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Development of large pseudocysts adjacent to the knee joint in rheumatoid arthritis. Assessment of radiological and histopathological approaches

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Abstract This study examined the pathogenesis of large pseudocysts adjacent to knee joints in rheumatoid arthritis (RA). The radiological and histopathological features of 17 large subarticular pseudocysts in 12 knee joints of 10 patients were analyzed. Nine of the 10 patients were classified as class 2 according to Steinbrocker's functional class. Eight large pseudocysts were located at the lateral femoral condyle, seven were at the proximal part of the tibia, one was at the medial femoral condyle, and one was at the patella. The large pseudocysts were divided into two groups according to whether they did or did not connect with the joint cavity. Serial radiographs revealed that all large pseudocysts in communication with the joint cavity had enlarged gradually over the past several months. They extended from the subarticular area toward the bone marrow. Histopathological findings confirmed that holes allowing communication were located at a transitional zone between the ligament and the hyaline cartilage, and that rheumatoid granulation tissue invaded the large pseudocyst through these holes. The results of this study indicate that large pseudocysts are formed by the extension of articular inflammation. Moreover, repeated extrinsic mechanical stress due to walking and the aggressive inflammatory nature of rheumatoid arthritis play important roles in the formation of large pseudocysts.

Key words Bare area · Bone cyst · Knee joint · Pseudocyst · Rheumatoid arthritis (RA)

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Introduction

Small cystic radiolucent lesions of juxtaarticular bone are one of the typical manifestations of rheumatoid arthritis (RA). Subarticular or subchondral pseudocysts, bone cysts, and geodes are used as synonyms to describe these cystic lesions.[1–7] They break out at the marginal zone "bare area" of the affected joint during aggressive inflammatory periods of RA. Microscopically, the presence of a connection between the cystic lesion and the joint cavity is often evident, and inflammatory granulation tissue penetrates the lesion.[1] Early studies suggest that the degree of physical activity performed by the patient and the increased intraarticular pressure accompanying joint effusions are related to the enlargement of cystic lesions.[2,8] Although lesions within a bone are usually multiple and small, lesions larger than a few centimeters in diameter occasionally are detected in the vicinity of large joints such as the knee, hip, and shoulder. These large subarticular pseudocysts sometimes enlarge gradually and cause spontaneous fractures that are difficult to manage.[3,4,9–12] Because detecting a connection between large subarticular pseudocysts and the joint cavity is sometimes difficult, opinion has been divided as to whether they arise from primary damage within the bone or by extension from arthritis.[2–7,13,14]

Thirty years after the first description of large subarticular pseudocysts observed at the proximal part of the tibia, the pathogenesis of this disorder remains obscure.[2] At least, questions remain concerning the development of large pseudocysts, i.e., whether they arise by extension of articular inflammation or from a primary focus within the bone. Furthermore, why most large subarticular pseudocysts appear at similar sites in the joints is also unknown. This study was undertaken to answer these questions by examining the radiological and histopathological features of large pseudocysts adjacent to knee joints in patients with RA.

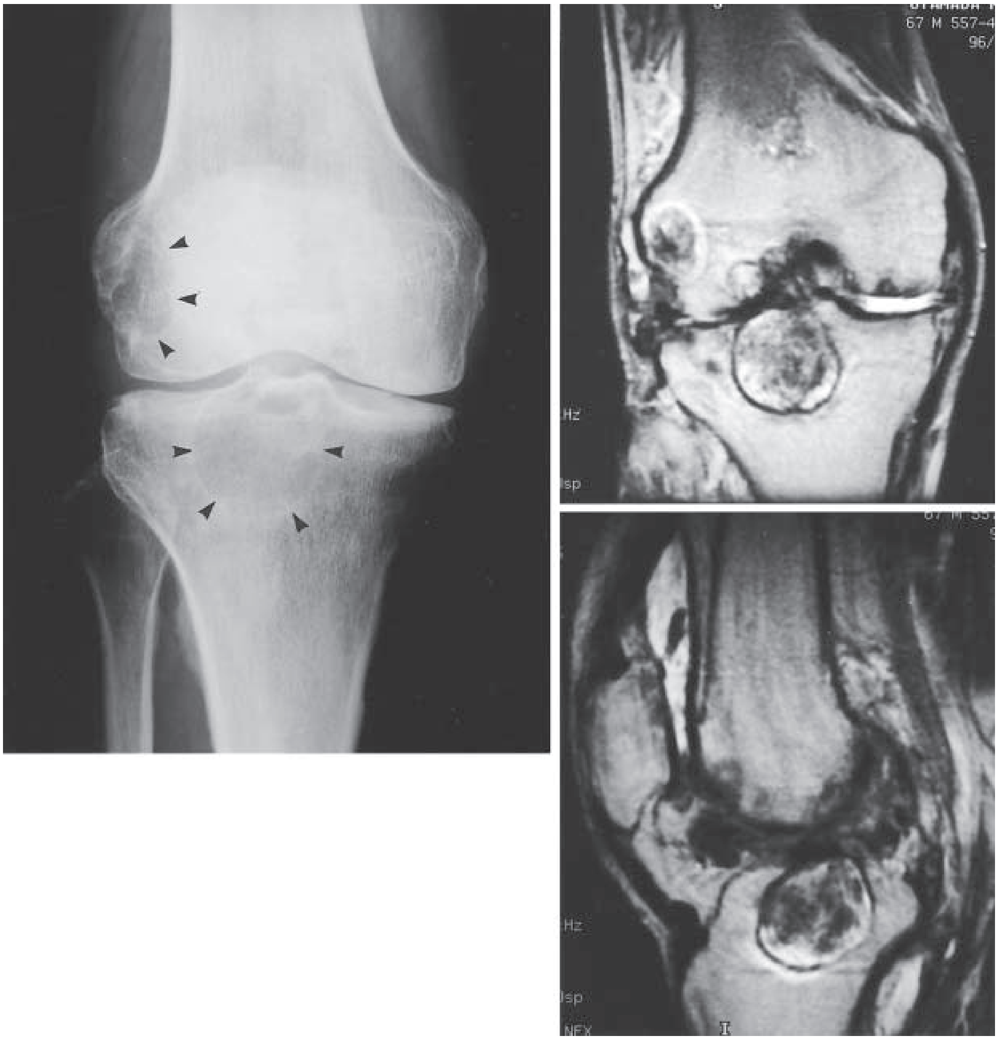

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Fig. 1. Radiography and magnetic resonance imaging showing large pseudocysts in the lateral femoral condyle and in the proximal part of the tibia. **a** *Arrow heads* indicate large radiolucent lesions in the juxtaarticular bone. **b** Sagittal and coronal T2-weighted MR images showing a heterogeneously high-signal mass

Materials and methods

Seventeen large pseudocysts adjacent to 12 knee joints were analyzed in 10 patients with RA who were treated between April 1990 and March 2000. All 10 patients fulfilled the 1987 revised criteria of the American College of Rheumatology for the diagnosis of RA. The clinical profiles of all patients and the locations of the large pseudocysts are shown in Table 1. There were 7 women and 3 men, with an age range of 50–77 years (66.1 $\pm$ 7.9), and the duration of their RA ranged from 4 to 29 years (13.9 $\pm$ 9.2). Nine patients were classified as class 2, and 1 patient was classified as class 3 according to Steinbrocker's functional classification system.[15] Of the affected knee joints, 4 were in each of Larsen's grades III, IV, and V. The pseudocysts were located at the lateral femoral condyle (n = 8), the proximal part of the tibia (n = 7), the medial femoral condyle (n = 1), and the patella (n = 1). Figure 1 shows typical large pseudocysts at the lateral femoral condyle and at the proximal part of the tibia. All patients were seropositive for rheumatoid factor and seronegative for antinuclear antibodies. No abnormalities in serum calcium, phosphate, or alkaline phosphate were observed in any patients during the study. Patients 1, 2, and 5 have had C-reactive protein (CRP) concentrations of 3.0 mg/dl or higher for the last few years.

Because most patients had longstanding RA, they had a history of therapy involving several disease-modifying antirheumatic drugs. Patients 1, 2, 4, 5, 8, and 9 were taking systemic prednisolone (dose range 5–10 mg/day). All patients presented with severe involvement of the knee joints, and consequently had been treated several times with intraarticular steroid therapy. Ten total knee arthroplasties and 2 synovectomies had been performed for 11 joints; the exception was the left knee of patient 7. Nine of the 10 knee joints were replaced with nonconstrained prosthetic joints, while the right knee joint of patient 5 required a constrained prosthesis due to marked damage. Patient 1 underwent synovectomy and a bone autograft after curettage of the large pseudocyst on his right knee. The first operation did not relieve his pain on walking, and thus total knee arthroplasty was performed upon the same knee 1 year later. Patient 2 underwent only synovectomy.

Radiographs of standard anteroposterior and lateral views of the knee joints were taken to detect the giant bone cysts. We adopted Larsen's grades to evaluate joint destruc-

Table 1. Clinical profiles of the 10 patients with rheumatoid arthritis and the location of large pseudocysts

Patient	Age	Sex	Duration of RA (years)	Class	Larsen's grade of the knee	Location of large cystic lesion	Type	Hole size (mm)
1	69	M	29	2	III right	Lateral femoral condyle	2	
					III left	Proximal part of tibia	1	3 × 4
						Proximal part of tibia	1	2 × 3
						×2	1	2 × 2
2	65	F	12	2	III right	Proximal part of tibia	1	3 × 3
3	61	M	28	2	IV right	Lateral femoral condyle	2	
4	62	F	7	2	III right	Lateral femoral condyle	2	
5	72	F	7	2	IV right	Lateral femoral condyle	1	2 × 1
						Patella	1	1 × 1
6	77	M	4	2	IV right	Lateral femoral condyle	2	
7	67	F	17	2	V right	Lateral femoral condyle	2	
					IV left	Proximal part of tibia	2	
8	63	F	20	3	V left	Lateral femoral condyle	2	
						Proximal part of tibia	2	
9	75	F	6	2	V right	Medial femoral condyle	2	
10	50	F	10	2	V right	Lateral femoral condyle	2	
						Proximal part of tibia	1	1 × 1

Class: Steinbrocker's functional class

tion in roentgen examinations. Magnetic resonance (MR) imaging was used to distinguish the cysts from other bone disorders. Sagittal, coronal, and axial spin-echo MR images were obtained. In the present study, cystic lesions within bone tissue were defined as large pseudocysts if they were greater than 20 mm in diameter. Tissue samples from the large pseudocysts, including their inner contents, were obtained during surgery. These samples were fixed in 20% formalin and embedded in paraffin. Tissue sections 2-μm thick were cut and stained with hematoxylin and eosin. Bone tissue was decalcified with EDTA after treatment with alcohol and then embedded in paraffin. Surgical findings, histological features, and serial radiographs of the large pseudocysts obtained over several years were examined.

Results

The 17 large subarticular pseudocysts could be divided into two groups, as described below, according to whether they connected to the joint cavity. Connection with the joint cavity was confirmed after resection of the damaged joint surface by arthroplasty. Type 1: large pseudocysts that communicated with the joint cavity by one small hole ($n = 7$). Type 2: large pseudocysts in which no connection with the joint cavity was detected ($n = 10$). The term bone cyst may be more appropriate than pseudocyst. The type and hole size of the large pseudocysts are shown in Table 1. The type-1 group included 5 large pseudocysts at the proximal part of the tibia, 1 at the lateral femoral condyle, and 1 at the patella. The type-2 group included 7 large pseudocysts at the lateral femoral condyle, 2 at the proximal part of the tibia, and 1 at the medial femoral condyle. Type 1 large pseudocysts had one communication hole each. Figure 2 shows the communication holes at the proximal part of the left tibia of patient 1. Analysis of serial radiographs

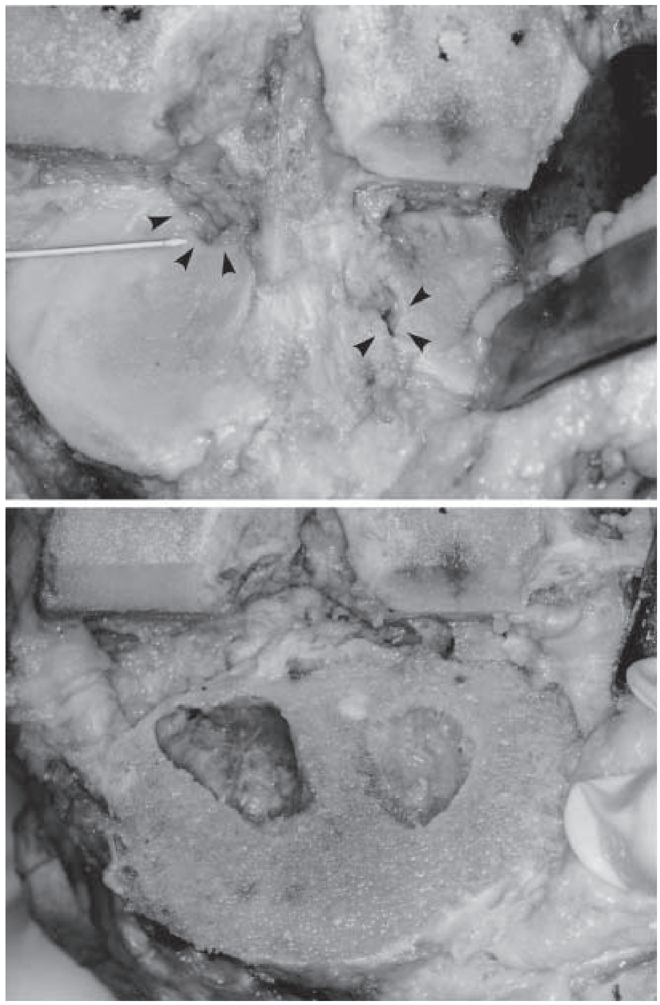

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Fig. 2. Operative findings of the left knee of patient 1. **a** *Arrow heads* indicate two holes adjacent to the ligaments. **b** The presence of large pseudocysts was confirmed after resection of the damaged joint surface. The type-1 pseudocysts had just one communication hole with the joint cavity

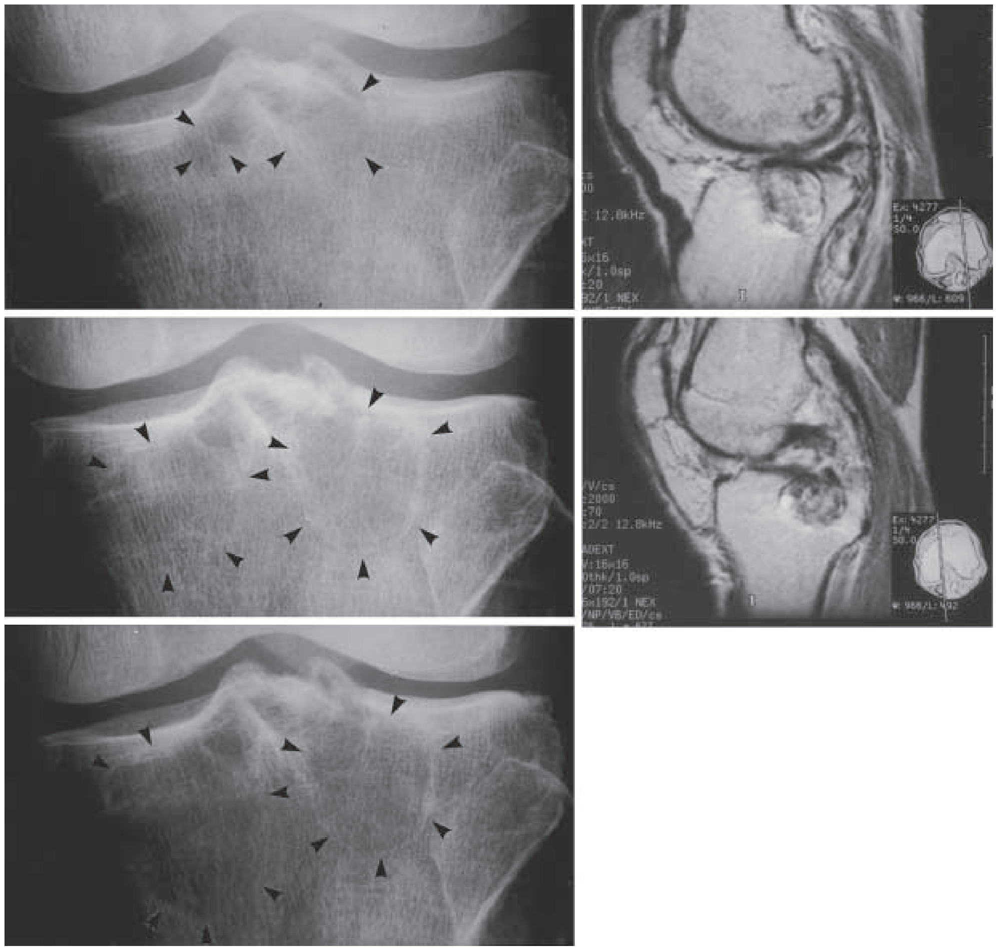

Fig. 3. Serial radiographs and magnetic resonance images of the left knee of patient 1. **a** November 1996, **b** July 1997, and **c** March 1998. *Arrow heads* indicate the radiolucent lesions in the proximal part of the tibia. **d**, **e** Sagittal T2-weighted MR images obtained in March 1998 showing two heterogeneous high-signal masses

revealed that all large type-1 pseudocysts had enlarged gradually over the past few months. They extended from the subarticular area toward the bone marrow. Serial radiographs and MR images of the left tibia of patient 1 are shown in Fig. 3. In contrast to type-1 pseudocysts, 8 of the 10 large type-2 pseudocysts had hardly changed in size over the last year, and were observed in a well-defined sclerotic margin in roentgen examination.

Although the 5 type-1 knee joints showed severe or intermediate synovial proliferation during surgery, the type-2 knee joints showed mild synovial proliferation or burnout. Hydrops (over 20 ml) was found in both knees of patient 1, the right knee of patient 2, the right knee of patient 5 (these joints involved large type-1 pseudocysts), the left knee of patient 8, and the right knee of patient 9 (these joints involved large type-2 pseudocysts). The large type-1 pseudocysts contained synovial fluid or whitish-gray gelatinous tissue, whereas those of type 2 contained pale yellow fibrous soft tissue.

Histological assessment of serial sections confirmed that the communication holes were located at a transitional zone (noncartilaginous area) between the ligament and the hyaline cartilage, and that rheumatoid granulation tissue had invaded the large pseudocyst through these holes (Fig. 4). The large type-1 pseudocysts all contained different amounts of granulation tissue which contained a moderate number of inflammatory cells, and this tissue was similar to that seen in synovial membrane with severe or intermediate proliferation in these joints. The granulation tissue often contained detached fragments of cartilage and bone. Osteoclastic activity was observed at the junction of the granulation tissue and bone trabeculae within the large type-1 pseudocysts. In contrast, most of the type-2 lesions involved cells that had degenerated and granulated tissue with fibrosis and mild inflammatory infiltrates, which suggested degenerated synovium (figures not shown).

Discussion

The large subarticular pseudocysts described in previous reports were extremely large and appeared mostly in the proximal part of the tibia. Consequently, operations were carried out to reconstruct pathological fractures or to distinguish the pseudocysts from other bone disorders.[3–5,7,13] In recent years, advances in MR imaging have allowed the detection of subarticular pseudocysts before they enlarge enough to cause severe damage. Our present results confirm that large pseudocysts adjacent to knee joints fre-

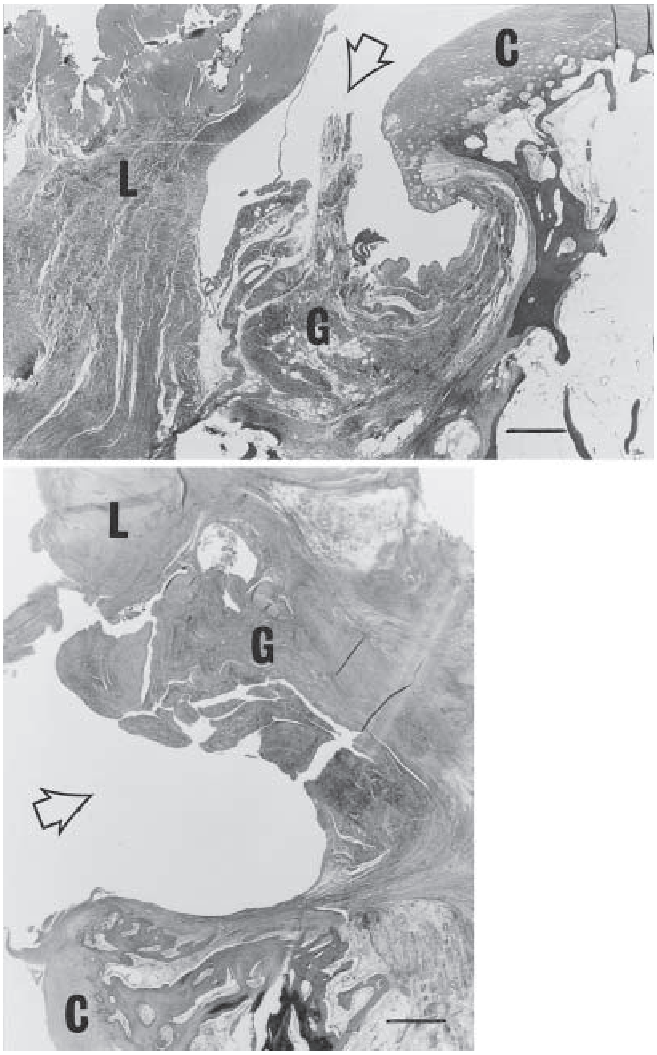

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Fig. 4. Microscopic findings around the holes between the cyst and the joint cavity (hematoxylin and eosin). The communication holes are located in the noncartilaginous area between the ligament and the hyaline cartilage. Rheumatoid granulation tissue invaded the large pseudocyst through these holes. *Bar* 1 mm. **a** *L*, anterior cruciate ligament; *C*, hyaline cartilage; *G*, granulation tissue. **b** *L*, lateral collateral ligament; *C*, hyaline cartilage; *G*, granulation tissue

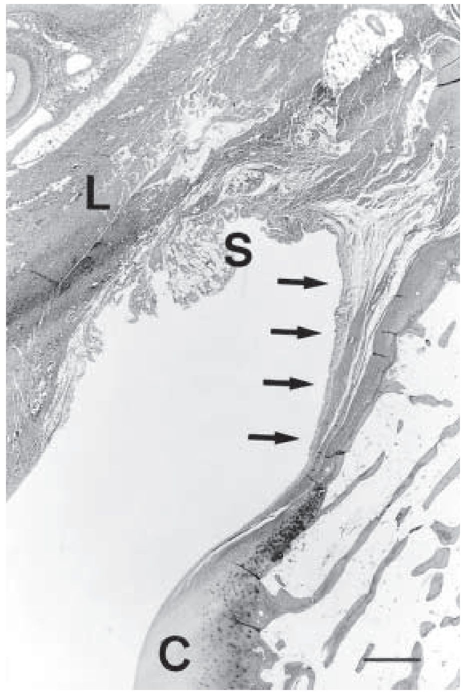

Fig. 5 Microscopic findings around the proximal attachment of the lateral collateral ligament in a normal joint (autopsy) (hematoxylin and eosin). *Arrows* indicate that the noncartilaginous area, known as the "bare area," is composed of much mesenchymal tissue. *Bar* 1 mm. *L*, lateral collateral ligament; *C*, hyaline cartilage; *S*, synovium

quently occur in the lateral femoral condyle as well as in the proximal part of the tibia.

In the present study, we divided the large pseudocysts into two groups according to whether they communicated with the joint cavity. The term "bone cyst" may be more appropriate for a lesion without a connection to a joint. In our patients, serial radiograph data and histological features strongly support the supposition that large pseudocysts that communicate directly with a joint are formed by extension of the articular inflammation. Judging from the location of the connection holes, some anatomical features of the attachment of the ligaments in the knee joint could be involved in the formation of large subarticular pseudocysts. All communication holes between the large pseudocysts and joint cavities were located in the noncartilaginous area adjacent to the attachment of the ligaments. Figure 5 shows the proximal attachment of the lateral collateral ligament in a normal anatomy. The noncartilaginous area, known as the "bare area," is composed of much mesenchymal tissue. The anterior and posterior cruciate ligaments are covered with synovial membrane, and the anatomical features surrounding the attachment site of these ligaments are similar to those at the proximal attachment site of the lateral collateral ligament. The rheumatoid inflammation arising in the synovium apparently extends to the noncartilaginous area, including the "bare area," and easily induces granulation changes such as edema, capillary proliferation, and inflammatory filtration in the mesenchymal tissue.

Although we observed that two pseudocysts of the lateral femoral condyle had enlarged gradually, these pseudocysts had no communication with the joint cavity. All connections of large pseudocysts with joint cavities were confirmed after resection of the damaged joint surface by arthroplasty. The ligament attachment of the lateral femoral condyle is usually retained during arthroplasty, and detection of the connection when the ligament has not been excised can be difficult. Large pseudocysts observed in the patella or medial condyle have each been described only once before.[2,3] These pseudocysts are evidently rare. The quadriceps ligament or medial collateral ligament may have been involved in their formation.

The noncartilaginous area is the transitional zone from hyaline cartilage to ligament tissue, and is the focus of extrinsic stress.[16] Our results also suggest that a mechanical factor is likely important for the development of large pseudocysts, as our type-1 pseudocysts had only one communication hole each. Most of our patients with large pseudocysts are able to walk. Repeated extrinsic mechanical stress due to walking may lead to damage at the transitional zone, and as a result, synovial membrane or pannus can easily invade bone trabeculae. Because the tibial attachment of the anterior and posterior cruciate ligaments is wider and stronger than the femoral attachment, the transitional zone of the tibial side is involved in stronger extrinsic stress than that of the femoral side.[17] The fact that large pseudocysts related to cruciate ligaments occurred at the proximal part of the tibia in most of our cases may be important. Although we found no clear correlation between the development of the large pseudocysts and the use of intraarticular or systemic steroid therapy in this study, pain suppression by analgesia may have resulted in the knees being subjected to much extrinsic stress.

The increased intraarticular pressure accompanying joint effusions has been suggested as an important factor in the enlargement of pseudocysts.[2] We detected hydrops of over 20 ml in 6 knees in the present study: 4 type-1 knees and 2 type-2 knees. Moreover, 6 of the 7 large type-1 pseudocysts were found in patients who have had CRP concentrations of 3.0 mg/dl or higher during the last few years. The results in the present study suggest that the aggressive inflammatory nature of RA plays a more fundamental role in the development of large pseudocysts than increased intraarticular pressure. Long-standing, severe arthritis can lead to the enlargement of pseudocysts by the continuous extension of articular inflammation. On the other hand, with alleviation of articular inflammation, the connection between the cyst and the joint cavity may gradually close up and become nearly obliterated. After being isolated from the joint cavity, secondary changes may develop inside the large cyst, such as fibrosis, degeneration, or necrosis of the contents. As inflammation is alleviated inside the large cyst, further enlargement of large bone cysts may cease. This process may explain the appearance of large pseudocysts (type 2) without a connection to the joint cavity.

References

1. Cruickshank B, Macleode JG, Shearer WS. Subarticular pseudocysts in rheumatoid arthritis. J Fac Radiol 1954;5:218–26.
2. Jayson MIV, Rubenstein D, Dixon J. Intra-articular pressure and rheumatoid geodes ("bone cysts"). Ann Rheum Dis 1970;29:496–502.
3. Jayson MIV, Dixon J, Yeoman P. Unusual geodes ('bone cysts') in rheumatoid arthritis. Ann Rheum Dis 1972;31:174–8.
4. Gohel V, Dalinka MK, Edeikin J. Giant rheumatoid pseudocyst. Clin Orthop 1972;88:151–3.
5. Magyar E, Talerman A, Feher M, Wouters HW. The pathogenesis of subchondral pseudocysts in rheumatoid arthritis. Clin Orthop 1974;100:341–4.
6. Magyer E, Talerman A, Feher M, Wouters HW. Giant bone cysts in rheumatoid arthritis. J Bone Joint Surg 1974;56-B:121–9.
7. Carter AR, Liyanage SP. Large subarticular cysts (geodes) adjacent to the knee joint in rheumatoid arthritis. Clin Radiol 1975;26:535–8.
8. Castillo BA, el Sallab RA, Scott JT. Physical activity, cystic erosions, and osteoporosis in rheumatoid arthritis. Ann Rheum Dis 1965;24:522–7.
9. Colton CL, Darby AJ. Giant granulomatous lesions of the femoral head and neck in rheumatoid arthritis. Ann Rheum Dis 1970;29:626–33.
10. Lowthian PJ, Calin A. Geode development and multiple fractures in rheumatoid arthritis. Ann Rheum Dis 1985;44:130–3.
11. Wordsworth BP, Mowat AG, Watson NA. Fracture through a geode in the proximal ulna. Br J Rheumatol 1984;23:110–2.
12. Jacobs AJ, Ginsburg WW, Bryan RS. Large geode in an elbow with spontaneous fracture. J Rheumatol 1982;9:340–1.
13. Nikpoor N, Aliabadi P, Poss R, Nusrat A, Weissman B. Case report 504. Skeletal Radiol 1988;17:515–7.
14. Fujii K, Tsuji M, Tajima M. Rheumatoid arthritis: a synovial disease? Ann Rheum Dis 1999;58:727–30.
15. Steinbrocker O, Traeger CH, Batterman RC. Therapeutic criteria in rheumatoid arthritis. JAMA 1949;140:659–62.
16. Resnick D, Niwayama G. Entheses and enthesopathy. Anatomical, pathological, and radiological correlation. Radiology 1983;146:1–9.
17. Girgis FG, Marshall JL, Monajem A. The cruciate ligaments of the knee joint. Anatomical, functional and experimental analysis. Clin Orthop 1975;106:216–31.