1% to 50% (Dejerine and Ceillier 1918; Coddington 1961; Guttman 1976). It most commonly affects the large proximal joints (Heller and Ringe 1979; Henderson and Reid 1981) and its aetiology is not yet known. Possible factors include local micro-trauma, disturbance of calcitonin and parathormone levels, and genetic disposition (Chantraine and Minaire 1981). Decreased blood flow and changes in pH may also be important (Bassett 1962; Nechwatal 1972).

We have studied the incidence of heterotopic ossification in patients with traumatic paraplegia and tetraplegia in an attempt to detect predisposing factors and define risk factors.

PATIENTS AND METHODS

From 1981 to 1986 we treated 413 patients for acute spinal-cord injuries in the Bergmannsheil Hospital in Bochum. The complete clinical records and radiographs

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of 356 patients followed up for a minimum of two years after injury were evaluated with regard to 28 variables.

Mean and standard deviation were calculated and statistical analysis performed according to the Student-Newman-Keul test or the paired Student's *t*-test for paired values.

RESULTS

There were 274 male and 82 female patients. Heterotopic ossification (HO) developed in 71 (20%); 23% of the male patients and 10% of the females developed HO (Fig. 1). The mean age of all patients was 35.4 years; 35.8 years in those without HO and 33.8 years in those with HO. There was a significantly higher incidence (29%) in patients between 20 and 30 years of age than in the other age groups.

In all, 127 patients had tetraplegia and 207 paraplegia; 22 had only a deficit of sensation. None of the last group developed HO, while 24% of the tetraplegic and 19% of the paraplegic patients did. In the group with HO, the spinal injuries were most commonly at C5 (24%) and C6 (18%) levels. Thoracic lesions were found at D5 (11%), D6 (10%), and D12 (15%). By contrast, in patients without HO the most common injury level was at L1 (26%) with fewer cervical and thoracic injuries: C5 (13%), C6 (11%), D5 (2%) and D6 (4%). Injury at D12 was about the same in both groups (12%).

However, the patients with heterotopic ossification showed a significantly ($p < 0.05$) higher proportion of Frankel A and B injuries (no useful motor function) than patients without such changes (Table I). In those without HO, 63.5% had no concomitant injuries as compared with 47.9% of patients with HO. In the group without

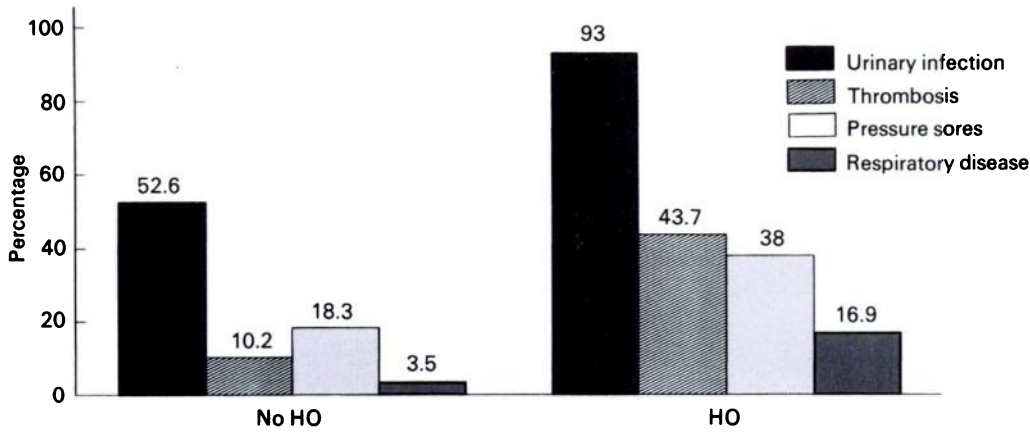


Fig. 1

Complications during time in hospital in patients with (HO) and without heterotopic ossification (No HO). Urinary tract infections, thrombosis, pressure sores and respiratory disease were all significantly more frequent in patients with HO.

Table I. Frankel grading of patients with and without heterotopic ossification on the day of injury and at discharge from hospital

Frankel grade	Injury		Discharge	
	Number	Per cent	Number	Per cent
<i>With HO</i>				
A	41	59.4	35	50.7
B	13	18.9	13	18.9
C	14	20.3	16	23.2
D	1	1.4	5	7.2
E	0	0	0	0
<i>Without HO</i>				
A	53	22.9	46	19.9
B	28	12.2	21	9.1
C	75	32.4	27	11.7
D	62	26.8	108	46.7
E	13	5.7	29	12.6

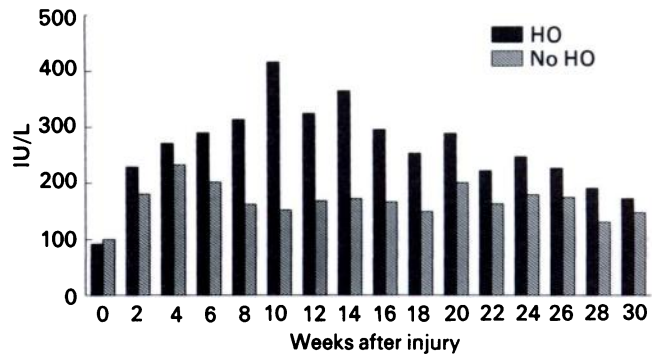


Fig. 2

Serum alkaline phosphatase levels in patients with (HO) and without heterotopic ossification (No HO) after injury.

Table II. Number and incidence of associated injuries in patients with and without heterotopic ossification

Site of injury	Without HO		With HO		
	Number	Per cent	Number	Per cent	
Cranial	I*	42	14.7	12	16.9
	II*	16	5.6	4	5.6
	III*	20	7.0	7	9.9
Thoracic	65	22.8	29	40.9	
Abdominal	14	4.9	4	5.6	
Upper extremity	21	7.3	8	11.3	
Lower extremity	37	13.0	11	15.5	
Pelvis	13	4.6	1	1.4	

*Cranial I: contusion without amnesia; II: contusion with amnesia; III: organic brain damage

Table III. Number and incidence of concomitant disease before injury in patients with and without heterotopic ossification

Disease	Without HO		With HO	
	Number	Per cent	Number	Per cent
Cardiovascular	37	13.0	5	7.0
Gastro-intestinal	13	4.6	3	4.2
Respiratory	11	3.9	1	1.4
Urogenital	14	4.9	5	7.0
Metabolic	9	3.2	2	2.8
Spinal	24	8.4	10	14.1
Dermal	4	1.4	0	0
Neurological	17	6.0	3	4.2
Psychotic	18	6.3	2	2.8
Alcoholism/drug dependency	11	4.9	3	4.2
Sensory organs	7	2.5	3	4.2
Undefined	7	2.5	0	0

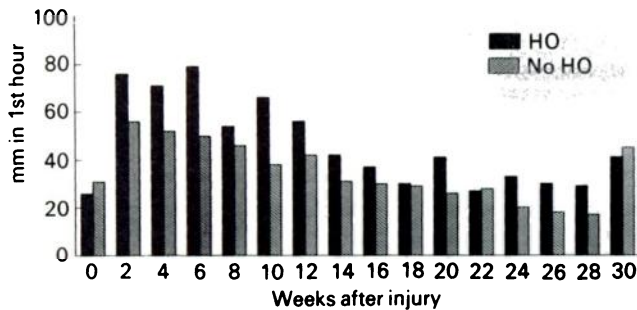


Fig. 3

Erythrocyte sedimentation rate in patients with (HO) and without heterotopic ossification (No HO) after injury.

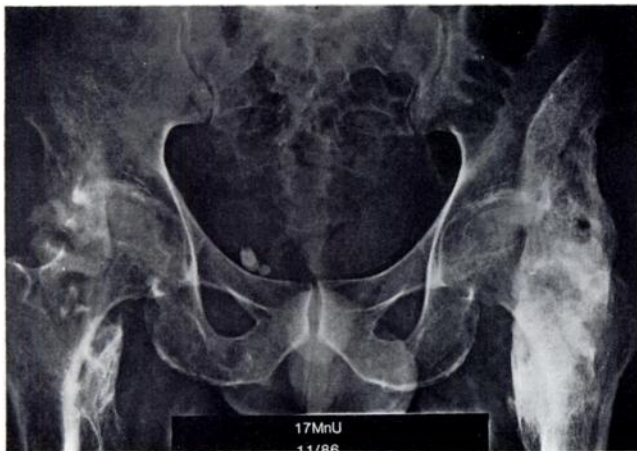


Fig. 4

Radiograph of both hips of a 37-year-old man 17 months after paraplegia. The left hip is completely ankylosed and the right hip has moderate restriction of movement.

HO, 27.3% of the patients also had a cranial injury; in the HO group 32.4% had injuries to the brain (Table II). Of the patients with HO, 31% had one, 5.6% two and 1.4% three concomitant diseases before injury, while in the group without HO 39% had one concomitant disease, 8.2% had two, 3.2% three, 1.8% had four and 0.7% five concomitant diseases. Patients without HO had a significantly higher percentage of cardiovascular disease ($p < 0.05$), while HO patients had a higher incidence of spinal problems before the injury (Table III).

Patients with spinal injuries may develop complications such as urinary tract infection, thrombo-embolism, pressure sores and respiratory disease. The number and the severity of these complications were higher in those with heterotopic ossification (Fig. 1).

Serum alkaline phosphatase levels increased in both groups from about 100 U/l at admission to more than 200 U/l at four weeks. After six weeks this increase was significantly greater in the patients with HO; it was greatest after ten weeks and continued at a significantly increased level up to 20 weeks after the initial injury (Fig. 2). Over the same time period, serum calcium increased from 4.2 mmol/l to only 4.6 mmol/l after ten weeks, and

there was never a significant difference in levels between the two groups. The erythrocyte sedimentation rate after one and two hours increased significantly ($p < 0.05$) from the day of injury to two weeks after injury. In the patients with HO it reached a maximum after six weeks of about 80 mm for the first hour and 110 mm for the second hour (Fig. 3).

New bone formation around only one joint was seen in 45.1% of the 71 patients with HO. Two joints were involved in 29.6%, three in 9.9% and four in 12.6%. There were five and 11 affected joints in the other two patients. The joints most often involved were the left hip (70.4%) and the right hip (57.8%). In 12 hips (13.2%) there was complete ankylosis in slight flexion (Fig. 4). Five elbows developed complete ankylosis in 60° to 100° flexion. Two knees became completely ankylosed.

DISCUSSION

The 20% incidence of heterotopic ossification in our series of patients with spinal-cord injuries is within the range of 1% to 50% that has been previously reported (Dejerine and Ceillier 1918; Coddington 1961; Wharton and Morgan 1970; Guttmann 1976). The localisation of the changes and the incidence of loss of movement also correlate with other reported series (Damanski 1961; Orzel and Rudd 1985) as does the percentage of ankylosis (Hardy and Dickson 1963; Wharton and Morgan 1970; Knudsen, Lundberg and Ericsson 1982; Garland et al 1983).

We found twice the incidence of HO in males (23%) than in females (10%). This may be explained by the hypothesis that HO is influenced by increased mobilisation of calcium from the skeleton, secondary to immobility, osteoporosis and venous stasis (Wharton 1975; Major, Resnick and Greenway 1980; Chantraine and Minaire 1981). However, this theory was not supported by the blood calcium levels: they did not increase significantly over 30 weeks and were no different in patients with or without HO.

There were more patients with mid-thoracic and cervical spine lesions in the group with HO, and more with Frankel grades A and B. This correlates with other reports that HO developed more often in patients with complete lesions (Scher 1976; Hernandez et al 1978; Chantraine and Minaire 1981; Knudsen et al 1982). We found no correlation with the fracture type or its treatment by surgical or conservative methods, or with the incidence of associated head injuries, although it is known that patients with cranial injuries alone may also develop HO. Couvée in 1971 reported 12 severe cases of HO requiring excision; in six of these patients a cerebral injury was the cause. Henderson and Reid (1981) found HO of the hand in one patient after severe head injury and coma and one after spinal-cord injury.

The only significant difference found was a higher incidence of thoracic injuries in the HO group. The

theory that previous trauma to an extremity may predispose to the development of HO is not supported by our study. We also found no significant difference in the incidence of pre-existing concomitant diseases before spinal injury in our two groups: previous medical history did not seem to be related to the risk of development of HO.

In our patients with HO, any pressure sores developed after HO; such sores therefore are unlikely to cause heterotopic ossification. We also consider that thrombosis and embolism are secondary to HO rather than causative. Heterotopic ossification produces narrowing of the veins; this may be an important predisposing factor for thrombosis and embolism (Orzel, Rudd and Nelp 1984; Orzel and Rudd 1985). We found an increased number of urinary tract infections in our HO patients, as has been reported by others (Dejerine and Ceillier 1918; Damanski 1961), but there is no satisfactory explanation for this. Urinary and respiratory infections were seen both before and after the development of HO, and both may contribute to its development by producing metabolic changes and release of inflammatory mediators.

Calcium mobilisation is a possible mechanism for the development of HO but, like other authors, we found no significant changes in serum calcium levels (Heilbrun and Kuhn 1947; Hossack and King 1967; Chantraine and Minaire 1981). The serum alkaline phosphatase level seems to be a more relevant guideline: this is manifest during the development of HO, but the increase, not the absolute value, appears to be predictive (Furman,

Nicholas and Jivoff 1970; Nechwatal 1972; Chantraine and Minaire 1981; Bilow 1982). Chantraine and Minaire reported that alkaline phosphatase levels increased about three to four days after the first clinical symptoms of HO developed, between two and ten weeks after injury. Orzel and Rudd (1985) found an increase in alkaline phosphatase level before the development of clinical symptoms. Monitoring of the alkaline phosphatase therefore may be a reliable method of early detection and of control of treatment.

Conclusions.

- 1) The overall incidence of HO in our series of spinal-cord injuries was 20%.
- 2) Males (23%) develop HO more than twice as often as females (10%).
- 3) Patients with HO had predominantly cervical and mid-thoracic spinal injuries, while thoracolumbar and lumbar injuries were more common in the group without HO.
- 4) HO was found more often in tetraplegic patients and in those with motor lesions (Frankel A and B).
- 5) Urinary tract and respiratory infections, pressure sores and thrombo-embolism were significantly increased in patients with HO.
- 6) The serum alkaline phosphatase level was significantly increased six weeks after the injury in patients with HO and may be a useful investigation for diagnosis and the control of management.

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