Periprosthetic low-grade hip infections

Erythrocyte sedimentation rate and C-reactive protein in 23 cases

Lennart Sanzén and Martin Sundberg

We followed 23 patients from the primary total hip arthroplasty to revision for a bacteriologically proven deep infection with a low virulent organism. The median time to revision was 14 (4–65) months. During this period, the maximum ESR value was median 50 (22–110) mm and the maximum CRP value was 35 (9–95) mg/L. 25 of the 98 CRP values recorded were normal (< 9 mg/L) and 22/89 ESR values were below 30 mm/h. In 6 patients, all CRP values were below 20 mg/L, but 5 of these patients had an ESR > 30 mm. Before the revision, normal values for both tests were found in only 1 patient. Both normal values and slight-to-moderate increases in ESR and/or CRP are consistent with a low-grade periprosthetic hip infection. We recommend that ESR should be determined preoperatively in all patients scheduled for total hip replacement to establish a baseline.

Department of Orthopedics, Malmö University Hospital, S-205 02 Malmö, Sweden. Tel +46 40-331000. Fax -336200
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The erythrocyte sedimentation rate (ESR) has been studied following both uncomplicated and infected total hip arthroplasties (THA) (Carlsson 1978, Forster and Crawford 1982, Aalto et al. 1984). Several authors have studied the postoperative course of C-reactive protein (CRP) following uncomplicated THA. In periprosthetic hip infections caused by bacteria of high virulence, high CRP and ESR values are common (Shih et al. 1987, Sanzén and Carlsson 1989). In low-grade infections with absence of fever, systemic illness, abscesses and fistulae, and without local clinical signs of inflammation, the courses of ESR and CRP are not well known. We reviewed the ESR and CRP data from 23 consecutive nonrheumatoid patients having periprosthetic low-grade infections caused by bacteria of low virulence.

Patients and methods

ESR and CRP are performed in all patients undergoing THA in our department, both preoperatively and at the outpatient follow-up visits. Among 3532 patients primarily operated on between 1978 and 1992, we identified 25 cases who had been revised for a periprosthetic total hip infection caused by low-virulent bacteria in the normal skin flora—i.e., bacteria which do not cause infections in healthy subjects without the presence of a foreign body. 2 rheumatoid arthritis patients were omitted. All patients had healed wounds without sinuses and were afebrile. No antibiotics were administered before or during the revision surgery until multiple (3–10) tissue biopsies had been collected from the bone-cement interface. The clinical suspicion of a periprosthetic infection was confirmed if the same bacterial strain had been grown in at least 2/3 or 3/5 biopsies. In cases with growth of 2 bacterial species, the second species was considered relevant if found in at least 2 biopsies.

There were 15 men and 8 women with a mean age of 68 (53–85) years at primary surgery. 18 patients had arthrosis, 3 failed osteosynthesis of femoral neck fracture, 1 congenital dislocation of the hip and 1 idiopathic femoral head necrosis (Table 1).

The revisions were performed by 2 surgeons with a special interest in handling periprosthetic infections. The interval between primary surgery and the revision with exchange of the prosthesis was median 14 (4–65) months. 10 patients were revised within 1 year following primary surgery.

All available ESR and CRP values preceding primary surgery until the revision were retrieved. CRP values before 6 weeks and ESR values before 12 weeks postoperatively were disregarded, as being influenced by the surgical trauma. The preoperative ESR and CRP values were missing in 3 and 4 patients, respectively. Thus 87 ESR and 98 CRP values remained for analysis. Depending on the length of the interval between the operations, the number of values for each patient ranged between 2–10 (median 4). Normal CRP values for our laboratory are < 9 or < 10 mg/L, which is shown in the figure as 5 mg/L.

Table 1. Patient data

A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S
1	1	72	89	1	1	<9	5		19	42	19	13	42	18	14	30	4	2
2	1	74	91	1	1	<9	16		24	69	41	17	69	13	41	52	5	1
3	1	54	92	1	4	<9	16		<9	44	<9		50	19	<9	30	5	3
4	1	59	88	1	2	<9	16	23			31	22	46	13	20	40	6	1
5	1	69	87	1	1	<9	17	20	<9	75	59	32	75	15	32	50	10	1
6	1	72	79	1	3	<9	25				46	29	45	21	34	28	11	1
7	2	65	85	1	1	<9	9	<9	10	20	26	43	58	44	26	58	11	1
8	1	76	83	1	1	<9	15	45	25	30	30	43	36	43	10	25	12	1
9	1	63	90	1	2	<9	11	<9	<9	38	41	40	95	47	11	95	12	4
10	2	69	89	4	1	11	25	43	23	75	57	41	110	41	57	110	12	2
11	2	73	89	2	1	<9	26	23	14	37	23	6	59	48	14	59	12	1
12	1	61	84	1	1	<9	7		25	31	95	56	50	29	95	48	14	1
13	1	57	92	3	1	<9	24				30	57	60	54	25	60	14	1
14	2	74	83	1	1	<9	8	40	40	16	60	67	41	21	60	27	16	6
15	1	70	90	1	1	<9	12	10	<9	21	10	7	40	66	<9	40	17	3
16	2	85	90	2	1	<9		10	35	70	35	16	70	16	30	57	17	1
17	2	67	91	1	1					56	35	76	38	76	35	38	19	1
18	1	65	81	1	1		4			52	40	83	49	62	20	30	21	6
19	1	78	90	1	2	<9	10	12			44	101	55	101	44	55	24	1
20	1	83	90	1	1	12	10		<9	18	18	112	50	113	9	50	26	5
21	2	65	86	2	1			16			<9		52	132	<9	51	32	1
22	2	53	78	1	1		11				<9		22	202	<9	13	50	1
23	1	62	83	1	1	<9	8	60	30	11	45	67	46	181	12	24	65	1

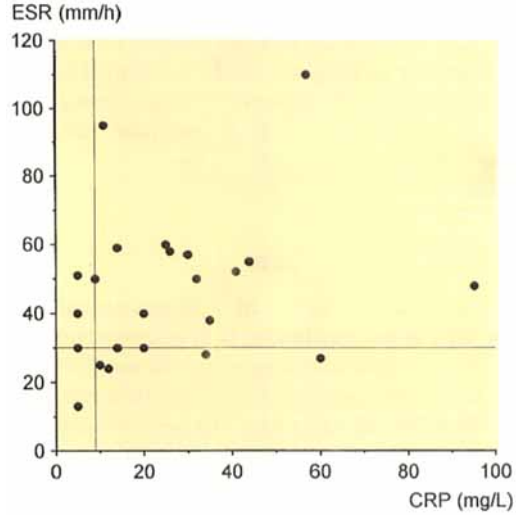
A Case
B Sex
  1 male
  2 female
C Age at primary arthroplasty (years)
D Operative year 19–
E Etiology
  1 arthrosis
  2 failed femoral neck fracture
  3 CDH
  4 osteonecrosis
F Prosthesis
  1 Charnley
  2 Charnley stem+Harris-Galante socket
  3 Lubinus
  4 cemented Omnifit
G CRP preop.
H ESR preop.
I CRP 6 weeks postop.
J CRP 12 weeks postop.
K ESR 12 weeks postop.
L Maximum CRP postop.
M weeks postop.
N Maximum ESR postop.
O weeks postop.
P CRP prerevision
Q ESR prerevision
R months to revision
S Bacteriology
  1 coagulase negative staph
  2 diphtheroids
  3 *Propionibacterium acne*
  4 *Peptococcus*
  5 G+ cocci
  6 mixed

ESR was determined during 1 hour with the Westergren method and CRP with immunoassay. The Mann-Whitney U-test was used for the statistical analysis.

Results

The median increase in ESR prior to revision, as compared to the preoperative value, was 31 (2–85) mm corresponding to 229 (12–764)%. 5 patients had an ESR value below 30 mm at the latest blood test before revision, the two lowest being 13 and 24 mm.

In 4 patients, CRP was < 9 mg/L prior to the revision, and 9–12 in 4 others (Figure). Normal values of CRP (< 9 mg/L) were found in 25/98 postoperative samples. 8 patients had at least two normal CRP values. In 3 patients, all CRP values were normal and in 6, all values were < 20 mg/L. However, all but 1 of these 6 patients had ESR values over 30 mm at least once. The exception, patient 22, was revised 4 years



Individual values of ESR and CRP before revision operation for a low-grade infection in 23 cases. Lines are drawn to show cut-off limits of 9 mg/L and 30 mm for CRP and ESR, respectively.

Table 2. Median (range) values of erythrocyte sedimentation rate and C-reactive protein in 23 deep periprosthetic hip infections from before the primary arthroplasty to revision for infection

	n	ESR (mm)	n	CRP (mg/L)
Before primary surgery	20	12 (4–26)	19	<9 (<9–12)
After 6 weeks		–	13	20 (<9–60)
After 12 weeks	15	37 (11–75)	15	19 (<9–40)
Maximum value	23	50 (22–110)	23	35 (<9–95)
Before revision	23	48 (13–110)	23	20 (<9–95)

Table 3. ESR and CRP values in patients revised for infection

Time to revision after the primary arthroplasty	ESR (mm)		CRP (mg/L)		
	<30	≥30	<9	9–19	>19
≤ 1 year (n 10)	4	27	10	6	22
> 1 year (n 13)	18	38	15	11	34

Table 4. Median of maximum ESR (mm) and CRP (mg/L) values and values before revision

Revision	≤1 year n 10	>1 year n 13	P-value [a]
ESR max	54	50	0.3
CRP max	36	35	0.6
ESR prerevision	45	48	0.7
CRP prerevision	23	20	0.8

[a] Mann-Whitney U-test

postoperatively and on two occasions, within 4 months before the revision, the ESR and CRP were normal. Before the primary THA, the median ESR (12 mm) and CRP (< 9 mg/L) were low and the median of the maximum registered values during follow-up until revision were 50 mm and 35 mg/L, respectively (Table 2).

In 10 patients revised within 1 year, 4/31 ESR values were < 30 mm. In 13 patients revised after 1 year, 18/56 values were < 30 mm. CRP values differed less (Table 3). Neither the maximum ESR and CRP values nor the values before revision differed between the 10 patients with infections that were revised in the first postoperative year and the 13 revised after 1 year (Table 4). The ESR and CRP showed no tendency to increase with time.

Staphylococcus epidermidis and closely related staphylococcal species were recorded as coagulase-negative staphylococci. They were cultured alone in 15/23 infections. The other infections were caused by diphtheroids in 2, *Propionibacterium acne* in 2, *Peptococcus* in 1 and unspecified Gram-positive cocci in 1 patient. There were 2 mixed infections, 1 caused by coagulase-negative staphylococci and *Propionibacterium acne* and 1 by *Peptococcus* and *Propionibacterium acne*. Coagulase-negative staphylococci were the commonest pathogens in patients revised both early and late after primary surgery.

Discussion

Low-grade periprosthetic infections following THA are often difficult to diagnose. Radiographic changes are nonspecific (Weissman 1983) and culture of aspirated joint fluid may give misleading results (Buchholz et al. 1981, Cuckler et al. 1991). Other authors have found a good correlation between cultures from fine-needle aspirations and tissue samples obtained at revision (Roberts et al. 1992, Lachiewicz et al. 1996). During surgery, frozen sections have been used with varying results, depending on the criteria used to define the infection (Athanasou et al. 1995). Glithero et al. (1993) studied low-grade hip and knee infections with granulocyte scanning. Sensitivity was only 37% and was best in knee infections. They concluded that sensitivity to insidious infections was lower than previously reported.

The diagnostic usefulness of ESR and CRP values is limited. ESR values are increased for a longer period following surgery than are CRP values and 1 year following an uneventful total hip arthroplasty, the mean ESR in 3 studies differed and were 13, 19 and 27 mm/h (Carlsson 1978, Aalto et al. 1984, Shih et al. 1987). Normal ESR values show substantial, age and sex-dependant variation (Böttiger and Svedberg 1967, Griffiths et al. 1984). Before surgery, CRP is present in only trace amounts in plasma. Following surgery, CRP can reach values of 200–400 mg/L within 48 hours. Normalization occurs within 3–6 weeks (Aalto et al. 1984, Choudhry et al. 1992, Larsson et al. 1992). These authors have assumed that an infection will cause a secondary rise or a persistent increase in CRP, but they have not presented data to support that view. Determinations of the CRP have facilitated the diagnosis of bacterial infections in many instances, but there are few reports on its use in orthopedic surgery (Hedström 1983, Waleczek et al. 1991, Schulitz and Assheuer 1994). These studies do not discuss chronic periprosthetic infections.

Cuckler et al. (1991) reviewed ESR determinations in 5 series totalling 168 periprosthetic hip infec-

tions and used a threshold of 30 mm/h. Specificity, sensitivity and accuracy were all around 80% and were slightly better than joint aspiration and white blood cell scanning. However, these 5 studies included infections caused by more virulent bacteria than those in the present study. In a group of patients revised for mechanical loosening, we found a median ESR before revision of 10 (1–28) mm (Sanzén and Carlsson 1989). Lachiewicz et al. (1996) reported a mean ESR of 32 mm in 116 uninfected hips before revision and 80 mm in 19 infected patients. 10 rheumatoid arthritis patients were included. In the present study, the average ESR before revision, 48 mm, was much lower. This difference in both infected and uninfected patients is remarkable and might be due to differences in technique or in the studied populations. We believe that the relative increase in ESR after the arthroplasty in the individual case is more relevant than comparison with an arbitrary normal upper limit.

To detect low-grade infections, we cannot use a CRP level of 20 mg/L as a limit. As shown in this study, repeated values close to the normal limit (< 9 mg/L) in patients without another reason for an increased CRP are consistently found in such cases. The risk of false positive results was analyzed in the earlier study from our institution (Sanzén and Carlsson 1989). We followed uncomplicated THA patients during the first 3 postoperative years, all within the duration of the present study. Among 233 CRP values in 50 patients, 203 were < 10 mg/L, 23 were 10–20 mg/L and 7 > 20 mg/L. A persistent slight increase in CRP was uncommon. Only 1 patient had more than 1 CRP value > 20 mg/L, and this was the only patient with a high CRP combined with an ESR above 30 mm. She also had an active sigmoiditis. In the same study, 9/33 patients revised for mechanical loosening had a CRP of 10–19 mg/L before revision, while the other patients had normal values. A Mann-Whitney U-test shows that the CRP values of these 33 patients were significantly lower than those before revision in the present series of 23 low-grade infections ($p = 0.00001$).

Another observation in the present study is that some patients with several normal assays of CRP at the same time had an increased ESR. CRP is a sensitive indicator of bacterial activity in chronic osteomyelitis (Hedström 1983), but the present series indicates that in some chronic low-grade periprosthetic infections there is not enough inflammation and tissue injury to stimulate the formation of CRP. At the same time, the ESR, which reflects changes in serum levels of immunoglobulins and fibrinogen, is often increased.

We conclude that even a slight increase in CRP or in ESR compared to the preoperative value in a patient with a painful hip prosthesis should make the surgeon aware of the possibility of a low-grade infection. It is our impression that the ESR is more sensitive and more valuable than CRP for indicating the presence of a low-grade periprosthetic hip infection.

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