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ORIGINAL PAPER

Percutaneous interface biopsy in dry-aspiration cases of chronic periprosthetic joint infections: A technique for preoperative isolation of the infecting organism

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Abstract
Purpose Preoperative identification of the infecting micro-organism is of paramount importance in the treatment protocol for chronic periprosthetic joint infections, as it enables selection of the most appropriate antibiotic treatment. Preoperative joint aspiration, the most commonly used sampling technique, has proven to have a broad range of sensitivity values and the frequency of dry aspirations has not been well assessed. In such dry-tap cases a biopsy sample could be an option. The purpose of this study was to assess the diagnostic accuracy of percutaneous interface biopsy (PIB) in isolating the infecting organism in cases of chronic Periprosthetic Joint Infection (PJI) and dry-tap event. The basic technique is to harvest and culture a sample from the periprosthetic interface membrane by a percutaneous technique in the preoperative period.
Methods A retrospective study was done involving 24 consecutive patients suspected of PJI and where no fluid was obtained from the joint. Culture results from a percutaneous interface biopsy (PIB) were compared with intraoperative tissue cultures at the time of revision surgery. In all cases, a two-stage replacement was done.
Results The sensitivity was 88.2%; specificity was 100%. Positive predictive value was 100%, while negative predictive value was 77.9%. Accuracy was 91.6%. No technique-related complication was observed.
Conclusion We conclude that PIB is a useful test for preoperative isolation of the infecting organism and could play a role in cases with dry-tap joint aspirations.

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Introduction

Prosthetic joint infection (PJI) can occur in 1–2% of patients receiving prosthetic joint arthroplasty [1–3] and can be a diagnostic challenge, especially in chronic cases [2, 4]. Bacteriological diagnosis is of paramount importance in any treatment protocol for PJI; reliable information on the causative micro-organism and its sensitivities is essential to selection of the appropriate antimicrobial therapy [5]. This can be difficult to accomplish in cases of low-grade chronic infection, due to factors such as a paucity of organisms in the joint fluid, highly fastidious growth, the biofilm nature of PJI, and the impact of any earlier antibiotic therapy. Sampling factors such as time delay, anaerobic environment or improper laboratory practice may also play a part [1, 2, 5–9].

Currently, the most-used technique for reaching a bacteriological diagnosis is evaluation of fluid aspirated from the joint [6, 7]. This technique carries some limitations. First, studies of preoperative joint aspiration show a wide variation in sensitivity values, ranging between 0.11 and 1.00 [6–8]. Low sensitivity values for fluid aspirates in chronic PJI are partly attributable to the fact that most micro-organisms in such infections grow in

biofilms, attached to the implant surface (sessile bacteria). Only a small percentage are free-floating (planktonic) bacteria in the surrounding tissue, released from the sessile population [9].

Another concern is the percentage of dry-aspiration cases, where no sample can be obtained for culture. To manage dry-tap cases, we have developed a technique of percutaneous interface biopsy (PIB). The rationale for the technique is based on the hypothesis that a tissue sample harvested directly from the periprosthetic interface membrane could supplement results obtained through joint fluid aspiration, due to the presence of a higher number of planktonic cells.

This study's objective was assessment of the diagnostic accuracy of PIB in identifying the infecting organism in cases of chronic periprosthetic joint infection.

Material and methods

A retrospective analysis was performed on 24 consecutive patients scheduled for two-stage revision, each of whom had undergone preoperative PIB, due to suspicion of chronic PJI (onset of infection four weeks after the index procedure) and dry joint aspiration; both knee cases and hip cases were included. All study patients complained of pain at the arthroplasty site. Infection of the prosthesis was considered highly probable, based on the following preoperative parameters [8]:

- History of wound infection or postoperative fever
- Clinical presentation of infection (fever, fistula)
- Haematological screening test: ESR > 30 mm/h and CRP > 10 mg/d
- Positive indium 11-labelled leukocyte scintigraphy

When at least one of these parameters was observed, and in cases where no fluid was obtained from the joint by aspiration, a PIB was done.

PIB technique protocol

The patient is taken off any antibiotic treatment for a minimum of 14 days [7, 8]. The patient is admitted to the orthopaedic unit. Informed consent is obtained in all cases. The procedure is performed in the operating theatre under spinal anaesthesia. The C-arm is used to confirm the correct entry point, and to guide a bone trephine of 4-mm diameter (Fig. 1). The target is the bone–prosthesis interface, or the bone–cement interface in cemented cases. Once the C-arm (Fig. 2) verifies correct placement, the trephine is introduced to a depth of about 10–15 mm, and the sample is collected. We harvest at least two sample cylinders (Fig. 3) from each interface. Samples are transferred to the microbiology laboratory in dry, sterile plastic containers. They are inoculated onto blood agar

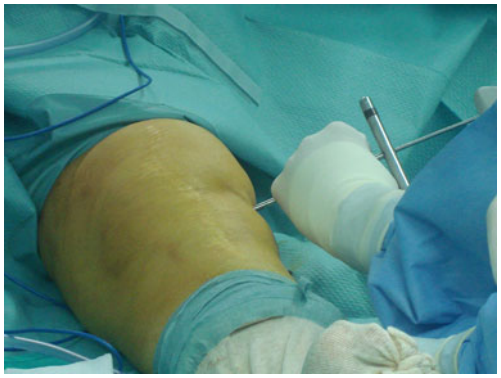

Fig. 1 The C-arm is used to confirm correct positioning of the entry point and to guide a bone trephine of 4-mm diameter

containing 5% sterile bovine blood, chocolate agar, and MacConkey agar plates (Biomérieux Inc., France). All are incubated at 37°C. Blood and chocolate agar cultures are incubated in a 5% CO_2 atmosphere for up to ten days, with daily reading of the plates. The MacConkey agar plates are incubated in air only, overnight. Additionally, brain-heart infusion broth (Oxoid) is inoculated and incubated at 37°C in air.

Finally, samples are also inoculated onto an enrichment broth for anaerobic cultures.

Media are checked daily for bacterial growth. Any growth on liquid media is sub-cultured onto a blood agar plate. Cultures are declared negative if no growth is visible at 14 days.

Micro-organisms are identified by standard microbiological procedures (API Systems, or VITEK from Biomerieux Inc., France). Susceptibility testing is by disc diffusion and E-test, according to recommendations of the Clinical and Laboratory Standards Institute.

The patient is discharged home the same day as the procedure.

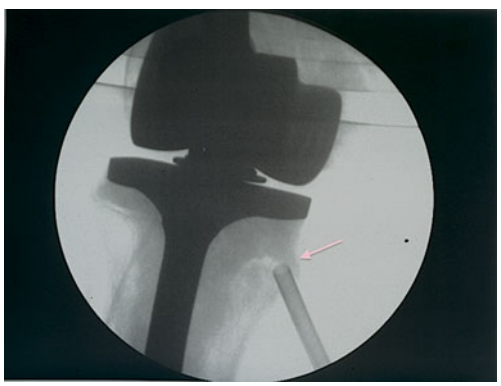

Fig. 2 The target is the bone–prosthesis interface or the bone–cement interface

Fig. 3 At least two sample-cylinders from each interface are harvested to culture

According our protocol, if there is a high suspicion of infection, a two-stage revision is performed, with at least six intraoperative samples obtained for culture and histological evaluation.

For analysis of the intraoperative results, the threshold was as follows. If 50% of the samples grew the same organism, this was regarded as a positive result for infection of the prosthesis. If growth was present in less than 50% of the samples, the decision regarding result was based on the clinical picture and the opinion of an expert on infectious diseases.

The final diagnosis of infection was made when the patient met at least one of the following criteria [8, 10–13]:

- Presence of a chronic sinus
- Presence of purulent fluid within the joint, observed during the surgery
- Positive culture from intraoperative samples
- Positive intraoperative histological evaluation

This article examines diagnostic accuracy for causal bacteria using sample cultures obtained through PIB in the preoperative period in patients with risk of infection and dry joint aspiration. We compared the results of preoperative PIB with those of cultures from intraoperative tissue biopsies. On the basis of this comparison, sensitivity, specificity, positive and negative predictive values and accuracy were calculated. We also observed for any technique-related complications.

Results

Between January 2007 and December 2010, 24 PIBs were done on 24 consecutive patients (ten hips and 14 knees) who subsequently underwent two-stage revision surgery due to suspicion of PJI and a dry-tap event. Retrospective analysis was completed on the 24 patients (13 women and 11 men) whose mean age was 70 years (range, 63–88 years old). Nineteen of the cases were primary operations while five were revision arthroplasties.

Seventeen patients (71%) were positive for infection in intraoperative tissue cultures. Similar numbers of samples were taken from infected and non-infected patients (average of 5.6 samples).

In patients with septic prosthesis, coagulase-negative *Staphylococcus* (CNS) was the most frequent microorganism found in surgical cultures (42%). The types of micro-organisms involved in infected prostheses are explained in detail in Table 1.

Finally, because no growth was observed in their intraoperative tissue cultures, and because histological analysis was negative for infection, seven patients (29%) were considered non-infected.

Preoperative PIB correctly identified infection in 15 of 17 patients (true positive).

In two of the 17 infected patients, PIB failed to show any growth (false negative). No false positives were encountered, that is, no case of positive preoperative biopsy, but negative intraoperative tissue sample. The remaining seven cases were considered true negatives for infection. Finally, there were no cases in which the microorganisms identified in preoperative biopsy were different from those found in the intraoperative tissue samples.

The number of samples collected using the PIB procedure was 3.7 per patient, on average.

The sensitivity of preoperative percutaneous interface biopsy (PIB) was 88.24% (95% CI, 62.2–97.9%). The specificity of the test was 100% (95% CI, 56–98.6%). The positive predictive value was 100% (95% CI, 74.6–99.3%). The negative predictive value was 77.8% (95% CI, 40.1–96%). The accuracy of a test is defined as the ratio of all correct results, both positive and negative, to the total number of results. The accuracy of PIB was 92% (Table 2).

With regard to complications, all patients were discharged home the same day as the procedure; no technique-related complications, such as bleeding, haematoma or biopsy tract infection, were recorded in any of the cases.

Table 1 Type and frequency distribution of infecting organism

Organisms	True positives (N=15)	False negatives (N=2)	False positives (N=0)
Staphylococcus (CNS)	5	2	0
S. aureus	4	0	0
E. coli	2	0	0
P. acnes	1	0	0
Corynebacterium	1	0	0
S. viridans	1	0	0
Peptostreptococcus	1	0	0

Table 2 Results cross tab

True result (intraop samples)			
PIB results	Infection	Non-infected	Total
Positive	15 (true positive)	0 (false positive)	15
Negative	2 (false negative)	7 (true negative)	9
Total	17 (infected)	7 (non-infected)	24

Sensitivity 88.2%, specificity 100%, accuracy 92%

Discussion

We describe a novel technique, which has demonstrated a high accuracy in preoperative isolation of the infecting microorganism, in cases of chronic PJI and dry articular aspiration.

To preoperatively identify the causative microorganism and determine its antibiotic profile, we must obtain and cultivate a sample from the pathological area; this is where problems can occur. The options are either a joint fluid sample obtained by aspiration, or a periprosthetic tissue sample collected through one biopsy technique or another.

Recently, new techniques have been developed to improve bacterial identification rates in chronic-PJI cases. One technique currently in vogue is ultrasound treatment of the removed implants, and culture of the resultant fluid [14]. Molecular methods (those based on PCR detection) have also been developed [7, 15]. Sonication seems to exhibit improved sensitivity in detecting infection, when compared with conventional tissue-sample cultures. Nevertheless some unanswered questions remain. For example, what is the role of the different bacteria found in the sonicated fluid, and what is the risk of contamination during manipulation of the explanted components? In any case, a very important drawback of sonication is that the results are postoperative —the prosthetic implants must be removed before sonication.

On another front, there are now molecular tests available, based on detection of the genetic trace of the bacteria involved. Such tests seem very promising, but they are also the subject of ongoing criticism. One significant challenge for any new molecular test will be to distinguish clinically important infections from mere traces of necrotic bacteria or contaminants [7]. An important drawback to the technique is the lack of identification of the antimicrobial susceptibility profile.

The most used sample, currently aspirated joint fluid, has a poor record of accuracy in isolating the infecting organism. In the literature, the sensitivity of preoperative aspirate cultures varies from 12% to 100% [6–8, 10–12, 16]. Because of this wide divergence, the technique's value in clinical practice remains unclear.

In a recent bibliographic search performed by Meermans et al. [17], spanning the period from 1988 to 2010, 29 different studies were found regarding joint aspiration sensitivity in PJI, for both hip and knee cases. A summary of these studies showed a joint aspiration sensitivity of 71% on average. In our preliminary study using PIB, we found a sensitivity well above this range (88.2%). We observed only two false negative cases. In both, coagulase-negative *Staphylococcus* grew in the intraoperative sample cultures, and histological examination was positive for infection. Our false negative cannot be attributed to the culture technique, since we used enrichment culture media, sub-cultured growth in liquid media, and followed a prolonged (14 day) culture protocol [16].

Another problem with joint aspiration is the frequency of dry aspiration. This is an important factor with low-grade infection, where a paucity of clinical signs is the norm. There is no accurate information in the modern bibliography concerning the rate of dry tap in joint aspirations. In a recent study investigating the utility of hip aspiration, dry tap was present in 32% of THAs [8].

Some investigators have used saline lavage as a means of retrieving adequate volume for culture studies. Ali et al. [8] reported a sensitivity of 83% after injection of 10 ml of saline into the joint, in cases where no fluid could be aspirated. The saline solution was reaspirated and inoculated in blood culture bottles. This is actually a question that is not well resolved at this time. We do not advocate the use of saline lavage, due to concern over the risk of infection, and of false positives.

The use of biopsy techniques in the chronic-PJI scenario has not often been reported in the modern literature. Some authors have used synovial biopsy, obtained by various techniques, in an attempt to improve outcomes, but with inconsistent results [17–19].

In a study of 145 TKAs scheduled for revision surgery due to component loosening, Fink et al. [18] showed that preoperative synovial biopsy, obtained using arthroscopic biopsy forceps, was superior to joint aspiration for diagnosis of periprosthetic infection. Aspiration had a sensitivity of 72.5% and specificity of 95.2%. Synovial biopsy had a sensitivity of 100% and a specificity of 98.1%. Moreover, Williams et al. [19] did not observe benefits from tissue biopsy, and did not advocate its use, due to the more invasive nature of the procedure. Our data show an accuracy level (92%) which is at least as good as the values achieved in such papers.

There is some support in the literature for the idea that the best sample to culture is the film of connective tissue, which can develop between bone and prosthesis, known as the "periprosthetic membrane" [9, 20–22]. Four histological types of periprosthetic membrane have been defined [21]. The specific septic membrane is the type II membrane; a

mixed type III membrane is also seen in infected cases. The correlation with detection of pathogens by bacterial culture methods seems to be very close for histological type II and III membranes.

The weaknesses of the study are its retrospective design and its small population, which made it difficult to find statistically significant results.

Another problem is that we have considered the results of intraoperative cultures as the standard against which the results of the test were to be evaluated. We are aware that there is a currently agreed gold standard for diagnosis of PJI [13]. We have used intraoperative tissue samples as our gold standard, even though in some series the rate of false negative cultures has been as high as 10% [23]. In truth, there is currently no certain alternative to intraoperative sampling, and there will not be, as long as the roles of other techniques such as sonication and molecular techniques remain undefined, and until prolonged culture protocols and enriched media have decreased the rate of culture-negative PJI [16].

In the course of this study we did not encounter any technique-related complications, but cannot ignore the possibility of unrecognised iatrogenic damage. We do recognise this possibility, though we believe it is not a significant issue. In our practice, we elect to use the technique only in symptomatic arthroplasties, where revision surgery is already planned. Thus, scraping the surface of the prosthesis or damaging the cement mantle is not of major importance. In no case has post-biopsy onset of infection been observed.

Because of the strong sensitivity (88%) and specificity (100%) values, and with a global accuracy of 92%, we believe that, based on the data obtained, PIB certainly has a place in the diagnostic armamentarium for PJI. This role should, for the present, be limited in cases of dry aspiration, where the value of saline lavage and re-aspiration has not been well defined, and in cases where there is high suspicion of infection despite negative joint fluid cultures.

Because of the more invasive nature of the procedure, and the higher costs it involves, a comparative study would be necessary to evaluate its use within the PJI diagnostic armamentarium.

Conclusion

Percutaneous interface biopsy (PIB) is a useful procedure for preoperative isolation and identification of the infecting bacteria, and determining its antimicrobial profile. Sensitivity, specificity and accuracy values connected with the procedure are high, and the complication rate is low. Thus, we can conclude that the biopsy technique could play a role in cases suspected of PJI despite negative joint aspiration culture, and in cases where no fluid can be aspirated from the joint.

Conflict of interest No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. All the authors have participated in this paper. We confirm that it has not been sent to any other journal. The current study achieved the IRB approval in our centre.

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