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〔Original Paper〕

Histological evaluation of the osteolysis after total hip arthroplasty

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SUMMARY

Using histological methods, tissues from revised hip replacement were investigated. Periprosthetic tissues were harvested separately from 24 acetabulum components, 34 proximal part and 28 distal part of femoral components in 41 patients. All cases demonstrated radiographic focal osteolysis. Tissue sections were analyzed for the presence of tartarate resistant acid phosphatase (TRAP). The analysis of variance showed no statistically significant differences between the groups (acetabulum vs. proximal part of the stem vs. distal part of the stem) for the number of polyethylene particles, and no statistically significant differences was seen between the groups for the number of TRAP positive multinucleated cells (MNCs). The number of polyethylene particles correlated with linear wear on the radiographs in every part. Correlation between the number of polyethylene particles and TRAP positive cells was shown in only acetabulum, while no correlation was found in both of proximal and distal part of the stem. These suggest close relationship between polyethylene particles and bone resorption in acetabulum, and unlikely in femur. It is assumed that the more variety of the mechanical stresses around femoral component than around acetabular component may affects the bone resorption and represents the difference of the manner of osteolysis between acetabulum and femur.

Key words: osteolysis, total hip arthroplasty, tartarate resistant acid phosphatase, polyethylene

I. Introduction

Osteolysis has been recognized as the major cause of long-term failure in total hip arthroplasty[1-5]. Many implant-derived biomaterial wear particles, mainly polyethylene particles, are found in periprosthetic tissues surrounding loosened components, forming a granulomatous tissue layer or membrane[6-8]. At present, it is widely accepted that these particles are phagocytosed by macrophages in the tissues, and these cells in turn release inflammatory mediators which stimulate osteoclastic bone resorption[4,5]. However, the

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development of prevention of this phenomenon has not been successful because the detail of the mechanism is not quite clear. The purpose of the present study is to elucidate the mechanism of osteolysis focusing on the polyethylene wear particles and multinucleated cells (MNCs) which are considered to be responsible for osteolysis.

II. Materials and Methods

Radiological assessment

All 41 cases demonstrated radiographic evidence of ballooning osteolysis. Osteolysis was defined as an appearance of cystic bone erosion that was absent on the immediate post operative radiograph. Time to surgical revision after implantation ranged from 26-262 months. Linear wear of the polyethylene was estimated on the anteroposterior radiograph by measurement of the change of the center of the femoral component relative to the acetabular shell following the method of Livermore. Semiquantitative gradings for wear were conducted as follows : -, 0～1 mm ; 1+, 1～3 mm ; 2+, more than 3 mm.

Histological assessment

Tissue Procurement

Sixty human periprosthetic tissues were harvested separately from 24 acetabulum components, 34 proximal and 28 distal part of femoral components in 41 patients undergoing revision total hip arthroplasty. Forty-eight specimens (21 acetabulum, 14 proximal femur, 13 distal femur) came from joints with a cemented prosthesis, and 38 specimens (3 acetabulum, 20 proximal femur, 15 distal femur) were obtained from joints in which cement had not been used. The prostheses were all radiographically loose, and clinically loose at surgery when subjected to manual manipulation.

At revision surgery, tissue specimens were harvested from an area of bone absorption.

Tissues were fixed in 10% buffered formalin and paraffin embedded.

Tartarate Resistant Acid Phosphatase Staining

TRAP staining was performed by a modification of a previously published method[9]. Briefly, 6 μm tissue sections were cut from paraffin embedded tissues. All slides were run in parallel for acid phosphatase alone or with 25 mmol/L sodium tartarate. Sections were incubated at 37℃ for 40 minutes in freshly prepared 0.1 mol/L Tris buffer, pH 5.0, containing 1.35 mmol/L naphthol AS-MX phosphate (Sigma Chemical Co., St. Louis, MO), 0.362 mol/L N, N-dimethylformamide, 3.88 mmol/L Fast Red TR salt, 0.5 mmol/L manganese chloride, and 25 mmol/L sodium tartarate. Slides were rinsed for 10 minutes and counterstained with hematoxylin. Synovial tissue from Pigmented Villonodular Synovitis (PVS) was used for positive control.

A modification of Mirra's grading system [10] was used to characterize the tissues as follows, depending on the number of MNCs or polyethylene particles in the microscopic fields: -, absent ; 1+, mild ; 2+, moderate ; 3+, severe. Polyethylene particles were identified intracellularly and extracellularly as strong birefringent fibers or granules that are visible under polarized microscopy.

Statistical analysis

The differences of the histological findings between each group (acetabulum vs. proximal part of the stem vs. distal part of the stem) and the correlation between the appearance of radiographical and histological features (linear wear vs. PE particles, TRAP positive cells vs. PE particles) in each part (acetabulum, proximal part of the stem, distal part of the stem) were analyzed statistically using nonparametric Mann-Whitney's U test and Spearman's rank correlation coefficient.

Ⅲ. Results

On the radiological assessment, the linear wear of the polyethylene was as follows, 10 cases of grade -, 14 cases of grade 1+ and 17 cases of grade 2+. Average time to surgical revision after implantation in each grading group was as follows, 126 months in grade -, 185 months in grade 1+ and 206 months in grade 2+. Correlation between the grading of radiological wear and the time to revision was found ($P<0.01$).

The morphological examination showed that numerous TRAP positive cells as well as scattered polyethylene particles existed in a fibrovascular stroma, similar to previous descriptions of the periimplant tissue. TRAP positive cells were mono- and multinucleated cells and were containing polyethylene particles intracellularly or extracellularly (Fig. 1a). Polyethylene particles were small irregular shaped fragments that were highly birefringent by polarized light microscopy (Fig. 1b). Table 1 and table 2 show the number of cases of each grade concerning polyethylene particles and TRAP positive MNCs. The analysis of variance showed no statistically significant difference between the groups (acetabulum vs. proximal

Table 1
No. of PE particles

part / grade	acetabulum	femur	
		proximal	distal
−	3	5	5
1+	3	5	8
2+	6	6	6
3+	12	18	9

Table 2
No. of TRAP positive MNCs

part / grade	acetabulum	femur	
		proximal	distal
−	4	3	2
1+	3	3	6
2+	6	11	9
3+	11	17	11

Fig. 1a
TRAP staining of the retrieved interface tissue
(Original magnification×200)

Fig. 1b
Polarized picture
(H-E staining, Original magnification×200)

part of the stem vs. distal part of the stem) for the number of polyethylene particles, showing a relatively low number in distal part of the stem. Likewise, no statistically significant difference was seen between the groups for the number of TRAP positive MNCs, showing a relatively high number in proximal part of the stem. The number of polyethylene particles correlated with linear wear on the radiographs in every part (acetabulum, proximal and distal part of the stem) ($P<0.01$) (Fig. 2). Correlation between the number of polyethylene particles and TRAP positive cells was shown in only acetabulum ($P<0.01$), while no correlation was found in both of proximal and distal part of the stem (Fig. 3).

IV. Discussion

The osteolytic reaction has been described in previous histological studies[2,11-13]. Various particulate materials, including cement, metal and polyethylene, have been cited as the primary cause of the osteolysis[2,11,12,14,15]. Though it is clear from the literature that any of these materials can cause osteolysis, the

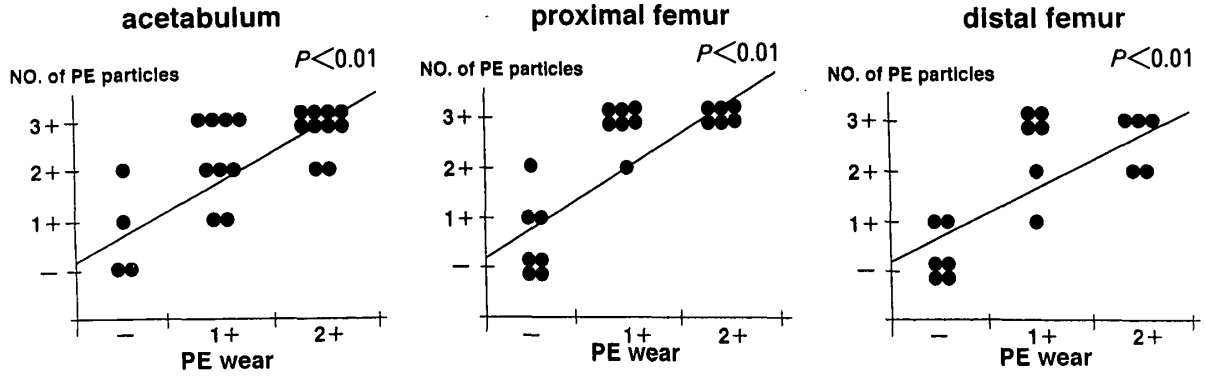

Fig. 2

The correlation between the appearance of radiographical and histological features (linear wear vs. PE particles) in each part (acetabulum, proximal part of the stem, distal part of the stem), Spearman's rank correlation coefficient

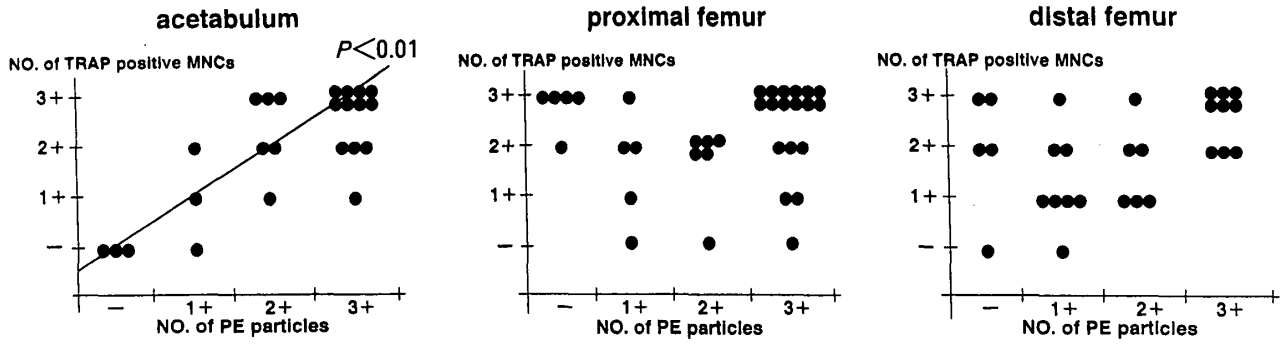

Fig. 3

The correlation between the appearance of histological features (TRAP positive cells vs. PE particles) in each part (acetabulum, proximal part of the stem, distal part of the stem), Spearman' s rank correlation coefficient

most common offending agent appears to be small particles of polyethylene[11,15,16]. The so-called effective joint space, as described by Schmarzried[3], refers to the path in the periprosthetic region for passage of the particulate debris away from the articulating surfaces. If the implant could be designed in such a way as to limit the effective joint space to the periarticular region, the osteolysis caused by the particulate debris could potentially also be restricted to the parts of the femur and of the pelvis immediately adjacent to the joint. In the present study, the results that there was no significant difference between two groups (acetabulum vs. femur) for the number of polyethylene particles and that the number of polyethylene particles correlated with linear wear indicate equivalent flow of polyethylene particles into both interfaces of acetabulum and femur. Furthermore, the result that no significant difference between two groups (acetabulum vs. femur) for the number of TRAP positive MNCs suggests the equivalent degree of bone resorbing reaction. However, this study demonstrated that the number of polyethylene particles correlated with that of TRAP positive cells only in acetabulum and not in proximal or distal part of the stem, suggesting close relationship between polyethylene particles and bone resorption in acetabulum, and unlikely in femur.

In total hip arthroplasty, it can be thought that the difference of the shape between acetabulum and femoral components results in the different pattern of mechanical stresses, the former being hemisphere and the stress spread almost equally, the latter being tubular and the stress varied widely like shearing, swinging, vibration and so on. The effect of these mechanical stresses on osteolysis is not clear. It is generally accepted that the proliferation and differentiation of osteoclasts require the direct contact with osteoblasts and M-CSF secreted from osteoblasts, and recent study showed that cyclic stretching of human osteoblasts affect proliferation and metabolism[17,18]. Then I can make the hypothesis about the mechanism of osteolysis that mechanical stress elicits proliferation of osteoblasts leading to proliferation and differentiation of osteoclasts, and then osteoclastic bone resorption is induced or accelerated. It is assumed that the more variety of the mechanical stresses around femoral component than around acetabular component may affects the bone resorption via osteoblasts and represents the difference of the manner of osteolysis between acetabulum and femur.

要　旨

[目的] 人工股関節置換術（THA）後の implant 周囲骨融解（osteolysis）の機序として，摩耗粉に対する異物反応および破骨細胞性骨吸収が主に考えられている。polyethylene particle（PE）と，その貪食や骨吸収に携わるとされる多核巨細胞に注目し，再置換術施行症例の病理組織学的検討を行った。

[方法] THA 施行後，osteolysis を認めた41症例の implant 周囲膜様組織を，①臼蓋底②大腿骨近位部③大腿骨遠位部の部位別に採取した。TRAP（酒石酸抵抗性酸フォスファターゼ）染色を行い，組織所見とX線所見に関し，評価を行った。

[結果] osteolysis 組織中の PE 数と TRAP 陽性多核巨細胞数は，どの部位間の比較においても有意差を認めなかった。X 線上の線摩耗量と組織中の PE 数の間には，全ての部位において有意な相関関係を認めた。一方，PE 数と TRAP 陽性多核巨細胞数の関係を部位別に見ると，臼蓋側では，有意な相関を認めるものの，大腿骨側では相関を認めなかった。

[考察および結論] 今回の検討から，THA 後の osteolysis 症例において，PE は臼蓋，大腿骨近位，大腿骨遠位のどの部位にも均等に流入していること，それぞれの部位での骨吸収反応の程度にも差がないことが示唆された。しかしその一方で，臼蓋側では PE と骨吸収の密接な関連が示唆されるものの，大腿骨側では，PE と骨吸収の直接の関連は否定的であった。つまり，臼蓋側の骨吸収には PE の流入が重要であるが，大腿骨側では，骨吸収は PE の流入のみでは起こりえないことが示唆された。THA においては，mechanical stress が臼蓋側と比べ大腿骨側でより多彩であり，それが骨吸収反応にも反映されるのではないかと考えられた。

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