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Review Article

Approaches to The Patient with Painful Total Knee Arthroplasty

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Abstract

Background: Total Knee Arthroplasty (TKA) is one of the most common procedures in or¬thopedic surgery and clinical success can be characterized by the revision rate and im¬provement of function, as well as the patient´s satisfaction and pain. Despite the clinical sucess of primary TKA with 10-year survival rates as high as 95%,about 20% of the patients after TKA are not completely satisfied with their outcomes for several reasons. Obvious causes of failure might be identified with clinical examinations and standard radiographs only, whereas the unexplained painful TKA remains a challenge for the surgeon. They can be classified into extra- and intraarticular disorders; the latter being divided into biological and mechanical origins. The onset of the pain after the operation and the differentiation between pain in motion and at rest are helpful to distinguish between mechanical and non-mechanical problems. An infection should be the first diagnosis to be ruled out in a painful TKA. It is generally accepted that a clear understanding of the failure mechanism in each case is required prior considering revision surgery.

Method: In the following review, a practical diagnostic algorithm is described for failure analysis in more detail. The evaluation of a painful TKA includes a detailed history with an extended analysis of the type of pain, thorough clinical examination including spine, hip and ankle, radiographic and laboratory analysis, as well as invasive examinations like joint aspiration and biopsies.

Conclusion: This diagnostic algorithm offers the reader an important tool for a sufficient failure analysis in almost all patients with painful TKA.

Keywords: Diagnostic Algorithm; Failure; Pain; Total Knee Arthroplasty

Introduction

Artificial joint replacement is probably one of the most successful and most common operations in the field of medicine [1]. The number of implantations of total knee endoprostheses (total knee arthroplasty; TKA) has been increasing continually in recent years and in the meantime, belongs to the most frequent and at the same time, most cost-intensive, intervention in orthopaedic and trauma surgery. Current figures show that approximately 190,000 primary TKA are being carried out per year in Germany. And an increasingly ageing population combined with higher levels of entitlement to benefits means that the number of implantations and the related costs can be expected to increase in the future. Revision leads to even more expenditure so this must be included in the prognosis for the financial and infrastructure requirements to be expected in the decades ahead. From the point of view of the patient, it is interesting to compare the functional benefit resulting from TKA with the risk of a potential revision operation.

Although the number of TKAs is increasing on a global scale at a faster rate than Total Hip Arthroplasty(THA), some studies have shown that the level of patient satisfaction following TKA is not as high as that reported for THA. The largest study that ad-

dressed this situation was carried out by [2] who investigated over 25,000 patients on the Swedish knee prosthesis register and found that over 8% of the patients were dissatisfied with their knee prosthesis. A large study of TKA patients in England and Wales was recently reported by [3]. They found that over 18% of the patients were dissatisfied with their prosthesis. Similar data were reported by a cross-sectional study carried out in Canada where approximately 20% of patients were dissatisfied with the result of their TKA [4]. This was particularly true for younger patients. Price, et al. [5] studied a cohort of patients who were 60 years of age or less at the time of surgery and found a survival rate for TKA of 82% after a follow-up period of at least 12 years. Over 40% of these patients reported modest or severe pain in the affected knee.

A meta-analysis by Lützner, et al. [6] involved a total of 20,873 TKA operations and revealed a revision rate of 4.4% after 10.7 years. The most common reason for revision surgery was aseptic loosening of one or more components (31%), infections (23%), polyethylene wear (16%), and patella-related problems (14%). The study also identified an age-related revision rate, with patients who were younger than 60 years of age at the time of implantation showing a revision rate of 7%. In contrast, patients between the ages of 60 and 70 years exhibited a revision rate of 5% and those who were older than 70 years a rate of 2.2%. All patients were assessed after a similar period of follow-up. In addition, the meta-analysis revealed a higher revision rate after cement less TKA (8.3%cement less versus 3.6% cemented) and in studies where there was a higher proportion of rheumatoid arthritis patients.

The reasons for pain in the area of a total knee endoprosthesis can be manifold. However, extra-articular causes can be differentiated from intra-articular causes (see Table 1).

Extra-articular causes	Intra-articular causes
Coxarthrosis	**Infection**
Neurological causes - Spinal canal stenosis - Radicular compression - Complex regional pain syndrome	Instability - on extension - on flexion/ midflexion - global
Vascular claudication	**Aseptic loosening**
Tendinopathies - Pes anserinus - Patellar tendon - Quadriceps tendon - Tractusiliotibialis	**Extensor apparatus** - Patella tracking problems - Overstuffing of pat.-femoral joint - Impingement of lat. patella facet due to undersized retropat. resurfacing - Retropatellar arthritis - Ruptured tendon Patellar tendon Quadriceps tendon
Periprosthetic fractures - Femur - Tibia - Patella	**Soft tissue impingement** - Patellar clunk - Popliteal tendon - Overhang of components
	Malalignment - Axial, rotation
	Polyethylene debris
	Osteolysis
	Arthrofibrosis
	Fracture of prosthesis components

Table 1: Extra- und intra-articular causes of pain associated with total knee arthroplasty.

In addition, because it has an effect on further treatment, a periprosthetic infection should always be considered first when the patient presents with a painful TKA until there is evidence to prove otherwise. Understanding the reasons for the pain represents a serious challenge for the treating physician. In addition to patient-specific data such as age, gender, low preoperative WOMAC scores, presence of co-morbidities, and psychological factors, patients with lower levels of preoperative osteoarthritis (less than Grade 3 or 4 as defined by Kellgren and Lawrence) have a much higher risk for postoperative pain and dissatisfaction with their knee implant [7].

A diagnostic algorithm is important for the assessment of a painful knee joint and can be used to obtain a detailed analysis of the condition of a painful prosthesis. This review is intended to illustrate the procedures we use in our clinic: in addition to the generation of a precise case history, especially the pain-associated history, it is important to carry out a thorough clinical examination of the affected knee and the neighbouring joints including the spinal column, the hips, and the ankles. Equally important is an instrument-based examination that includes clinical chemistry for assessing inflammation parameters such as CRP and leukocyte count, as well as a radiological examination with a standard radiograph in two views. If required, a CT or a 3-phasebone scintigraphy can be carried out in special cases. If results are inconclusive, we employ invasive procedures such as joint aspiration and biopsy.

The Diagnostic Algorithm

Case History

Joint replacement is similar to treatment of other illnesses and conditions in that a detailed case history is the most important source of information for the clinician. In this case, it is most important to localize the pain, when it occurs (under load or at rest), as well as the intensity and duration of the pain. It is also important to discover how long after the implantation the pain started occurring. If the knee was always painful following the operation, this

would suggest that there are mechanical or kinetic problems with the prosthetic or that there is a previously unrecognized periprosthetic infection. Brown, et al. [8] introduced the concept of the four I's for pain that occurs soon after surgery: incorrect indication, infection, instability, and impingement of soft tissue. Mechanically induced pain occurs during joint movement or when walking. If the pain only occurs at rest, this is less likely to be the result of a mechanical defect and more likely to be the result of a periprosthetic infection or neuropathic pain (see Table 1). If the preoperative pain continues to be felt at the same intensity after surgery, this suggests extra-articular pain or an incorrect initial diagnosis. Pain that begins within the first year following implantation is most likely to be the result of a periprosthetic infection, incorrect rotation or soft tissue impingement. Pain that begins later than one year after surgery is probably the result of osteolysis, loosening or a periprosthetic infection. The location of the pain can also provide important information about the actual cause. Ventral pain, particularly when it occurs while walking uphill or ascending stairs, indicate problems associated with the patellofemoral joint.

Clinical Examination

A subsequent physical examination will also provide information about the cause of the pain. Poor mobility suggests the existence of kinematic or mechanical problems but can also be caused by periprosthetic infections and by complex regional pain syndrome type I. Ligament instability can easily be identified. In such cases, it is important to check the stability of the knee at different flexion angles because the main structures around the knee have various supportive functions for Varus-valgus stability in the different flexion positions. Thus, the stability of the knee should be examined in extension in a midway flexion angle and at 90° flexion. Since the posterior capsule is mainly responsible for stability during complete extension, the function of the lateral ligaments is best tested at a slight flexion of 20°; the function of the posterior part of the medial ligament can be assessed during slight flexion and of the anterior part of the medial ligament when the knee is flexed to 90°. The lateral ligament and the tractus iliotibialis are tested with an extended knee and the popliteal tendon preferably tested with the knee flexed to 90°.

The mobility of the patella should also be examined while knee movement is being assessed. Any tendency for lateralization of the patella could indicate a malrotation of the femoral or tibial components, or both. If pressing on the patella during knee extension also causes pain, or movement of the patella is painful, it is probable that there are complications with the patellofemoral joint. If the patella has not been resurfaced, it is possible that the problems are caused by secondary retropatellar arthritis. Impingement problems can be diagnosed during full extension of the knee. The patellar clunk syndrome occurs most often with posterior stabilizing prostheses of older design where, during extension, a mass of soft tissue springs out of the femoral prosthesis notch and elicits a palpable mechanical catching, or clunk, phenomenon [9]. Another impingement syndrome involves the mechanical catching of the popliteal tendon on the posterolateral border of the femoral component, the tractus iliotibialis on the anterolateral border of the tibial component, and the pes anserine us on the anteromedial border of the tibial component. This often involves oversized prostheses with protruding borders. If this is tibial, then the main location of the pain is medial. If femoral, a lateral overhang of the patellar shield can lead to irritation of the soft tissue. If the knee is warm to the touch, there is reason to believe that an inflammatory component, including a periprosthetic infection, is involved. Similarly, a recurrent effusion in the joint is indicative of an inflammatory intra-articular process. Pain emanating from the hip or the spinal column should always be considered with respect to a differential diagnosis, which is why those areas should always be examined as well.

Laboratory Tests and Radiological Examinations

The nature of the subsequent tests and examinations is dependent on the information obtained from the case and pain histories and the physical examination. Until proven otherwise, it should always be assumed that a painful knee prosthesis is caused by an infection. Thus, an assay for determining the level of CRP is one of the first tests that should be carried out. Standard radiographs can be used to evaluate a number of different causes for the painful knee prosthesis. Loosening of prosthetic components can be recognized by changes in the position of the prosthesis and by observing a change in the radiolucency with time [10]. Marx, et al. [11] reported a sensitivity of 77% for radiological detection of loosening of the femoral component and of 83% for the loosening of the tibial component; specificity was assessed as 90% for the femoral component and 72% for the tibial component. Osteolysis (caused by polyethylene abrasion debris, for example) and periprosthetic infections are usually identifiable in standard radiographs (Figure 1).

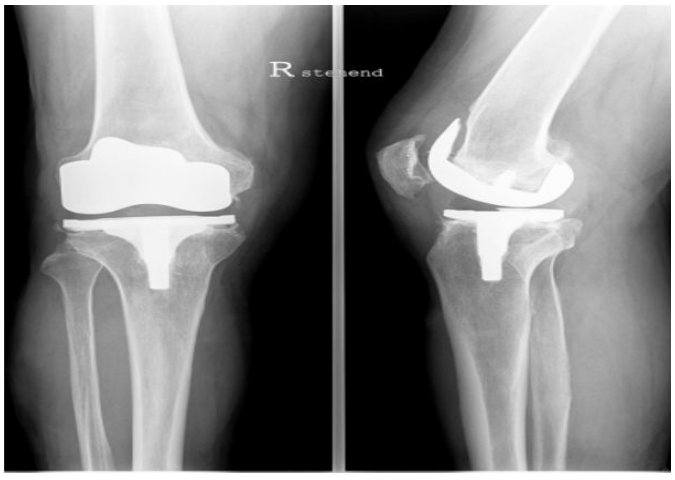

Figure 1: Radiograph in two planes of a 77-year-old male patient showing radiolucent lines and osteolyses around the femoral and tibial component as a sign of implant loosening.

Computer Tomography (CT) is recommended if there is any ambiguity and for determining the extent of the osteolysis. Radiological analysis of the long-leg view enables a better assessment of the axis alignment of prostheses than the routine radiographical procedure in two views (Figure 2).

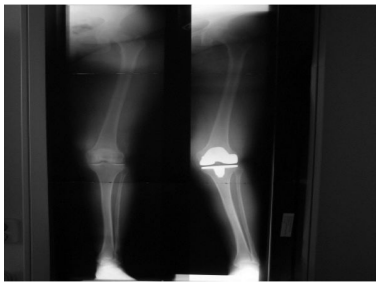

Figure 2: Long-leg radiograph of the left leg of a 65 year of female patient 3 months postoperatively showing a malaligned total knee arthroplasty.

If a malrotation is suspected, long-leg analysis is only useful when there is no flexion contraction and the leg is rotated correctly (patella ventrally orientated) during the exposure. In this case, a tangential view of the patella is useful (Figure 3).

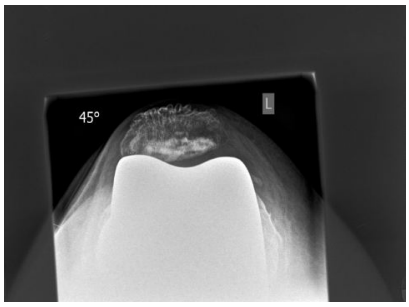

Figure 3: Tangential radiograph of the right knee of a 78-year-old male patient showing a lateral tilt of the patella as a sign of malrotation (internal rotation) of one of both components of the total knee arthroplasty.

If there is suspected malrotation of the femoral and/or the tibial components, this is best evaluated by a rotation CT, whereby the reference line for the femoral component is the trans epicondylar axis [11,12] (Figure 4a-4b).

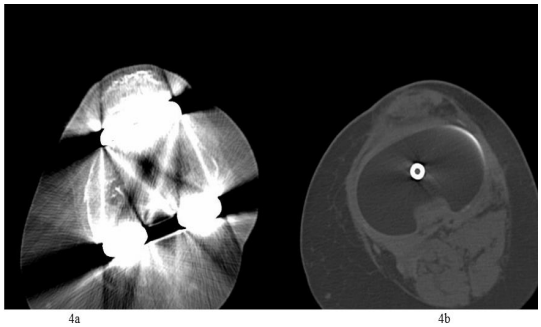

Figure 4: Rotational CT-Scan of a total knee arthroplasty showing internal rotation of the femoral and tibial component of patient of Figure 3. Figure 4a: Rotation-CT of the femoral component showing internal ration of the component in relation to the trans epicondylar line. Figure 4b: Rotation-CT of the tibial component showing internal rotation of the tibial component in relation to the tibial tubercle.

Radiological examination during flexion with Varus and valgus stress enables the visualization of an instability that has been identified during the physical examination [13]. Any AP-radiograph should be compared to previous radiographs whenever possible if the clinical findings indicate the following conditions: polyethylene abrasion, osteolysis, radiolucency, component overhang, subsidence, or translation of the tibial component (Figure 1). The lateral radiograph should be examined for the following parameters: size of the femoral component, posterior femoral offset, position and thickness of the patella, slope of the tibial component, and subsidence or translation of the tibial component (Figure 1). A radiograph tangential to the patella should be examined for the following: tilt and/or misalignment of the patella, overhang of the femoral component, lateral patellofemoral impingement, and thickness of the patella (Figure 3).

3-phase bone scintigraphy is often carried out in cases of painful knee implants although its implementation and interpretation should be regarded with some scepticism. In cases of unicondylar knee arthroplasty, bone always accumulates around the components of the prosthesis, probably as a result of ossification processes occurring at the prosthesis. Thus, 3-phase bone scintigraphy is not utilizable in such cases. Where total knee replacements and axis-aligned prostheses are concerned, this methodology is first applicable to the diagnosis of prosthesis loosening one year after surgery at the earliest [14,15]. Smith, et al. [16] report a sensitivity of 92.3% for this technique when used for diagnosing prosthesis loosening together with a specificity of 75.9%, a positive predictive value of 64.9% and a negative predictive value of 95.0%. Accumulation of radionuclide around the whole prosthesis indicates that loosening has occurred, especially in the case of axis-aligned prostheses (Figure 5).

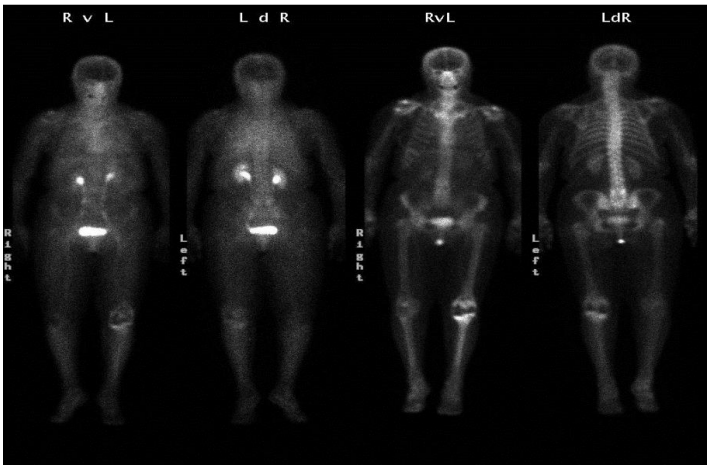

Figure 5: Three-Phase-Szintigraphy of a 74 year of female patient with an increased accumulation of radionuclide around the tibial component as a possible sign of tibial component loosening.

Scintigraphy can also be useful in the verification of secondary retropatellar arthritis as the reason for the pain following total knee arthroplasty. The so-called "Hot patella" displays a greatly increased uptake of tracer and provides diagnostic evidence for initiating secondary patellar resurfacing [17].

Invasive Procedures

As already mentioned, diagnostic procedures addressing painful TKA include those that lead to the exclusion of periprosthetic infections. The AAOS guidelines [18] recommend that further diagnostic procedures should only be carried out when the CRP level is greater than 10 mg/L. Since our own studies have clearly shown that approximately 10% of patients with periprosthetic infections exhibit CRP levels less than 10 mg/L, we recommend that further diagnostic procedures should be initiated if the CRP level is less than 10 mg/L and the patient presents with undefined pain associated with the TKA [19] (see Table 3). The different diagnostic methods currently available for determining, or for excluding, the presence of a periprosthetic infection can be classified as direct or specific methods, where the pathogen is identified and its sensitivity to antibiotics tested, and indirect or unspecific methods where those parameters are not assessed. Indirect, unspecific methods only provide evidence or proof of an infection but leave the question of the identity of a pathogen, or its sensitivity to antibiotics, unanswered. Thus, specific methods of investigation should be well-established components of the diagnostic armamentarium used to determine a periprosthetic infection (see Table 2).

Direct or specific tests	Indirect or unspecific tests
Laboratory: If required PCR (no resistance assay)	**Laboratory:** CRP, BSR. IL-6
Aspirate: With incubation	**Aspirate:** With cell count in aspirate Alpha-Defensine
Biopsy: With incubation	**Biopsy:** Histological examination by normal technique or with frozen section
	Imaging: X-ray, sonography, scintigraphy, leukocyte scintigraphy, FDG-PET

Table 2: The different diagnostic methods for identifying or excluding the presence of a periprosthetic infection

One of the specific methods for providing evidence for the identity of the pathogen is the pre-operative aspiration of the joint. The predictive value of the preoperative joint aspirate is, however, very much under discussion in the medical literature. Quoted sensitivities range from45% to 100%, and specificities from 81% to 100% (see Table 3).

	CRP	Aspiration	Incubation	Histology	Biopsy
Positive [n]	29	29	31	36	40
Negative [n]	85	100	103	100	103
False positive [n]	20	5	2	5	2
False negative [n]	11	11	9	4	0
Sensitivity (±95% confidence interval)	**72.5%** (±13.8%)	**72.5%** (±13.8%)	**77.5%** (±12.9%)	**90.0%** (±9.3%)	**100%** (±0%)
Specificity (±95% confidence interval)	**80.9%** (±7.5%)	**95.2%** (±4%)	**98.1%** (±2.6%)	**95.2%** (±4.1%)	**98.1%** (±2.6%)
Positive predictive value (±95% confidence interval)	**59.2%** (±13.8%)	**85.3%** (±11.9%)	**93.9%** (±11.2%)	**87.8%** (±10.0%)	**95.2%** (±6.4%)
Negative predictive value (±95% confidence interval)	**88.5%** (±7.5%)	**90.1%** (±5.6%)	**92.0%** (±5.0%)	**96.1%** (±3.7%)	**100%** (±0%)
Accuracy	**78.1%**	**89%**	**92.4%**	**93.8%**	**98.6%**

Table 3: Results of the diagnostic methods applied to 145 knee revision arthroplasties [19].

The reasons for the poorer results are given as contamination of the aspirate by, for example, bacteria from the skin flora, the presence of bacteria that are difficult to grow in culture, such as facultative anaerobes and Gram-negative bacteria, and the localisation of antibiotics that had not been discontinued before joint aspiration [20-23]. Moreover, the actual method of analysing the aspirate varies greatly between investigators, particular where culture medium and incubation times are concerned. Specific methods for identifying the bacteria should only be employed when the patient is no longer receiving antibiotic treatment; antibiotics not only make the identification of the bacteria more difficult, they are also of limited therapeutic value in cases of chronic periprosthetic infection. If antibiotics have been administered, they should be discontinued for at least 14 days - better would be four weeks - before the joint fluid is aspirated [20,22,24,25].

Symptoms of a systemic infection are uncommon following discontinuation of antibiotics but, if these do appear, the patient should undergo surgery immediately. In our opinion, the purpose

of this operation should be to bring about local relief of the joint and to obtain material for diagnostic analysis. At this stage, we recommend treatment with a broad-spectrum antibiotic, at least until the antibiotic sensitivity of the organism is known. Subsequently, a specific local and systemic antibiotic treatment should be initiated. In addition,a sufficiently long incubation time - we use 14 days - is essential for the further analyses [19,26-29]. This extended incubation period is necessary because the bacteria that cause a periprosthetic infection occur in very small numbers in the biofilm and are often in a sessile state that is characterized by a slow rate of bacterial multiplication [26,30-33]. In a study of 110 periprosthetic infections of hip and knee joints, we were able to show that after an incubation period of 7 days, only 70% of the infections were demonstrable and that bacterial growth in the remaining 30% only became apparent during the second week of incubation [28]. It should also be noted that a significant increase in contamination of the cultures during the second week of incubation could be avoided by exercising extreme care when setting up the test. Employing a sufficiently long incubation led to a reported accuracy of 90% for the diagnosis of a periprosthetic infection by testing the aspirate [34,35]. In our own study of 145 knee revision arthroplasties, we attained a sensitivity of 72.5% and a specificity of 95.2% together with positive and negative predictive values of 85.2% and 90.1% respectively. This result corresponded to data from an earlier pilot study and are comparable to data reported in other studies [19,36] (see Tables 3 and 4).

Author	N	Sensitivity	Specifity	PPV	NPV	Accuracy
Barack [20]	53[a]	75 %	96 %	75 %	96 %	93 %
Duff [24]	39	100 %	100 %	100 %	100 %	100 %
Fuerst [36]	75	69 %	97 %	85 %	92 %	91 %
Glithero [48]	54[b]	89 %	97 %	94 %	95 %	94 %
Kordelle [39]	39	50 %	100 %	100 %	50 %	67 %
Levitsky [22]	72[b]	67 %	96 %	75 %	94 %	91 %
Morrey [38]	73	45 %	c	c	c	c
Panousis [49]	92[b]	70 %	95 %	78 %	92 %	90 %
Steinbrink [29]	2158[d]	82 %	96 %	87 %	94 %	92 %
Teller [50]	166[b]	28 %	99 %	83 %	90 %	90 %
Virolainen [41]	69[b]	75 %	100 %	-	-	-

Table 4: Results reported for the microbiological culture of joint aspirate for the diagnosis of a periprosthetic infection of a knee TEP. (a = without previous antibiotic treatment; b= knee and hip TEP; c = all infected; d = only hip TEP)

In our opinion, it is the failure to incubate the aspirate for a long enough time that could have resulted in the poorer sensitivities of pre-operative aspiration reported in other studies (for example, 46.1% reported by [37], 45% reported by [38], and 50% reported by [39]. However, many reports fail to mention the actual time of incubation and this suggests that the standard time of 3 days was employed in such cases.

Another direct and specific diagnostic method involves the biopsy of periprosthetic tissue. Using arthroscopic biopsy forceps, 5 samples of the periprosthetic tissue and synovium are taken from different areas of the knee joint, close to the affected prosthesis. Each of the synovial samples is placed in separate sterile tubes and, along with the joint aspirate, transferred to the microbiological laboratory within an hour of sampling. The samples are then streaked onto blood agar for purposes of further differentiation. Special medium is used to detect anaerobic organisms. All samples are then incubated for 14 days. The results are evaluated according to the parameters proposed by [40-42]. Thus, a periprosthetic infection is regarded as being present when at least one of the following conditions is fulfilled:

- Evidence of the same pathogen in at least two of the samples
- Evidence of a pathogen in at least one sample and evidence of at least five neutrophilic polymorphonuclear leukocytes per high power field (x 400) in the histological preparation, based on the reports by [42-45].

Evidence of bacteria in just one sample in the absence of any histological evidence, is regarded by [41] as a contaminant arising from the sampling phase or from the subsequent culture procedure. In our study of 145 knee revision arthroplasties, we could show that this preoperative diagnostic method is superior to aspiration and that an infection can be accurately confirmed or excluded from the clinical evaluation. We achieved a sensitivity of 100%, a specificity of 98.1%, a positive predictive value of 95.2%, and a negative predictive value of 100%; this calculates to an accuracy of 98.6% [19] (see table 3).

The biopsy has an advantage over other diagnostic methods of verifying a periprosthetic infection in that it combines several methods of detection in one, namely the bacteriological and histological examination of several samples of the synovium. The

relatively small surgical incision required and the associated low level of risk, combined with the high diagnostic value, has made the biopsy a standard procedure for the diagnosis of periprosthetic infections of the knee in our clinic. In our opinion, biopsy should be preferred over a second joint aspiration (as recommended by [46]) if there is any doubt attached to the diagnosis, i.e., if the result of the first aspirate analysis is suspected to be falsely positive or falsely negative.

The biopsied material can also be investigated histologically for other causes of the joint pain, such as allergic reactions or inflammatory responses associated with prosthesis debris. In fact, the histological examination of the periprosthetic tissue is the only reliable method for assessing an allergic response to the implanted prosthesis or to the cement. Thus, the sign of an allergic reaction Type IV in the histological section is the accumulation of eosinophilic granulocytes, the visualization of which can be enhanced by immunohistochemical staining techniques. Epicutaneous testing and the lymphocyte transformation test are not suitable for providing evidence of a local allergic reaction to the implanted knee prosthesis.

The latter discussion illustrates why the biopsy of periprosthetic tissue has become an essential diagnostic tool in our clinic when a periprosthetic infection, an allergic reaction, or an inflammatory response to implant debris has to be verified in cases of painful knee prostheses. Tissue can also be biopsied in cases of loosened prostheses although, because revision surgery will be carried out anyway, arthroscopy is not necessary. Arthroscopy of the knee can be useful when the prosthesis is not loosened and iatrogenic damage to the prosthesis surface is to be avoided. It can also be useful for specifying an impingement syndrome (patella clunk syndrome), and to treat impingement problems or joint mobility restrictions caused by ingrowth of soft tissue.

Conclusions

The techniques discussed in this chapter have been designed to identify the causes of pain associated with a knee prosthesis. It is important to note that a painful knee prosthesis should never be operated upon without first discovering the cause of the pain, and especially not undergo revision surgery. Mont, et al. [47] only achieved 41% good and excellent results after revision of 27 prostheses in patients with unexplained pain. Ultimately, psychosomatic causes of the pain also have to be excluded in such cases.

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