Accumulation of Fatty Marrow in the Osteonecrotic Hip Mimicking Joint Infection

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Abstract

Background Factors such as lipids or cholesterol crystals in body fluids can cause a spurious elevation of leukocytes (WBC) in an automated cell count. This artifact can occur in automated WBC counts of hip fluid from femoral head osteonecrosis (ON), and an erroneous diagnosis of septic arthritis can be made.

Question/purposes We describe the frequency of this artifactual leukocytosis in femoral head ON and how to differentiate it from septic arthritis.

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

This work was performed at Seoul National University Bundang Hospital.

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Methods From September 1997 to June 2004, 414 patients (486 hips) with femoral head ON were scheduled to undergo THAs. Although we had no pre-operative suspicion of infection, we intraoperatively suspected concomitant pyogenic arthritis in eight patients (eight hips) because pus-like fluid gushed from the joint during the operation. To confirm the presence or absence of infection we intraoperatively evaluated the joint fluid with automated blood cell count and microscopy. The automated WBC count was elevated in all eight patients. In seven of the eight patients, WBCs were not identified under microscopic observation and the leukocytosis of automated cell counting was considered to be erroneous. These seven patients underwent THAs. The minimum followup was 3 years (average, 45 months; range, 36–60 months).

Results These seven patients were considered to have a spurious elevation of WBC (range, 4500–18,400/mm³; mean, 8970/mm³) in an automated cell count. The prevalence of the spurious leukocytosis was 1.4% (7/414) in osteonecrotic hips. In all seven patients, we observed numerous fat cells and globules instead of WBCs under microscopic observation. No bacteria were seen in the smear and culture of the joint fluid. The seven patients underwent THAs, and no patient had a subsequent deep wound infection as of the last followup.

Conclusions Fatty joint effusion in an osteonecrotic hip may appear like pus and erroneously can be interpreted as leukocytes in an automated cell count. In this situation, a microscopic evaluation of joint fluid smear should be performed to determine the presence of infection and the treatment method.

Level of Evidence Level III, prognostic study. See Guidelines for Authors for a complete description of levels of evidence.

Introduction

Conventionally, orthopaedic surgeons make a diagnosis of septic arthritis when joint fluid appears turbid and the WBC count is elevated in cell counting of joint fluid even without clinical symptoms of septic arthritis because these symptoms might not be evident in the early stage of infection or low-grade infection.

Liquefied fat of bone marrow is yellow and turbid and may simulate pus. In collapsed femoral head ON, marrow fat leaks into the hip through the osteochondral defect. If pus-like fluid gushes from the joint during the THA, and an automated WBC count of the joint fluid shows leukocytosis [20], orthopaedic surgeons make a diagnosis of septic arthritis and delay THA owing to fear of infection developing after the arthroplasty [23]. Surgeons may treat these patients with débridement or resection arthroplasty and subsequent use of antibiotics. Accordingly, hospital stays are prolonged, medical costs are increased, and patients have substantially greater physical limitations and a reduction in their health-related quality of life [2, 3].

In September 1997, we performed a THA for a patient with collapsed femoral head ON. During the operation pus-like fluid gushed from the hip and the patient's WBC count was elevated in an automated cell count of the joint fluid. The patient had no symptoms or suggestive laboratory findings of infection preoperatively. We were unsure whether the patient had an infection and we hesitated performing the THA. Subsequently we questioned whether these cell counts could erroneously suggest infection.

We therefore asked: (1) how frequently an artifactual elevation of WBC count occurs in automated cell counting of the joint fluid in femoral head ON; (2) how to distinguish this artifactual leukocytosis from true septic arthritis; (3) whether to do a THA or delay performing it in patients with artifactual leukocytosis; and (4) whether an infection occurs in these patients after THA.

Patients and Methods

From September 1997 to June 2004, we scheduled 414 patients (486 hips) with femoral head ON to undergo THAs. According to the Ficat system [11], 75 hips had Stage II-B ON, 302 had Stage III, and 109 had Stage IV. In eight of these 486 hips (eight patients), pus-like fluid gushed from the joint during the operation (Fig. 1). We had not suspected septic arthritis during the preoperative evaluation of these eight patients because they had no fever and their preoperative laboratory findings did not suggest infection. To confirm the presence of infection

Fig. 1 An intraoperative photograph shows the yellowish and turbid hip fluid that looks like pus.

Fig. 2 An intraoperative smear from infected hip fluid shows numerous neutrophils (Stain, Diff-Quik; original magnification, $\times 400$).

and decide whether to perform or delay the THA during the operation we collected joint fluids and sent them to the laboratory for automated WBC counting and direct microscopic observation intraoperatively. The design and protocol of this retrospective study were approved by the institutional review board of Seoul National University Bundang Hospital, and all patients were informed that their medical data could be used in a scientific study; all patients gave consent for publication of the data concerning their cases.

According to the automated blood cell counting, all of the eight patients had an elevated WBC count. One patient had neutrophil aggregation under microscopic observation (Fig. 2). This patient was considered to have an early stage or a low virulence of septic arthritis and was treated with débridement and irrigation; this patient was excluded from

Table 1. Characteristics of the patients in this study

Patient	Gender	Age (years)	Ficat stage	Cause of ONFH	Laboratory findings before THA			WBC (joint fluid)	Culture	Time to normalization after THA (days)		
					WBC*	ESR [†]	CRP [‡]			WBC*	ESR [†]	CRP [‡]
1	M	32	III	Idiopathic	5800	21	12	6400	Negative	14	21	14
2	M	39	IV	Alcohol	7500	18	5	8600	Negative	0	15	10
3	M	29	IV	Steroids	9700	2	5	4500	Negative	5	10	7
4	M	40	IV	Alcohol	7300	13	10	18,400	Negative	0	18	12
5	M	63	III	Alcohol	5900	16	3	7400	Negative	5	10	9
6	M	33	III	Alcohol	11,000	2	7	7700	Negative	5	14	10
7	M	43	IV	Idiopathic	7100	16	9	9800	Negative	7	14	12

*mm³ (range, 0.0–8.0 mm³); [†]mm/hour (range, 0.0–10.0 mm/hour); [‡]mg/L (range, 0.0–9.0 mg/L).

the current study. In the remaining seven patients, who are the subjects of this study, WBCs were not identified under microscopic observation. The leukocytosis of automated cell counting was considered to be an artifactual elevation attributable to lipid material, and these seven patients underwent THAs. All seven patients were followed for at least 3 years after THA and the latest followup was at an average of 45 months (range, 36–60 months) after the operation. All seven patients were males with a mean age of 40 years (range, 29–63 years). The Ficat stages were III in three patients and IV in four patients. The causes of ON were alcohol induced in four patients, idiopathic in two, and steroid induced in one. Preoperatively, the WBC count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) level of these patients were within normal ranges (Table 1).

THAs in all patients were performed through a posterolateral approach. Because the joint capsule was distended, we aspirated the joint fluid using a 16-gauge needle. The fluid sample was collected in a Vacutainer® tube (BD Company, Franklin Lakes, NJ, USA) containing ethylene diamine tetra-acetic acid (EDTA) anticoagulant and sent to the laboratory for WBC count, smear, and culture to determine the presence of infection.

The cell counts were obtained with a Coulter STKS Cell Counter (Coulter Corporation, Hialeah, FL, USA), which uses an electrical impedance-based technology for cell counting. In normal synovial fluid, the WBC count is less than 200/mm³ [18]. Leukocytosis of joint fluid is defined as a WBC count of 2000/mm³ or greater [12].

Hematoxylin and eosin stains were performed for the joint fluid smears to identify the cells in the fluid and to distinguish an artifactual leukocytosis from true leukocytosis. All slides were reviewed by one clinical pathologist (SJK), and total and differential numbers of WBCs were manually counted using the Neubauer counting technique [22]. The reported coefficient of variation (CV) of this method was approximately 6.5% for normal and increased

WBC counts [22]. Aerobic and anaerobic cultures of the joint fluid were performed.

When there was no evidence of leukocytosis in the microscopic examination of the smears, patients underwent THA as scheduled regardless of automated WBC counts. Cementless fixation was used for the acetabular cup and femoral stem in all patients.

After surgery, we carefully monitored clinical signs of infection including fever, pain, tenderness, local heat, swelling, or redness of the surgical wound for 2 to 3 weeks in the ward. The WBC count, ESR, and CRP level of each patient were examined twice per week during hospitalization and once per week after discharge until they were normalized.

After discharge patients were routinely followed at 6 weeks, 3, 6, 9, and 12 months, and every 6 months thereafter. During the followup period, we carefully monitored clinical signs and laboratory findings of infection, and the Harris hip score was used for evaluation [15]. An ESR greater than 30 mm/hour and a CRP level greater than 10 mg/L were considered to be suggestive of infection [26]. Followup radiographs were examined with particular attention being paid to the occurrence of infection. A progressive radiolucency, loosening of the prosthesis, and periosteal reaction were considered to be suggestive of infection [4]. The 6-week AP and cross-table lateral radiographs were considered to be the baseline studies for radiographic comparison. Fixation of the femoral component was determined using the method of Engh et al. [9], and fixation of the acetabular component was determined using the method of Latimer and Lachiewicz [19]. Osteolytic lesions, if present, were defined according the criteria of Engh et al. [8]. The lesions were recorded according to the three zones described by DeLee and Charnley [7] on the acetabular side and the seven zones described by Gruen et al. [14] on the femoral side. Final radiographic analysis was performed at the latest followup.

Results

The seven hips comprised 1.4% of 486 osteonecrotic hips that underwent THAs during the study period. At surgery, all of the seven femoral heads had an osteochondral crack at the surface of the necrotic portion of the femoral head, through which the marrow space communicated with the joint space (Fig. 3). In automated cell counting, the number of WBCs ranged from 4500 to 18,400/mm³ (mean, 8970/mm³). In all seven patients, microscopic evaluation of the fluid revealed numerous fat cells and globules and the manual cell count revealed a scarce number of WBCs (Fig. 4). The smear and culture identified no bacteria in joint aspirates for all seven patients.

Fig. 3 An osteochondral crack was present at the surface of the necrotic portion of this extracted osteonecrotic femoral head.

Fig. 4 An intraoperative smear of the hip fluid shows fat globules and fat cells. No leukocytes are visible (Stain, hematoxylin and eosin, original magnification, $\times 400$).

The WBC and CRP after surgery were normalized within 3 weeks (Fig. 5A–B), and the ESR was normalized within 5 weeks (Fig. 5C). No patient had any symptoms or laboratory findings suggestive of infection during the follow-up period, and the preoperative mean Harris hip score improved from 54 (range, 43–61) points to 92 points

Fig. 5A–C Serial changes of (A) WBC count, (B) CRP level, and (C) ESR after THA are shown. For all seven patients, the WBC count and CRP were normalized within 3 weeks. The ESR was normalized within 5 weeks in all seven patients. The numbers next to the symbols in these illustrations refer to the seven patients.

Fig. 6A–B (A) An AP radiograph of the hip of a 40-year-old man shows femoral head osteonecrosis with collapse. (B) An AP hip radiograph obtained 5 years after surgery shows no evidence of infection such as implant loosening, periosteal reaction, or progressive radiolucency.

(range, 89–96) at the latest followup. No patient had loosening of implants, any periosteal reaction, or any focal osteolytic lesion around the implants. All of the acetabular cups and femoral stems had radiographic evidence of bone ingrown stability at the time of the last followup (Fig. 6).

Discussion

Advanced femoral head ON is frequently treated with a THA. However, in the presence of septic arthritis, we believe the THA should be delayed until the infection is resolved to avoid the near certainty of postoperative infection [5, 13, 24]. Therefore, if surgeons find yellow and turbid joint fluid during the operation, they usually make a diagnosis of septic arthritis and perform debridement or resection arthroplasty instead of THA. Lipid or cholesterol crystals in body fluids can cause a spurious elevation of WBCs in the automated cell count [10, 25]. This artifact can occur in the automated WBC count of hip fluid containing marrow fat from an osteonecrotic femoral head and an erroneous diagnosis of septic arthritis can be made. This spurious elevation of WBCs in fat-contaminated body fluid is well known to physicians in the laboratory department. However, most orthopaedic surgeons are unaware of the spurious infection. Therefore, we studied the frequency of this artifactual leukocytosis in femoral head ON and how to differentiate it from a true septic arthritis.

We acknowledge limitations to our study. First, our study included a small number of patients. Nevertheless, to avoid a prolonged hospital stay, increased medical costs, and prevent morbidity, we think it is worth reporting that the yellowish turbid fluid mimicking joint infection might gush from the hip in advanced femoral head ON and that the cell counter misread the fluid to be a joint infection. Second, we cannot explain why the joint fluid exhibits such pus-like appearance in some patients but not in others, although osteonecrotic femoral heads frequently collapse and bone marrow is exposed to the hip space.

In all of our seven patients, gross examination revealed the joint fluid to be yellowish and opaque and the initial automated instrument cell counter reported elevated WBC counts. All seven patients had femoral head collapse and a Ficat Stage III or IV lesion. Thus, we speculated that the marrow fat leaked into the joint space through the osteochondral crack at the surface of the necrotic femoral head, appeared like pus, and caused an artifactual leukocytosis in the automated cell count.

Most of the currently used automated cell counters use electrical impedance or light scattering to obtain a WBC count. The electrical impedance-based technology determines the number and size of cells by detecting and measuring the changes in electrical resistance when a cell in a conductive liquid passes through a small aperture. These cells are analyzed in an electro-optical flow cell. The cell volume is determined by the impedance. Cell counters using this technology seem to capture greater than 75% of the current world market of automated cell counters. The light scattering-based technology determines the cell number and size by detecting the forward angle scatter of a laser-generated monochromatic light [22].

In certain situations, abnormal characteristics of the sample interfere and erroneous counts are obtained [25]. The most common causes are the presence of nucleated erythrocytes and failure of all the erythrocytes to lyse. Other causes include the presence of giant platelets, platelet aggregates, fibrin strands, the presence of a cryoglobulin or paraprotein, and the presence of malaria parasites [1, 6, 16]. Hyperlipidemia is also reportedly a cause of falsely elevated WBC count [1]. A Coulter STKS, which was used in our study, determines the number and size of cells by a technology of electrical impedance. The size of the normal marrow fat cell is approximately 76 μm , which is much larger than that of the leukocytes ranging from 10 to 20 μm [20]. We speculated that the fat cell membrane might have been ruptured in several fat cells and fat globules were released from the fat cells. Some shrunken fat cells and released fat globules, which were similar in size to leukocytes, might have been counted as leukocytes. This might have generated a bias of electrical impedance in the Coulter STKS cell counter, thereby also

interfering with the WBC count in our patients. Cell counters, which are based on light scattering technology, also showed an artifactual elevation of WBC count when the blood sample was contaminated with subcutaneous adipose tissues [27].

Concomitant septic arthritis of the hip can occur in patients with femoral head ON, especially when the patient is immune compromised or has sickle cell anemia [17, 21]. When septic arthritis is confirmed under microscopic identification of an aggregation of neutrophils, THA should be delayed until the infection is resolved to prevent a catastrophic result. However, joint fluid containing fat material leaking from an osteonecrotic femoral head can have the appearance of pus and an automated cell counter can report a spurious leukocytosis attributable to the adipose tissue or lipids. In such a situation, microscopic examination of the smear must be performed to avoid a false diagnosis of septic arthritis.

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