Research Paper Medical Science

Heterotopic Ossification after Primary Total Knee Arthroplasty

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ABSTRACT

Introduction: Heterotopic ossification is a less known but an agonizing complication after primary total knee arthroplasty. Early detection can help in treating it at an earlier stage so that the patient returns back to normal ambulatory life at the earliest.
Method: With an aim to find the earliest predictors of heterotopic ossification in patients, who had undergone primary knee arthroplasty, a prospective study was carried and quarterly assessment was done using biochemical markers and conventional plain radiography in 34 patients with primary total knee arthroplasty.
26 patients underwent bilateral total knee arthroplaties and 8 patients underwent unilateral total knee arthroplasties - total 60 total knee arthroplasties in 34 patients.
Results: Only one out of 34 patients (60 total knee arthroplasties) developed heterotopic ossification and had significant limitation of range of movement in the affected joint. We found changes in biochemical markers in the patient who developed heterotopic ossification in our study. There was a transient decrease in serum calcium and transient increase in inorganic phosphate at 3 months follow up. While the serum calcium was raised in subsequent follow ups. Serum alkaline phosphatase was initially normal and was subsequently raised. Plain radiograph showed changes of heterotopic ossification 6 months after total knee arthroplasty.
Summary: Biochemical markers (serum calcium, inorganic phosphate and alkaline phosphatase) may be useful indicators of developing heterotopic ossification in a knee joint following arthroplasty at early stage so that the prophylactic therapy can be administered at appropriate time so as to enable the patient to get back to normal life at the earliest.
Key words: Total knee artroplasty,, Heterotopic ossification, Biochemical markers.

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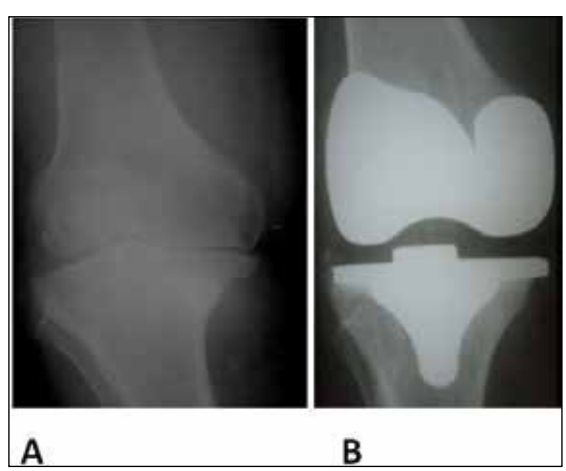
Introduction:
Heterotopic ossification is the formation of new bones in the soft tissues around knee joint. To our knowledge the occurrence is not yet reported in any study done in India.

Extensive heterotopic ossification can cause significant limitation of range of movement of the knee joint so that the basic purpose for which knee arthroplasty was carried out is defeated. Hence it was decided to study whether patterns of biochemical markers and sequential radiographs could help in early detection of this entity so that it is detected before it gets established and treated at very early stage so as to enable the patient to resume active life at the earliest.

Materials and Methods:
34 patients having severe pain and limited range of movement in knee joint enrolled for primary total knee arthroplasty were prospectively studied. Clinically 26 patients had severe osteoarthritis in both the knees and 8 patients had severe osteoarthritis of single knee. Plain radiographs of these patients were also obtained. All were treated surgically with total knee arthroplasty (26 patients underwent bilateral total knee arthroplasties and 8 patients underwent unilateral total knee arthroplasties - total 60 total knee arthroplasties in 34 patients) using the same design of implant.



Titles of figures.
Figure 1 : A & B
Plain radiographs of the patient
A: Radiograph of knee joint showing severe osteoarthritis.
B : Plain radiograph of the knee joint after total knee arthroplasty.

Within one week of surgery their blood samples were obtained to evaluate the levels of serum calcium, inorganic phosphate and alkaline phosphatase (biochwmical markers). Plain radiographs were also done. Same blood tests and radiographs were repeated after one month and every 3 months thereafter for one year.

Results :
All the patients were above 40 years of age with severe osteoarthritis limiting normal day to day activities. All were treated surgically with total knee arthroplasty. Only one out of 34 patients developed heterotopic ossification. Severely restricted painful knee movements were present in this patient. We found changes in biochemical markers in the patient who developed heterotopic ossification in our study. There was a transient decrease in serum calcium and transient increase in inorganic phosphate at 3 months follow up. While the serum calcium was raised in subsequent follow ups. Serum alkaline phosphatase was initially normal and was subsequently raised. ESR was raised in a patient who developed heterotopic ossification at all follow up visits.

Table 1: Blood test reports (Biochemical markers) and plain radiography report of all patients at follow up visits:

Parameter	Result in January 2009	Result in April 2009	Result in November 2009
Serum levels			
Calcium (normal :8.5-10.5 mg/dL)	Low in 1	Rise in 1	Normal
Inorganic Phosphate (normal: 2.5-5.5 mg/dL)	Raised in 1	Normal	Normal
Alkaline Phosphatase (normal: 80-290 IU/L)	Normal	Raised in 1	Raised in 1
ESR (normal:0-10mm at 1 hour)	Raised in 1	Raised in 1	Raised in 1
Plain Radiograph Positive findings	None	One	One

Plain radiograph showed changes of heterotopic ossification 6 months after total knee arthroplasty.

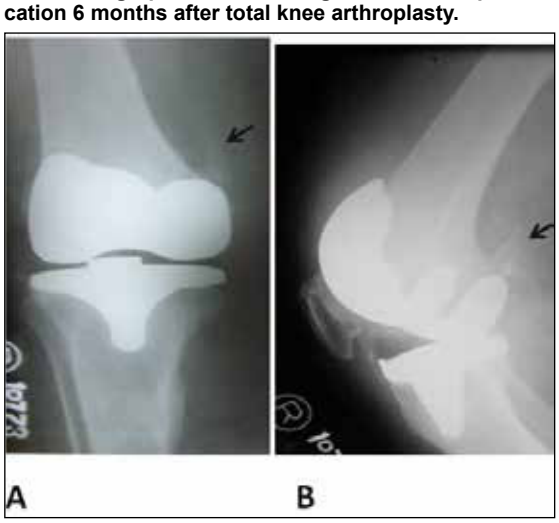


Figure 2 : A & B
Plain radiographs of the patient 6 months after total knee arthroplasty showing development of heterotopic ossification (Arrow)

This patient was started on treatment with Capsule Indomethacin 75 miligram per day for one and half months. Pain was reduced and movements were improved significantly with this early treatment.

Discussion:
The incidence of heterotopic ossification (HO) following primary knee joint arthroplasty has been quoted to be between 3 to 9% in western population as mentioned in almost all references [1-8]. In this study only one out of total 60 knees operated showed heterotopic ossification. The incidence (1.6 %) was thus the least amongst all that has been quoted in the literature [1-8]. One study [9] quotes the rate of heterotopic ossification to be 23-56% following revision total knee arthroplasty.

Significant difference was seen between range of movement in the patient who developed heterotopic ossification and those who did not develop heterotopic ossification. This finding is in agreement with observation by other researchers [1-4] that advanced heterotopic ossification delimits function and benefits of arthroplasty.

Hasegawa M, Ohashi T and Uchida A[5] have reported that patients with heterotopic ossification had findings which raised suspicion of early infection after surgery in the form of fever, erythema, warm and swollen knees.The single positive patient reported in this series had no such findings.

Hasegawa M, Ohashi T, Uchida A. [5] have also reported that the blood examinations were normal in the patients who had heterotopic ossification in their study. We found changes in biochemical markers in the patient who developed heterotopic ossification in our study. There was a transient decrease in serum calcium and transient increase in inorganic phosphate in the first quarter follow up. While the serum calcium was raised in subsequent follow ups, inorganic phosphate was normal. Serum alkaline phosphatase was initially normal and was subsequently raised. ESR was raised in a patient who developed heterotopic ossification at all follow up visits. We believe that the above described biochemical marker pattern may be sensitive indicator of development of heterotopic ossification.

Plain radiograph of knee was positive from second quarter follow up onwards. Hence it is not useful as an early predictor of heterotopic ossification. As to the site of heterotopic ossification, Rader CP, Barthel T, Haase M, Scheidler M, Eulert J. [2] found largest ossifications in anterior distal femur. The study reported by Hasegawa M, Ohashi T, Uchida A. [5] too describes distal femur as the commonest site. In our study also heterotopic ossification was seen in antero-medial aspect of femur.

Commonly reported risk factors for the development of heterotopic ossification include periosteal damage during surgery, increased preoperative spinal bone mineral density, postoperative effusion, forced manipulation, heavy built, male gender and presence of infection [2, 3,5,6,7-10].The factor which could explain the occurrence of heterotopic ossification in the positive case in our study was that there was history of excessive forced manipulation and periosteal trauma during surgery. She was an average built female and she had no focal infection. Her spinal bone mineral density was however not done due to unavailability of the facility.

Various studies [1, 2 and 6] have recommended following treatment modalities for prophylaxis in high risk primary cases:

A] Radiotherapy – either four hours before or within 72 hours of surgery given as a single dose of eight gray.

B]Cap. Indomethacin – 75 milligrams per day for one and half month.

Excision of primary heterotopic ossification is to be considered only when the heterotopic ossification has matured (around 18 months post surgery) and significantly hampers day to day activities. For recurrence following excision of primary heterotopic ossification combined treatment with Cap. Indomethacin and radiotherapy is found to be effective.

Certain studies [1] have pointed out that no conclusive evidence exists to routinely use of prophylaxis against heterotopic ossification and further state to use it only in patients

with significant risk factors. Use of lumbar spinal bone mineral density [3]is also proposed as an earliest indicator of chances of developing heterotopic ossification. Patients who undergo knee replacement surgery usually have such severe osteoarthritis that their range of movement is limited. Thus they are bedridden and hence their bone mineral density is expected to be low.

Hence we are against the use of preoperative spinal bone mineral density. Moreover in our country the cost and availability of bone densitometry facility warrants the use of other methods to predict heterotopic ossification at the earliest.

This study thus proposes that the pattern of triple biochemical markers described here may be used as the earliest test to detect development of heterotopic ossification. Moreover, blood tests are readily available and economical.

Summary:

Typical pattern of biochemical markers i.e. a transient decrease in serum calcium and transient increase in inorganic phosphate in the peri operative stage coupled with a normal serum alkaline phosphatase may be used as the earliest predictor of developing heterotopic ossification in high risk patients so that the prophylactic therapy can be administered at appropriate time so as to enable the patient to get back to normal life at the earliest.

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