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Technical note

Histological analysis of surgical samples and a proposed scoring system for infections in intervertebral discs

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ABSTRACT

Back pain remains one the most prevalent types of pain and disability worldwide. Infection is estimated to be the underlying cause in approximately 0.01% of patients. Despite recent evidence demonstrating prominent infection rates, a standardised algorithm for diagnosis of disc infection is lacking. Histopathological evaluation can aid in confirming inflammatory changes and also in identifying degenerative changes. Hence, standardising practice through a clear scoring system with regards to inflammation and degeneration may have some utility in the clinical setting. To our knowledge no such systems exist specifically for intervertebral disc infection. A literature review of current methods of scoring inflammation and degeneration in spine surgery and orthopaedic surgery was performed. Based on the current evidence, a scoring system for disc inflammatory and degenerative changes was proposed. We propose four domains for consideration: (1) granulation tissue, (2) dense fibrosis, (3) chronic inflammatory cells, and (4) neutrophil count. The non-standardised nature of diagnosing infections and degeneration in the spinal surgery literature means that this scoring system is currently of particular value. Based on a literature review, our proposed method for diagnosis incorporates a combination of histopathological criteria expected to increase diagnostic sensitivity in the setting of disc infection. Overall, scoring can be applied to surgically obtained material and integrated directly into routine pathological practice.

1. Introduction

Back pain remains one the most prevalent types of pain and disability worldwide, representing almost 4% of the total disability-adjusted life years and ranked sixth on the World Health Organization global disability-adjusted life year rankings [1]. Estimated to affect up to two-thirds of the population aged between 50–69 alone, 80% of people experience back pain at some point in their lives [2,3]. Despite increases in diagnostic imaging, pain management and surgical intervention the overall burden of disease remains steady [4].

Infection is estimated to be the underlying cause in approximately 0.01% of patients, with the number expected to rise in the setting of an ageing Western population and chronic disease [5,6]. In addition, as speculated by Albert et al. in 2013, another link between chronic low back pain secondary to disc infection may exist [7]. Albert et al., in a 2013 randomised controlled study of antibiotic treatment for patients with disc herniation demonstrating Modic type 1 changes on MRI, illustrated better results across all measured outcomes at both 100 days and 1 year follow-up in comparison to a placebo group. This has led to controversy regarding disc infection rates. Separate systematic reviews have estimated the pooled rate of positive surgical disc specimen infection rates to be at 34% and 36.2% respectively (n = 11 and nine studies, respectively) [8,9]. In 2015 Ganko et al. indicated that the proportion of infection in patients with disc pathology was higher than those without (37.4% *versus* 5.9%, odds ratio 6.1). However, the most commonly identified organism, *Propionibacterium acnes*, is a known commensal organism – questioning its role in the underlying pathological mechanism of disease [9].

Despite recent evidence demonstrating prominent infection rates, a standardised algorithm for diagnosis of disc infection is lacking. Histopathological evaluation can aid in confirming inflammatory changes and also in identifying degenerative changes. Histopathological microscopic analysis of surgically obtained specimens has been demonstrated to be cost beneficial in patients with

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a preoperative clinical diagnosis, with the estimated cost of laboratory testing to be at approximately US $24.75 [10]. Despite this, it is not routinely performed, with current diagnostic modalities and definitions varying amongst laboratories. Techniques across facilities differ in levels of sensitivity and specificity, with no definitive "criteria" for diagnosis of disc infection currently established throughout the literature, to our knowledge. Aseptic surgical sampling from the spine and paraspinal tissue has been demonstrated in multiple studies [11–14].

Hence, standardising practice through a clear scoring system with regards to inflammation and degeneration may have some utility in the clinical setting. To our knowledge no such systems exist specifically for intervertebral disc infection. Current recommendations by the American Academy of Orthopaedic Surgeons (AAOS) in regards to periprosthetic joint infections recommend a combination of inflammatory markers, frozen specimen, and microbiological testing, amongst other investigations (including radiological scanning, polymerase chain reaction) [15,16], however the generalizability of these recommendations in the setting of intervertebral discs has not been reported on previously. The present report reviews the current evidence for histopathological analysis of infections, and a new scoring system for diagnosis of disc infections and degeneration is proposed.

2. Criteria for infection

With current debate surrounding the presence of commensal organisms within disc specimens, the major caveat of diagnosis is that positive growth alone may not demonstrate clinically important pathology [9]. This further adds to the challenge of defining what criteria, both histopathological and clinical, should be utilised and what their limits should be.

As demonstrated by Carricajo et al. in 2007, intraoperative surgical specimens obtained from multiple sites including paraspinal muscles, the ligamentum flavum and from the nucleus and annulus of the intervertebral disc are possible, however specimens may be contaminated during the harvesting process, transportation or laboratory treatment stages. In addition, there are currently no spine-focused studies linking intraoperative sample findings and clinical manifestations, to our knowledge. While literature is available in the setting of joint surgery, discrepancy remains around similar issues. Reported differences also exist between sample processing, namely positive culture diagnosis and microscopic frozen section findings.

Pandey et al. compared the results of microbiological, histopathological and clinical techniques of diagnosis and reported correlations between the findings. In a cohort of 91 patients clinically suspected of periprosthetic joint infection, 79 demonstrated positive cultures and inflammatory activity. Two of 91 cases were positive on culture but not on histopathological testing, while 10 demonstrated the converse. The reported sensitivity of microbiological culture alone, using clinical diagnosis as a comparison, was 89%. Overall the combined method yielded sensitivity of 87.8% [17]. In the setting of disc infection samples, the major concern of culture remains aseptic sampling and contamination [9,18].

Recent studies indicate that the quantification of inflammatory cells and markers appears to be of clinical relevance in the determination of an underlying infection across tissues. In 1973 Charosky et al. described frozen section tissue examinations obtained from 20 patients, 10 with intraoperative positive cultures, and 10 with negative cultures. From the patients with positive cultures, five had 2+ scores for acute inflammation and five had 2+ scores for chronic inflammation, proposed indicators of infection. More recent studies have analysed a variety of inflammatory components as an alternative for infection diagnosis, including neutrophils, plasma cells, lymphocytes and inflammatory markers (including interleukins, C-reactive protein [CRP] and erythrocyte sedimentation rate [ESR]). Similarly, the presence of local tissue destruction and surrounding fibrosis has also been demonstrated to be of some benefit [19]. Table 1 summarises the definitions and results of various histopathological studies evaluating intraoperative infection rates. Evidently, there is a lack of agreement between authors regarding the cut-off for definitive diagnosis.

Using frozen section tissue examination, to our knowledge Fehrin and McAlister have published the only study characterising infection based on the holistic spectrum of inflammatory cells as opposed to neutrophils alone. They reported that of 107 patients who underwent revision joint arthroplasty, histological frozen section evidence yielded a sensitivity of only 18.2% in detecting occult periprosthesis infection, significantly lower than the reported figures of other studies.

Using neutrophils alone, a prospective study (n = 175) by Lonner et al. in 1996 analysed frozen section specimens, defining infection as >10 neutrophils per high power field, yielding a sensitivity of 84% and a specificity of 99%. However, the external validity of this finding may be questioned, as seven out of 19 positive cultures identified were contaminated [20]. In a separate project, perioperative frozen sections retrieved by Athanasou et al. in 104 patients undergoing hip arthroplasty demonstrated a sensitivity of 90% and a specificity of 96% [19]. To validate these figures a recent meta-analysis (pooled n = 3269) by Tsaras et al. demonstrated the pooled diagnostic odds ratio of frozen section sampling using neutrophil cell counts >5 per high power field to be 54.7 (95% confidence interval 31.2–95.7). This value increased (odds ratio

Table 1
Review of the literature for frozen section sensitivity and specificity for diagnosis of periprosthetic joint infection

Study	Inclusion criteria for diagnosis of infection	Exclusion criteria	Sensitivity	Specificity
Mirra et al. [26]	>5 stromal PMN in separate HPF (OM × 500)	Surface fibrin, inflammatory exudates	NA	NA
Abdul-Karim et al. [27]	>5 neutrophils in separate HPF (OM × 400)	Surface fibrin, inflammatory exudates	NA	NA
Feldman et al. [28]	>5 PMN leukocytes per high power field in ⩾5 separate HPF	If less than 5 HPF	100%	100%
Charosky et al. [29]	Acute or marked chronic inflammation, no quantification	NA	NA	NA
Fehring and McAlister [30]	Evidence of acute inflammation, no quantification	Three patients with "moderate chronic inflammation"	18.2%	89.5%
Lonner et al. [20]	⩾10 PML per HPF in ⩾5 separate HPF	If less than 5 HPF	84%	89%
Athanasou et al. [19]	>5 PML, lymphocytes or plasma cells per HPF in ⩾10 fields	If less than 10 HPF	90%	96%
Pandey et al. [17]	Average of 1 "inflammatory" cell per HPF in ⩾10 HPF	If less than 10 HPF	97.8%	99.0%
Spangehl et al. [31]	⩾5 stromal neutrophils in any HPF	NA	80%	94%
Banit et al. [32]	⩾10 PML per HPF in ⩾5 HPF	If less than 5 HPF	67%	93%
Pandey et al. [33]	Average of ⩾1 PMN/HPF in ⩾10 HPF	NA	100%	97%
	Average of ⩾5 PMN/HPF in ⩾10 HPF		72%	100%
Musso et al. [34]	>5 PML per HPF in at least five separate microscopic fields	NA	50%	94.9%

HPF = high power fields, NA = not available, OM = original magnification, PML = polymorphonuclear leukocytes, PMN = neutrophils.