Synovectomy for septic arthritis

Early versus late synovectomy studied in the rabbit knee

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Thirty rabbits with established unilateral septic arthritis of the knee after inoculation with *Staphylococcus aureus* received cloxacillin 50 mg/kg x 2 i.m. and probenecid 250 mg x 1 p.o. from Day 3 to 21. In 26 knees, synovectomy was performed 3, 5, and 7 days after the inoculation, and four knees were not operated on. Further, synovectomy was performed in eight noninfected knees. The rabbits were killed 3 or 7 weeks after the operation, and the specimens were examined macroscopically and microscopically. All the cultures taken postoperatively and at killing were negative. Infected knees synovectomized on Day 3 differed, although marginally, 3 weeks postoperatively from the operated on, uninfected group; a minor loss of cartilage cellularity and glycosaminoglycans was observed, but there were no changes indicating arthrosis. At 7 weeks postoperatively, this difference was more pronounced. If synovectomy was performed at a later stage, increased destruction was observed: after 7 days of infection, all the knees presented cloning and vascular crossing of the tidemark, indicating arthrosis, which did not differ from those knees treated with only antibiotics. We conclude that synovectomy performed early in the course of infection may stop the destructive influence of enzymes and of the synovial membrane leading to irreversible changes in the cartilage.

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Synovectomy in septic arthritis may decompress the joint effectively through removal of the purulent fluid and the synovial membrane. The content of cartilage-destroying enzymes (Curtiss and Klein 1963) and antigenic bacterial debris (Cromartie et al. 1977) is effectively eliminated to preserve the cartilage. Controversy still exists about the value of the treatment, and the procedure has only been described sporadically in small clinical series (Cauchoix and Duparc 1962, Ballard et al. 1975, Gérard et al. 1977, Tørholm et al. 1983, Riegels-Nielsen and Jensen 1984). In a previous rabbit experiment, we have shown that treatment exclusively with systemic antibiotics does not prevent destruction of articular cartilage once bacterial arthritis has been established (Riegels-Nielsen et al. 1989).

We have now used our rabbit knee infection model (Riegels-Nielsen et al. 1987) to evaluate the effect on cartilage destruction following surgical synovectomy.

Material and methods

Forty-four rabbits (New Zealand white type SsC: CPH; weight 3 to 4 kg) were used for the experiments. The right knees of 36 rabbits were inoculated with 10^3 *Staphylococcus aureus*, phage type 3C, the characteristics of which were tested before and after each experiment (Riegels-Nielsen et al. 1987). A group of 8 rabbits (Group A) were not inoculated, and thus remained uninfected. The rabbits underwent daily veterinarian control, and all the procedures were performed under anesthesia. After 72 hours, the infection was verified by a diagnostic puncture. Immediately following this puncture, all the rabbits received antibiotic therapy for a period of 3 weeks with intramuscular cloxacillin 50 mg/kg × 2, with the second dose preceded by probenecid 250 mg p.o. (Riegels-Nielsen et al. 1989).

All the inoculated joints developed the classical signs of septic arthritis, and had positive cultures of *Staph. aureus*, phage type 3C. The initial clinical course of infection was similar to our earlier experiments (Riegels-Nielsen et al. 1987 and 1989).

Two rabbits died of unrelated diseases during the observation period, and 4 rabbits were excluded because the patella was dislocated at killing; thus, there were 38 specimens for evaluation.

The inoculated rabbits (n 30) were divided into four groups: synovectomy was performed on Day 3 in 11

knees (Group B), on Day 5 in eight knees (Group C), and on Day 7 in seven knees (Group D), whereas synovectomy was not performed in 4 rabbits (Group E), which served as a control as regards the course of infection, and were thus treated with only antibiotics. The 8 noninfected rabbits (Group A) were synovectomized in the same fashion as above, serving as controls regarding the effects of surgery (Table 1). Postoperatively, the knees were aspirated daily through a cannula for 4 days, and the exudate was cultured.

The synovectomy was always performed on the right knee through a medial parapatellar incision under aseptic conditions. After opening the knee, specimens were taken from the joint fluid and synovial tissue for bacterial culturing. All the available synovial tissue was removed, and the joints were rinsed with Ringer's lactate. The wound was closed in layers with absorbable sutures (Vicryl® 4–0). Postoperatively, the rabbits were allowed to move about freely in standard cages.

The rabbits were killed with an overdose of nembutal 3 or 7 weeks after synovectomy. Bacterial cultures were taken from the joint fluid and synovial tissue, the cartilage was examined according to Salter's histologic-histochemical scoring system (Salter et al. 1981, Riegels-Nielsen et al. 1987), and the loss of glycosaminoglycans (GAGs) was evaluated with safranin-O stainability (Rosenberg 1971). All the specimens were examined blindly by the same author (PR-N) as in earlier series (Riegels-Nielsen et al. 1987 and 1989) to obtain an equivalent evaluation. The Mann-Whitney rank sum test was used for the statistical analysis.

Results

All the cultures from the postoperative joint aspirates and from the synovial fluid and tissue sampled at killing were negative, and all the cultures from the noninfected cases (Group A) were negative.

Macroscopic appearance

After 3 weeks, the noninfected knees (Group A) had normal synovial fluid, and a thickened synovial-like membrane had regenerated. The cartilage was unchanged. In the infected and synovectomized knees (Groups B, C, and D), the cartilage had lost its normal, shiny appearance. The synovial membrane was edematous, and there were inflammatory changes and an increased amount of turbid synovial fluid. No erosion or pannus was observed.

After 7 weeks, the synovial membrane had almost normalized in Group A, and the cartilage was normal. In the primarily infected groups (B, C, and D), the synovial membrane was still thickened, together with an inflammatory reaction; and all three groups exhibited an increased amount of turbid joint fluid. In Group B, minor marginal pannus was observed in two knees; but this was present in all the knees from Groups C and D. In Group E, with a spontaneous course of infection after antibiotics, the findings were identical with Group D.

Microscopic appearance

The thickened synovial membrane was heavily infiltrated with leukocytes, and the vessels were dilated in all the groups after 3 weeks. Reduction of cartilage cellularity and increased cloning were seen in the nonoperated on and late synovectomized groups (Table 1). Pannus was also observed in these groups together with marginal erosion (Table 1). The histologic appearance was equivalent in the noninfected knees and in those to be synovectomized on Day 3 ($P = 0.2$). The GAG depletion was increased in the operated on groups, and became microscopically more evident with the increased time lapse between inoculation and synovectomy (Table 1).

Only slight differences were encountered between 3 and 7 weeks of observation in the rabbits synovectomized on Day 3, whereas signs of cartilage destruction increased with time in rabbits synovectomized on Days 5 and 7 ($P < 0.001$). In nonoperated on cases, vascular crossing of the tidemark was observed, with cloning of chondrocytes, resulting in a significantly increased average score ($P < 0.001$). Similar changes were seen after 7 weeks of observation in rabbits synovectomized on Day 7 (Table 1).

Discussion

In our infection model (Riegels-Nielsen et al. 1987), the first irreversible joint changes are seen after a course of about 5 days as marginal cartilage erosion if no treatment had been instituted. In the present series, the combined treatment with antibiotics and synovectomy was performed when the joints had a confirmed and clinically well-established infection. In order to simulate most clinical situations, the synovectomy was performed 3, 5, and 7 days after the inoculation of the bacteria.

Table 1. Septic joint morphology scores according to the histologic-histochemical system of Salter et al. (1981)

Group	Rabbit (No.)	Infection	Synovectomy (day)	Killed (week)	Tidemark broken	Histologic-histochemical scoring: Cellularity	Erosion	Clonus	Pannus	Safranin-O staining	Cumulated Score
A	1	–	0	3	0	1	0	0	0	0	1
	2	–	0	3	0	1	0	0	0	0	1
	3	–	0	3	0	1	0	0	0	1	2
	4	–	0	3	0	1	0	0	0	1	2
	5	–	0	7	0	1	0	0	0	0	1
	6	–	0	7	0	1	0	0	1	1	3
	7	–	0	7	0	1	0	0	0	0	1
	8	–	0	7	0	1	1	0	0	1	3
B	9	+	3	3	0	1	0	0	0	1	2
	10	+	3	3	0	1	0	0	0	1	2
	11	+	3	3	0	1	0	0	0	1	2
	12	+	3	3	0	1	0	0	0	2	3
	13	+	3	3	0	1	0	0	0	2	3
	14	+	3	7	0	2	0	0	0	2	4
	15	+	3	7	0	1	0	0	1	2	4
	16	+	3	7	0	2	0	0	0	3	5
	17	+	3	7	0	1	1	0	0	2	4
	18	+	3	7	0	1	1	0	0	1	3
	19	+	3	7	0	1	1	0	0	2	4
C	20	+	5	3	0	1	1	0	0	3	5
	21	+	5	3	0	1	1	0	0	3	5
	22	+	5	3	0	1	1	0	1	2	5
	23	+	5	3	0	1	0	0	0	3	4
	24	+	5	7	0	2	1	0	1	2	6
	25	+	5	7	0	3	2	0	1	2	8
	26	+	5	7	0	2	1	0	1	3	7
	27	+	5	7	0	2	1	0	1	3	7
D	28	+	7	3	0	2	1	1	1	2	7
	29	+	7	3	0	2	1	1	1	2	7
	30	+	7	3	+	2	1	1	1	3	8
	31	+	7	3	+	3	1	1	1	3	9
	32	•	7	7	+	3	1	2	1	3	10
	33	+	7	7	+	3	2	3	1	3	12
	34	+	7	7	+	3	1	2	1	3	10
E	35	•	–	7	0	2	1	2	1	2	8
	36	+	–	7	+	2	1	1	1	2	7
	37	+	–	7	+	3	1	1	1	3	9
	38	+	–	7	+	2	1	1	1	3	8

Scores: 0 indicates normality, 3 maximal changes
Cellularity: Amount of living cartilage cell
Erosion: Loss of cartilage matrix
Cloning: Number of dividing cartilage cells
Pannus: Degree of synovial cartilage overgrowth
Safranin O: Loss of stainability (GAG loss)
Tidemark: Borderline between normal and ossified cartilage.
Vascular crossing indicated by +

The synovial membrane has been found to regenerate in rabbit knees about 60 days after synovectomy (Mitchell and Cruess 1967a, b). In our noninfected, but synovectomized, knees (Group A), the synovial membrane had almost regenerated 7 weeks postoperatively; but a minor reduction in cartilage cellularity and superficial GAG loss was evident, visualized semiquantitatively by the diminished stainability of safranin O, which might have been caused by the natural pain-induced immobilization (Salter et al. 1981) or by the operative trauma (Reimann et al. 1982), with increased activity of lysosomal enzymes (Mitchell and Cruess 1967a). However, the total score following synovectomy of the normal rabbit knee joint remained below the point of irreversibility, which corresponds to a level of about 5 points in the scoring system (Riegels-Nielsen et al. 1987).

When synovectomy was performed on the third day of infection, the synovial membrane did not regenerate into normal tissue, but remained thickened with

inflammatory changes in spite of negative cultures. The cartilage changes remained minor, but the GAG loss was more severe than in the uninfected knees. In these cases the prolonged articular effusion may have maintained the enzymatic lysosomal activity. The average score after 7 weeks of observation reached a level where permanent changes in the cartilage can be observed microscopically (Riegels-Nielsen et al. 1987), even though the infection was cured. However, cloning— i.e., cell division in the cartilage—and vascular crossing of the tidemark, which are signs indicative of arthrosis (Mankin et al. 1971, Lane et al. 1977, Bullough and Jagannath 1983), were not observed in this group. Synovectomy performed later during the course of infection, when cartilage changes were more pronounced, did not improve the score as compared with the findings in an earlier experiment with antibiotic treatment alone (Riegels-Nielsen et al. 1989). Further, the results of synovectomy performed 5 or 7 days after inoculation did not differ significantly from the spontaneous course of the unoperated on and infected knees.

The postoperative course of this experimental series seemed to follow those described in some clinical series (Cauchoix and Duparc 1962, Ballard et al. 1975, Gérard et al. 1977, Törholm et al. 1983, Riegels-Nielsen and Jensen 1984). The clinical relevance of our experimental results indicates that synovectomy may be an effective adjuvant in the therapy of joint infections. If a beneficial outcome is to be expected, the procedure must be performed meticulously and at an early stage of the disease.

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