

# Hydroxyapatite crystal deposition causing rapidly destructive arthropathy of the hip joint

Jae-Hyuk Yang, Kwang-Jun Oh<sup>1</sup>, Dilbans S Pandher<sup>2,3</sup>

## ABSTRACT

Destructive arthropathy of the hip joint can be attributed to various etiologies like rheumatoid arthritis, aseptic necrosis of the femur head, Charcot's joint, subacute septic arthritis, and tubercular arthritis. A disease that results in much rapid destruction of the hip joint and is not associated with clinical syndrome of above mentioned disease has been reported way back in 1970. However, no evidence-based study has been published to support hydroxyapatite (HA) crystals as a probable cause of rapidly destructive arthropathy of the hip joint. We report a case with microscopic and biochemical confirmation of HA crystal deposition causing destructive arthropathy of the hip joint.

**Key words:** Hydroxyapatite crystal, rapidly destructive hip arthropathy, scanning electron microscopy

## INTRODUCTION

Rapidly destructive arthropathy was first described by Postel and Kerboul<sup>1</sup> as a disease characterized by a higher average age of onset than other arthropathies, unilateral involvement, almost always appears to start in normal hip, and in several months, it takes on the characteristics of ordinary arthrosis with moderate pain and early roentgenographic signs. Then, in a matter of a few weeks, it starts to degenerate, and in 6 to 12 months, the destruction of the joint can be extreme. Inoue *et al.*<sup>2</sup> have reported that new bone formation and osteophytes, typical of osteoarthritis, is not observed in rapidly destructive arthropathy. Komiya *et al.*<sup>3</sup> have studied bone resorptive factors in joint fluid, though they did not specify any etiology that results in activation of these factors. Hydroxyapatite (HA) crystals have been associated with several forms of

arthritis and peri-arthritis in and around the joints; however, no study has reported HA crystals as a cause of rapidly destructive arthropathy of the hip. Identification of crystals remains a problematic issue since there is no simple, reliable analytic procedure available. We describe a case of destructive arthropathy of the hip joint which was primarily induced by HA crystals.

## CASE REPORT

A 66-year-old male patient presented with 6-month history of intermittent pain in his right hip joint, which rapidly worsened over last few weeks. The pain was dull aching in nature, localized to the right hip joint, and exacerbated by movement at the hip joint. Range of motion was significantly reduced. Neurological examination was normal. There was no history of fever, trauma, infection, preceding systemic illness, prolonged drug intake, or previous surgery of the hip joint. The general clinical examination was unremarkable.

Total leukocyte count was 5 510/ $\mu$ l; E.S.R was 31 mm/hr, and C.R.P. was 2.45 mg/dl. Serum calcium, phosphorus, and alkaline phosphatase levels were normal, as were the liver and renal function tests. Rheumatoid factor and antinuclear antibodies were negative.

Plain radiograph of the right hip revealed severe destruction and flattening of the femoral head with mild sclerosis and minimal osteophytes [Figure 1]. Magnetic resonance imaging (MRI) showed foci of low signal intensity (best seen on T1-weighted images) around posterior aspect of greater and lesser trochanter, consistent with the suspicion of calcification [Figure 2a]. T2-weighted images showed

Department of Orthopaedic Surgery, Seoul Veterans Hospital, Seoul,  
<sup>1</sup>Joint Replacement and Trauma Service, Department of Orthopaedic Surgery, Konkuk University Medical Center, Seoul, Republic of Korea,  
<sup>2</sup>Oxford Super-Specialty and Trauma Hospital, Jalandhar, <sup>3</sup>SGL Charitable Hospital, Subhanpur, Kapurthala, Punjab, India

**Address for correspondence:** Dr. Dilbans Singh Pandher, Department of Orthopaedic Surgery, Oxford Super-Specialty and Trauma Hospital, Bhagwan Mahanvir Marg, Lajpat Nagar, Near Nakodar Chowk, Jalandhar, Punjab – 144001, India. E-mail: dilbans@yahoo.com

Access this article online	
Quick Response Code:	Website: www.ijoonline.com
	DOI: 10.4103/0019-5413.87139

destruction of the right femoral head, fluid collection in the joint space, thinning and destruction of the acetabular cartilage, and a cystic mass lesion with increased signal

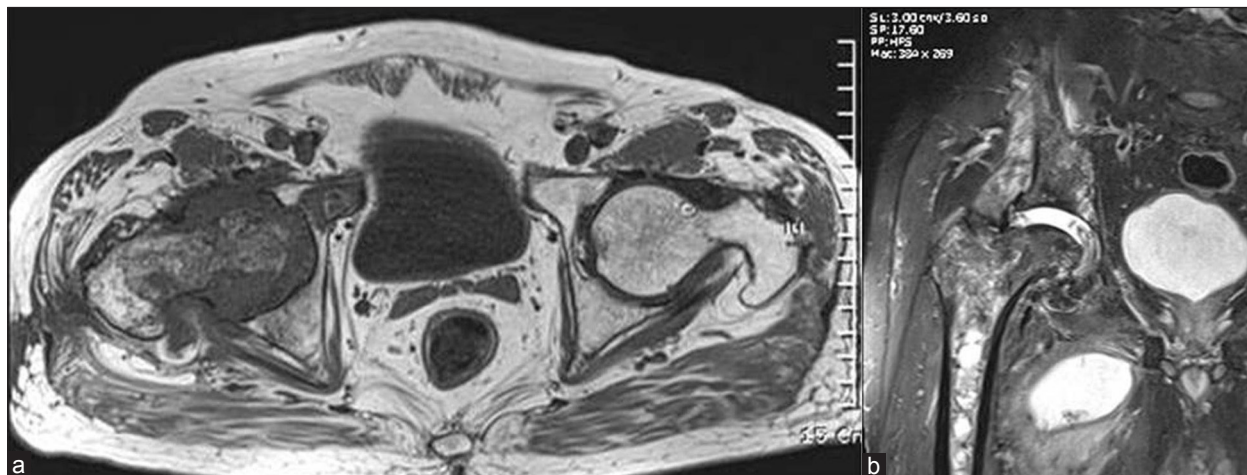


**Figure 1:** Radiograph of the pelvis (anteroposterior view) with both hip joints shows severe destruction of the right femoral head with mild subarticular sclerosis and minimal osteophytes

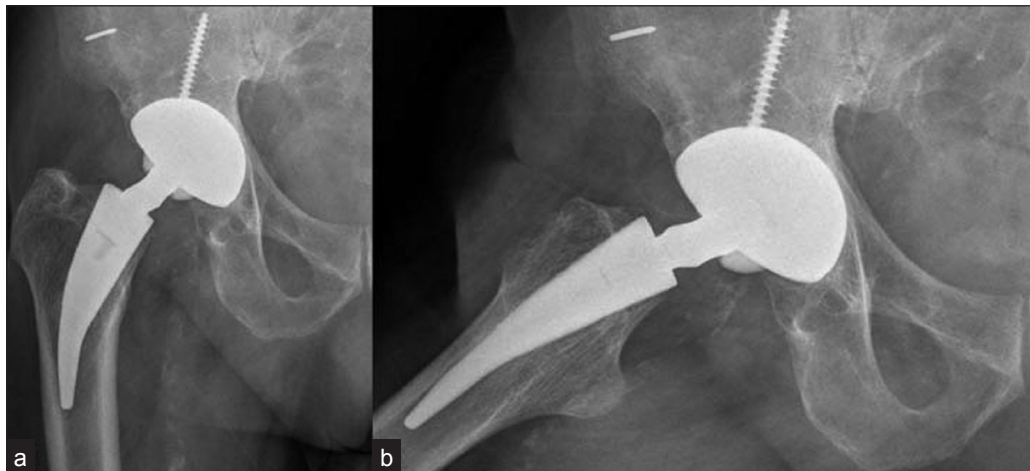
intensity and wall enhancement, in the adductor muscle group [Figure 2b].

Sonography-assisted aspiration of the hip yielded serosanguinous fluid. Fluid analysis results showed a normal total cell count and cultures for bacteria, fungi, and acid fast bacilli were negative. Alizarin red S staining was strongly positive. Polymerase chain reaction test for *Mycobacterium tuberculosis* was negative. Polarized microscopy demonstrated amorphous non-rhomboid or needle-shaped crystals which were negatively birefringent.

After thorough discussion with patient regarding prognosis of total hip arthroplasty (THA), surgery was planned. Patient underwent uncemented THA [Figure 3]. Peroperative tissue sample for frozen biopsy was sent to rule out infection. A sample of synovium and capsule were sent for microscopic and histological examinations.



**Figure 2:** (a) T1-weighted MRI shows low signal intensity areas around the trochanteric region. (b) T2-weighted MRI shows destruction of the right femoral head, high signal intensity effusion in the joint space, thinning and destruction of the acetabular cartilage, and cystic lesion with wall enhancement in the adductor muscle group



**Figure 3:** (a) Follow-up X-ray (anteroposterior view) showing (a) well-placed total hip prosthesis on right side (b) Frog leg view of right hip joint showing well-placed total hip prosthesis

Microscopy revealed diffuse villous proliferation of the synovium with diffuse deposits of bluish, acellular, amorphous material intermixed with fibrin. There was insignificant inflammatory cell infiltration. The amorphous material showed extensive calcium deposits with von Kossa stain [Figure 4a]. Histopathologic examination of the tissue specimen demonstrated extensive synovial hyperplasia and hypertrophy with marked calcium and fibrin deposits, marked degeneration of articular soft tissue, and fat necrosis with dead bony trabeculae. Subsequent scanning electron microscopy (SEM) examination revealed small densely packed microspheroids of roughly spherical or elliptical shape with uniformly dense or with less dense centers [Figure 4b]. The diagnosis of destructive arthropathy of the hip joint induced by HA crystals was established. The patient is followed up at 2 years and 8 months with good outcome.

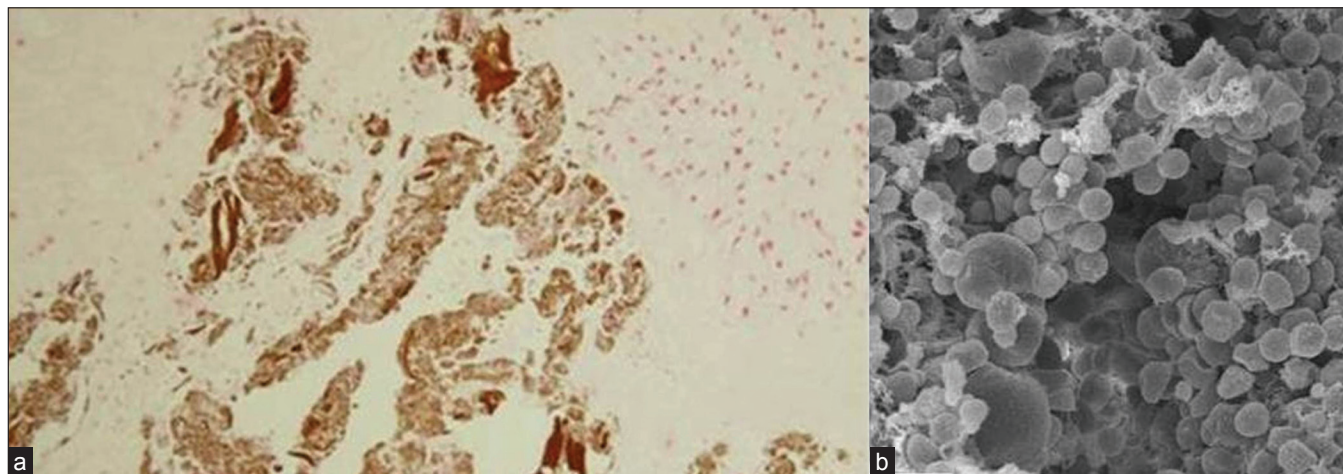
## DISCUSSION

The factors responsible for the intra-articular accumulation of crystals and their role in producing joint disease have always been a topic of debate. HA crystals commonly found in osteoarthritic synovial effusions and frequency of crystal deposition in articular cartilage are significantly higher in osteoarthritis patients.<sup>4</sup> In knee joint osteoarthritis, HA crystal deposition is common (30-60% cases),<sup>5</sup> and the damage to the joint has been correlated with the amount of crystals deposited in the joint.<sup>5,6</sup> Crystals usually are deposited in the connective tissues of joint, often long before clinical presentation of acute arthritis. They may be found in the synovium, cartilage, joint capsule, and periarticular tissues.<sup>7</sup> It is generally accepted that solute excess of a crystal due to decreased ionized calcium or inorganic phosphate levels in the ambient joint fluid initiate crystal release,<sup>8</sup> but this may also require alteration of the

articular connective tissue matrix. The shedding of crystals may also result from local trauma, surgery, drug therapy, acute illness, or hemodialysis.<sup>9</sup> In present patient, there were no predisposing factors that could be associated with calcium and phosphate metabolic alterations, or an increase in the solubility of the intra-articular deposits. Although the pathogenesis of HA-induced arthropathy is poorly understood, Komiya *et al.*<sup>10</sup> have found elevated levels of IL-1 $\beta$  in the joint fluid of affected patients as well as increased secretion of matrix metalloproteinase by the affected synovium, suggesting that excessive production of these bone resorptive factors may mediate the rapid joint destruction. The crystals stimulate the synovial cell to secrete collagenase and neutral protease.<sup>11</sup> These enzymes may damage the articular structures and also may release additional tissue-bound basic calcium phosphate crystals to continue the cycle.

HA-associated arthropathy may radiographically be confused with other disease entities such as osteonecrosis with secondary arthritis, rheumatoid arthritis, neuropathic arthropathy, or septic arthritis. In most cases, however, clinical history and laboratory findings are sufficient to exclude these entities. The radiographic findings in our case were incompatible with simple osteoarthritis, in view of paucity of osteophytes, lack of cyst formation, and very mild subarticular sclerosis. MRI findings of low signal intensity corresponding to calcification and increased signal intensity representing edema and cystic mass lesion were also consistent with those previously reported about HA deposition disease (HADD).<sup>12,13</sup>

Alizarin red S staining of synovial fluid is a sensitive but not specific method of detecting HA crystals. Test is considered positive when the orange red-stained clumps are present in every field.<sup>14</sup> In present case, results of synovial fluid analysis



**Figure 4:** (a) Light micrograph shows diffuse villous proliferation of the synovium, absence of inflammatory infiltrate, and extensive calcium deposits (Original magnification,  $\times 40$ , von Kossa stain). (b) Scanning electron micrograph shows small densely packed microspheroids of roughly spherical or elliptical shape compatible with hydroxyapatite crystals (Original magnification,  $\times 701$ )

and histopathology showing large number of alizarin-positive bodies and findings of synovial hyperplasia, fibrosis with fragments of calcified material, respectively, were found to be compatible with HADD.<sup>12,13</sup> Particularly, we confirmed the crystal morphology using the SEM. HA crystals themselves are very small—only 70 to 250 Å in diameter. SEM with energy dispersive analysis (EDA) represents more specific techniques that provide both morphologic data and molar ratios of elemental constituents. SEM of HA crystals reveal small irregular-shaped microspheroids with uniformly dense or less dense centers. EDA showed a calcium/phosphorus molar ratio of approximately 1.7:1, which is compatible with HA crystals.<sup>15</sup>

Destructive arthropathy primarily attributed to HA crystals has already been reported and confirmed in the glenohumeral (Milwaukee shoulder), knee, and elbow joints.<sup>16-18</sup> The threshold of suspicion for HA crystal-induced arthropathy is low among the practicing consultants. This report emphasizes on considering it as a distinct subset of osteoarthritis that may cause relatively rapid destruction of the involved joint in a manner different from the primary osteoarthritis. Further research is required to establish modes of early diagnosis of the disease and role of medical management of early disease to prevent rapid destruction of the joint.

## REFERENCES

- Postel M, Kerboull M. Total prosthetic replacement in rapidly destructive arthrosis of the hip joint. *Clin Orthop Relat Res* 1970;72:138-44.
- Inoue A, Higuchi F, Bekki S, Fujita A, Shiba N. Immune reaction blamed for RDC syndrome's sudden hip damage. *Rheum News Int* 1989;17:3-7.
- Komiya S, Inoue A, Sasaguri Y, Minamitani K, Morimatsu M. Rapidly destructive arthropathy of the hip. Studies on bone resorptive factors in joint fluid with a theory of pathogenesis. *Clin Orthop Relat Res* 1992;284:273-82.
- Ohira T, Ishikawa K. Hydroxyapatite deposition in osteoarthritic articular cartilage of the proximal femoral head. *Arthritis Rheum* 1987;30:651-60.
- Gibilisco PA, Schumacher HR Jr, Hollander JL, Soper KA. Synovial fluid crystals in osteoarthritis. *Arthritis Rheum* 1985;28:511-5.
- Halverson PB, McCarty DJ. Identification of hydroxyapatite crystals in synovial fluid. *Arthritis Rheum* 1979;22:389-95.
- Dieppe P, Doherty M, Macfarlane D. Introduction. Crystal-related arthropathies. *Ann Rheum Dis* 1983;42Suppl 1:1-3.
- Halverson PB, Cheung HS, McCarty DJ. Enzymatic release of microspheroids containing hydroxyapatite crystals from synovium and of calcium pyrophosphate dihydrate crystals from cartilage. *Ann Rheum Dis* 1982;41:527-31.
- Halverson PB, Carrera GF, McCarty DJ. Milwaukee shoulder syndrome. Fifteen additional cases and a description of contributing factors. *Arch Intern Med* 1990;150:677-82.
- Komiya S, Inoue A, Sasaguri Y, Minamitani K, Morimatsu M. Rapidly destructive arthropathy of the hip. Studies on bone resorptive factors in joint fluid with a theory of pathogenesis. *Clin Orthop Relat Res* 1992;284:273-82.
- Cheung HS, Halverson PB, McCarty DJ. Release of collagenase, neutral protease, and prostaglandins from cultured mammalian synovial cells by hydroxyapatite and calcium pyrophosphate dihydrate crystals. *Arthritis Rheum* 1981;24:1338-44.
- Chow HY, Recht MP, Schils J, Calabrese LH. Acute calcific tendinitis of the hip: case report with magnetic resonance imaging findings. *Arthritis Rheum* 1997;40:974-7.
- Kuroda H, Wada Y, Nishiguchi K, Ninomiya T, Takahama A, Sato S, *et al.* A case of probable hydroxyapatite deposition disease (HADD) of the hip. *Magn Reson Med Sci* 2004;3:141-4.
- Paul H, Reginato AJ, Schumacher HR. Alizarin red S staining as a screening test to detect calcium compounds in synovial fluid. *Arthritis Rheum* 1983;26:191-200.
- Halverson PB, Cheung HS, McCarty DJ, Garancis J, Mandel N. "Milwaukee shoulder"-association of microspheroids containing hydroxyapatite crystals, active collagenase, and neutral protease with rotator cuff defects. II. Synovial fluid studies. *Arthritis Rheum* 1981;24:474-83.
- Halverson PB, McCarty DJ, Cheung HS, Ryan LM. Milwaukee Shoulder syndrome: Eleven additional cases with involvement of the knee in seven (basic calcium phosphate crystal deposition disease). *Semin Arthritis Rheum* 1984;14:36-44.
- Hernandez-Molina G, Crispin JC, Kimura-Hayama E, Rull-Gabayet M. Chronic destructive elbow arthropathy associated with hydroxyapatite crystals in a patient with systemic lupus erythematosus. *J Clin Rheumatol.* 2006;12:194-5.
- McCarty DJ, Halverson PB, Carrera GF, Brewer BJ, Kozin F. "Milwaukee shoulder"-association of microspheroids containing hydroxyapatite crystals, active collagenase, and neutral protease with rotator cuff defects. I. Clinical aspects. *Arthritis Rheum* 1981;24:464-73.

**How to cite this article:** Yang J, Oh K, Pandher DS. Hydroxyapatite crystal deposition causing rapidly destructive arthropathy of the hip joint. *Indian J Orthop* 2011;45:569-72.

**Source of Support:** Nil, **Conflict of Interest:** None.