Serum Interleukin 8 Levels Correlate With Synovial Fluid Levels in Patients With Aseptic Loosening of Hip Prosthesis

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Abstract: Levels of inflammatory cytokines (tumor necrosis factor α, interleukin [IL] 6, and IL-8) in serum from patients with osteolysis on radiographs after hip arthroplasty [osteolysis(+), n = 28], patients without osteolysis after hip arthroplasty [osteolysis(−), n = 24], and nonoperated healthy subjects [controls, n = 20] were determined. In addition, cytokine levels in synovial fluid from patients undergoing revision total hip arthroplasty (n = 14) for loosening were measured and compared with each other and with the area of osteolysis on radiographs. Serum IL-6 and IL-8 levels were significantly higher in the osteolysis(+) group than in the osteolysis(−) or the control groups. Furthermore, a significant correlation was found between the serum and synovial fluid IL-8 levels and between synovial fluid IL-8 levels and the area of osteolysis in patients undergoing revision total hip arthroplasty. Therefore, serum IL-8 levels could be a useful periprosthetic osteolysis marker. **Key words:** aseptic loosening, periprosthetic osteolysis, serum, synovial fluid, cytokines, interleukin 8.

With improved cementing technique and implant design, the longevity of total hip arthroplasty (THA) has been prolonged. However, periprosthetic osteolysis with resulting aseptic loosening has been considered to be the most important factor that affects the long-term success of THA, and periprosthetic osteolysis, in turn, has been linked to the action of several inflammatory cytokines, prostaglandins, soluble adhesion molecules, and growth factors [1-3].

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Currently, the extent of periprosthetic osteolysis can only be estimated by its appearance on plain radiographs, and another useful diagnostic method has not yet been established. Although there have been several reports which have dealt with the relationship of cytokine levels either in serum [4,5] or in synovial fluid [6-10] and periprosthetic osteolysis, use of their levels as a marker for monitoring osteolysis has not been documented, and to the best of our knowledge, there has been no report concerned with the relationship between cytokine levels in serum and those in synovial fluid in patients with aseptic loosening of hip prostheses.

We have therefore conducted the current study to determine levels of inflammatory cytokines (ie, tumor necrosis factor α [TNF-α], interleukin [IL] 6, and IL-8) in serum obtained from patients diagnosed with osteolysis on plain radiograph after THA or bipolar hip arthroplasty, patients without osteolysis after THA, and healthy subjects.

The results were compared among the relevant groups. In addition, we have analyzed the cytokine levels in synovial fluid in patients undergoing revision THA for aseptic loosening due to osteolysis and have investigated the correlation between serum, synovial fluid levels, and the area of osteolysis.

Materials and Methods

Osteolysis

Osteolysis was defined as radiolucent areas of a bone more than 2 mm in width and progressive on the anteroposterior or on the lateral radiographs. Nonprogressive and linear radiolucent areas less than 2 mm in width were not considered osteolysis. After the radiograph was digitized, the area of osteolysis was outlined and measured using an image analysis program (National Institutes of Health Image program, Bethesda, Md). The area of radiolucency around the acetabular component or the femoral component, or around both, was measured on anteroposterior or on lateral radiographs, and the total amount was considered as the area value of osteolysis.

Patients

A total of 72 patients were divided into 3 groups as follows:

- An osteolysis(+) [OL(+)] group consisted of 28 patients with arthroplasties who had osteolysis around the acetabular or femoral component, or both.
- An osteolysis(−) [OL(−)] group consisted of 24 patients with arthroplasties who had no osteolysis around the acetabular or femoral component.
- A control group consisted of 20 nonoperated healthy subjects.

Table 1. Details of the Patients in Each Group

	OL(+)	OL(−)	Control
Total Samples	28	24	20
Sex (male/female)	4/24	1/23	6/14
Mean age (range)	65.6 (39-82)	66.1 (49-84)	63.0 (54-77)
Mean implant duration, mo (range)	147.1 (60-264)	65.3 (23-148)	–
Cemented/uncemented	11/17	3/21	–
THA/BHA	15/13	24/0	–

BHA indicates bipolar hip arthroplasty.

Table 2. Mean Serum Levels of Cytokines

	OL(+) (n = 28)	OL(−) (n = 24)	Control (n = 20)
TNF-α	2.51 ± 0.32 (0.49-7.66)	2.15 ± 0.26 (0.71-6.18)	2.01 ± 0.17 (0.92-3.15)
IL-6	3.31 ± 0.70 (0-16.9)*	1.11 ± 0.28 (0-4.97)	0.67 ± 0.23 (0-3.01)
IL-8	21.7 ± 1.91 (6.13-49.6)*	11.2 ± 1.08 (0-21.7)	11.2 ± 1.34 (0-21.6)

Values are expressed as pg/mL ± SEM (range).
*$P < .01$ (Mann-Whitney U test) compared with OL(−) group and the control group.

Details of the patients are given in Table 1. Patients with autoimmune diseases, allergies, infectious diseases, or cancer were excluded from this study. All patients or their relatives gave informed consent for blood and synovial fluid samples to be obtained for this study. The procedure was carried out after approval by the Hiroshima University School of Medicine Ethics Committee.

Sample Preparation

Peripheral venous blood samples were collected from all patients in serum separator tubes and then centrifuged at 3000 rpm for 15 minutes. The separated serum was aliquoted and stored at −70°C until assayed. Similarly, synovial fluid samples were collected at revision THA and then centrifuged at 3000 rpm for 15 minutes to remove cells and other debris. The supernatant was aliquoted and stored at −70°C until assayed.

Cytokine Assays

Inflammatory cytokine levels (TNF-α, IL-6, and IL-8) in serum and synovial fluid were measured using quantitative, noncompetitive, sandwich enzyme-linked immunosorbent assays (Quantikine, R&D Systems, Minneapolis, Minn). The

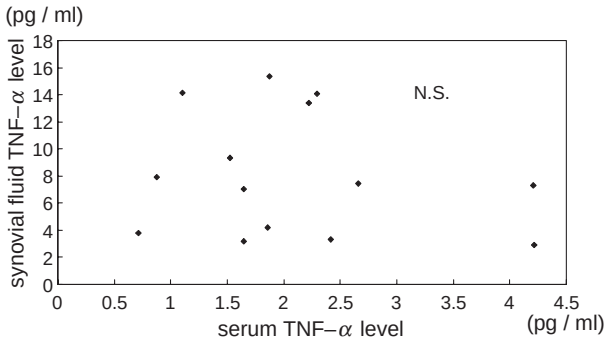

Fig. 1. Comparison between serum TNF-α level and synovial fluid TNF-α level.