Periprosthetic joint infections

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Infection is a dramatic complication of total joint surgery. Infection mechanism, pathogen, clinical presentation, and patient related factors dictate the treatment and they should be used as guides to optimal treatment protocol. The prompt diagnosis and treatment of infection will minimize the morbidity. No single test is able to show the presence of infection in every case. Diagnosis of infection is always a combination of available tests and clinical knowledge.

If acute infections are treated without delays the prosthesis may be saved. In chronic infections the two stage treatment protocol is still the best choice. However, especially with elderly patients with many comorbidities, suppression treatment with antibiotic only must be kept in mind.

Mechanism of infection

Infections can be divided into four main categories: Acute intraoperative infections, delayed postoperative infections, acute hematogenous infections and chronic infections, table 1.

Acute intraoperative infections are contaminations and they can be further divided into immediate and early infections. This was formerly the most common mechanism of infection. In some series the widespread use of profylactic antibiotics and laminar airflow conditions have altered especially the rate of intraoperative infections (1) but this is a bit controversial (2). It seems that the rate of acute postoperative infections has been quite constant during the last decade. In acute infection the onset of symptoms is very rapid. These infections are relatively easy to diagnose. The early acute infection usually shows characteristic clinical (pain, warmth and effusion of the joint) and laboratory features (elevated C-reactive protein and blood leucocyte level).

Delayed postoperative infection is also a contamination. Diagnosis of delayed postoperative infection is more problematic. The joints are commonly the ones that have not "healed properly". Patients are not happy with the outcome, tenderness, impaired function and pain still exist after several months after surgery. During the first postoperative months the distinction between delayed postoperative infection and normal postoperative pain and dysfunction is clinically very demanding, sometimes impossible. Laboratory tests are not helpful. C-reactive protein and blood leucocyte levels are often elevated in delayed infections, but occasionally also in non-infected cases. Radiographs show infections very late if ever and bone scans usually show normal postoperative changes also in infected cases.

Hematogenous infections are not surgery related. The primary focus of infection is most often in pulmonary or urinary track or in dental area. Skin problems and poor nutrition are also common findings. Hematogenous infection can act as an acute infection with classical characteristic clinical and laboratory features. The joint has been asymptomatic and the onset of symptoms is rapid. Hematogenous infection is often a septic disease with classical septic clinical and laboratory features.
Table 1. Classification of periprosthetic joint infections. Acute intraoperative infections can be divided into the immediate and early infections, and late chronic infections can further divided into the late chronic and late chronic "acutized" infections. These categories help to determine the treatment.

<table>
<thead>
<tr>
<th></th>
<th>Immediate 0-3 weeks</th>
<th>Early 3 wk-3 months</th>
<th>Delayed 3-24 months</th>
<th>Acute hematogenous</th>
<th>Late chronic &gt;24 months</th>
<th>Late chronic &quot;acutized&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local symptoms</td>
<td>Swelling</td>
<td>Swelling</td>
<td>Swelling</td>
<td>Swelling</td>
<td>None or mild swelling</td>
<td>Bad joint becomes even</td>
</tr>
<tr>
<td></td>
<td>Pus</td>
<td>Slow rehabilitation</td>
<td>Warmness</td>
<td>Pain</td>
<td>and/or warmth</td>
<td>worse</td>
</tr>
<tr>
<td></td>
<td>Pain</td>
<td>Warmness</td>
<td>Pain</td>
<td>Heat</td>
<td>Pain</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Redness</td>
<td>Pus discharge</td>
<td>Redness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heat</td>
<td>Heat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic symptoms</td>
<td>Fewer Sepsis possible</td>
<td>None</td>
<td>None</td>
<td>Fewer Sepsis possible</td>
<td>None</td>
<td>May be fewer</td>
</tr>
<tr>
<td>CRP</td>
<td>High</td>
<td>Normal or elevated</td>
<td>Normal or slightly elevated</td>
<td>High</td>
<td>May be elevated</td>
<td></td>
</tr>
<tr>
<td>X-ray</td>
<td>Normal</td>
<td>Normal</td>
<td>RLL's possible</td>
<td>Normal</td>
<td>RLL's possible</td>
<td>RLL's possible</td>
</tr>
</tbody>
</table>

The diagnosis of chronic infection depends on the duration of symptoms. These infections can further be divided into late chronic and late chronic activated infections. The acute phase constitutes the first six weeks, following subacute phase, after which the infection is called chronic.

The chronic infection is the most difficult to diagnose. Chronic infection can be a contamination or a hematogenous infection from origin. Distinction between aseptic loosening and infection is important for prediction of the final outcome after revision arthroplasty but also for the choice of surgical management. In chronic infections laboratory and radiological findings are often normal. Chronic infection is usually clinically silent, but it may activate and act as an acute infection with classical symptoms. It is, however, important for the choice of the treatment to distinguish the chronic infections from the true acute hematogenous infection. In true acute infection the joint has been functioning well before rapid onset of symptoms whereas in “acutized” chronic infection there has been some kind of problems (at least minor) with the joint also earlier.

The most usual bacterial source in postoperative contamination infections is staphylococcus aureus. Staphylococcus epidermidis is also quite common. In chronic infections staphylococcus epidermidis and aureus are the most common pathogen but streptococcus (5–10%), anaerobic pathogen (5%) and multibacterial infections are not uncommon. Acute hematogenous infections are caused most often by gram-positive cocci, staphylococcus aureus, beta-hemalytic streptococci, entococcus specian, but rarely by a gram negative pathogen (3–6).

The prosthesis acts as a large foreign body and it can be colonized by micro-organisms. Experimental studies have shown that especially polymethylmetacrylate (bone cement), stainless steel, cobalt-chromium alloy and polyethylene, that are the main constituents of prostheses, all have increased susceptibility to infection (7,8). Especially stafylococcus epidermidis has a high rate of adhesion to polyethylene. Bacterial resistance to antibiotics is related to the production of a glocoalyx slime that impairs antibiotic access and killing by host-defence mechanisms (9,10).

**Risk factors of infection**

The best way to prevent an infection is to minimize all risk factors. However, patients who need prosthesis are usually elderly and have also other diseases. Rheumatoid patients may have medications that impair bone formation. Arthroplasty is always a compromise between existing risk factors and hope for better function. Prior surgery of the joint is a significant risk factor. The risk is significantly higher if surgery is undertaken within one month of the prior arthroplasty. This is sometimes necessary in revision arthroplasties. Ex-
ceeding operation time is another risk factor. Studies have shown that if the operation lasts more than 2.5 hours the risk for infection rises significantly. However, the patient related factors are the most important factors. Comorbidities, such as diabetes mellitus and rheumatoid arthritis, increase the risk of infection, as does poor nutrition and obesity. Immunosuppressive therapy and compromised immune status also increase the risk of infection. Compromised social factors, mental retardation, smoking and use of alcohol have been shown to be related to higher infection rate. Poor hygiene and use of narcotics should be considered as contraindications for arthroplastic surgery.

**Diagnosis of infection**

As mentioned previously the early acute infection usually shows some characteristic clinical and laboratory features, whereas the diagnosis of subacute or low grade chronic infection is more problematic. In septic postoperative infections wound drainage is considerable and even pus may be found. C-reactive protein and blood leucocyte level are clearly elevated. In acute haematogenous infection the wound may seem normal, but patients have clear tenderness and pain in motion. Clinical series, however, have shown that it is not possible to differentiate between the delayed or chronic infection or aseptic loosening by clinical signs (6). Pain, especially pain at rest, is more often related to chronic infections, but also associated with aseptic loosening. Swelling, tenderness and warmth of the joint area are also seen in both cases. The blood white cell count is significantly higher in patients with infection compared to aseptic loosening. The average value can, however, still be within normal range. The blood white cell count is therefore rarely abnormal in chronic infections and is not helpful for ruling out infections. The blood C-reactive protein level is more helpful. CRP level is significantly higher in infections compared to aseptic loosenings, but normal C-reactive protein level does not rule out chronic infection. It must also be determined whether any other factors associated with raised C-reactive protein level, such as rheumatoid arthritis, other infection, any inflammatory condition or neoplasm, is present.

Radiographs are widely used in follow-ups. However, distinction between aseptic loosening and infection is difficult. Clinical follow-up series have showed that radiological findings such as loosening and osteolysis are common on both septic and aseptic failures. A common radiological scaling of loose vs. not loose is not diagnostic. Bone scans are found to be very helpful but problems exists with them too. The sensitivity of Technetium-99m bone scan is in most series around 0.4 and the specificity 0.95 (6,11). The analysis seems to be very specific but negative bone scan does not necessarily rule out infection. The scan might be occasionally negative in patients who have infection but have an inadequate blood supply of the bone (11). Also, normal postoperative changes are difficult to differentiate from low grade infection.

Intraoperative frozen section gram staining (12,13) and aspiration biopsies (14,15) have been found insensitive to detect occult septic loosening. However, the use of histological grading system based on the number and the type of the inflammatory cells suggested by Mirra et al. (16) has showed significantly better results (17,18).

Duff et al. (19) reported in their analysis of 43 knees preoperatively aspirated that the preoperative aspiration of the knee was the most helpful study for diagnosis or exclusion of infection with 100% sensitivity and specificity. Erythrocyte sedimentation rate, peripheral leukocyte count and radiographs correlated poorly with infection (19). The best results are obtained from pre- and perioperative joint aspirations and tissue sample cultures (6,19). An additional benefit of joint aspiration is the possibility to identify the organism responsible for infection and its antibiotic-sensitivity profile. However, a special attention must be addressed to prevent contamination. PCR from joint aspiration has been used lately in exceeding numbers. It is relatively sensitive and specific. PCR, however, is not able to show antibiotic-sensitivity profile. It is clear from various studies that no single test is able to show the presence of infection in every case. Synovial fluid leucocyte differential of >65 % neutrophils and / or leucocyte count over 1700 / µl (20) or over 1100 / µl (21) are sensitive and specific tests for a periprosthetic joint infection at least in knee joint.

Classical clinical signs, laboratory tests, special imaging studies and joint aspirations have all yielded a notable rate of false negative results.

**Management of infection**

Management of infection is a combination of surgical treatment and antibiotic therapy. Selection of surgical treatment dictates the antibiotic regimen. The goal of the treatment should be final eradication of the pat-
Surgical management of infection

The type of infection dictates the treatment protocol. Debridement with retention of the prosthesis seems to be potentially successful treatment for early postoperative infection or acute hematogenous infection, if performed within the first two-three weeks after the onset of symptoms (31). It is an attractive treatment option because of lesser morbidity and reduction in cost. The results have, however, been quite variable (22,32,33). In acute postoperative infections within three weeks of operation the prosthesis could be saved. As mentioned these patients have septic symptoms. Intra-articular synovectomy, debridement of all infected tissue with lavage can be recommended within the first three weeks, however, the results decline by time significantly. Radiological evidence of osteolysis is associated with high rate of failure (1). In delayed postoperative infections the distinction between normal postoperative pain and loss of function and infection is difficult. The symptoms are less dramatic. If infection is suspected more than four weeks after operation prosthesis can usually not be salvaged. If symptoms are not severe the status could be followed and if infection still suspected after several weeks the joint aspiration should be undertaken. In case of infection two stage exchange is recommended.

Acute hematogenous infection can happen anyti-
me. The onset of symptoms is rapid, patient had not have any signs of pain or tenderness in the joint previously. Acute hematogenous infections can be treated with synovectomy, debridement of all infected tissue, lavage, replacement of all polyethylene inserts and retention of the prosthesis if not loose. Antibiotic therapy for six weeks is accompanied to treatment protocol (1–3). The source of the original infection has to be removed.

In failed arthroplasties the distinction between aseptic loosening and chronic infection is important for the choice of surgical management between direct one stage exchange or delayed two-stage reconstruction. The one-stage exchange means that implant removal and new implantation are done in the same operation. In two stage exchange the implant is removed, intracapsular synovectomy and power lavage is undertaken. The joint space is filled with antibiotic-cement spacer. I.v. antibiotics are administered for at least six weeks and after that a new operation is performed. Synovectomy and power lavage is repeated and new prosthesis is implanted. The one-stage exchange of infected prosthesis is associated with higher rate of reinfections, and should therefore only be used in the treatment of aseptic loosening or with patients having chronic infection with low grade pathogen and poor general medical condition. However, there is some evidence that the overall results in infected cases can be improved by careful selection of patients (34). Delayed two-stage reconstruction with the use of antibiotic-impregnated bone cement provides the highest rate of success in treatment of infection and the best long-term functional results (1,23,32,33,35–37). Antibiotic bone cement seems to protect against hematogenous infection for some months after operation.

The results of resection arthroplasties are quite good in terms of eradication, but the procedure is seldom used due to impaired function. It does not seem to decrease the risk of death. Resection arthroplasty should be reserved for patients whose medical condition is poor and who have a history of failed prosthesis sparing surgery.

Infection remains to be one of the most dramatic complications of joint arthroplastic surgery. The risk for infection remains the rest of the life. The most effective way to treat infection is to avoid them. Therefore, selection of patients, minimizing the risk factors and using skillful and experienced operative team can not be underestimated. The financial outcome of infection is significant. Long morbidity and hospital stay, expensive antibiotic regimen, and repeated operative treatment is a real challenge for the patient and for the health care system. In future the rate of infections might even decrease but the total number of infection is going to exceed due to the increasing number of arthroplastic operations worldwide. Although, the goal of treatment has to be the eradication of the pathogen, modern effective management of patients with prosthesis infection should not be directed only toward the eradication of the infection but also toward the restoration of the optimal function.

References:


