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REVIEW

Diagnosis and Treatment of Spondylodiscitis: Current Concepts

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ABSTRACT

Spondylodiscitis is infection of intervertebral discs and adjacent vertebral bodies with a variety of causes ranging from haematogenous spread or direct inoculation from interventional and surgical procedures. It is a rare disease with 3% mortality, and most clinicians have low exposure and find the management challenging. Our review aims to provide an evidence-based approach to inform readers of current concepts in the care of spinal infection. The commonest pathogen is *staphylococcus aureus*. Radiographs, blood cultures and biopsies yield high false-negative rates, leading to delays in diagnosis, and treatment challenges. Therefore, a high level of awareness is required to avoid mismanagement. We recommend a thorough checklist of investigations from the outset in order to avoid missed diagnosis of spondylodiscitis and associated conditions, and improve microbial yield. We also review available evidence on non-operative and surgical options, including emergency surgical intervention.

Key words: Spondylodiscitis; Spinal Epidural Abscess; Full Endoscopic Discectomy; Post-discectomy infections

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INTRODUCTION

Spondylodiscitis is defined as a primary infection in the vertebral body with secondary infection to neighbouring vertebral bodies. However, in some circumstances the osteomyelitis of the vertebral body pre-exists the discitis. It has multiple causes, but is most commonly due to *staphylococcus aureus*. Other important causes not to miss are tuberculosis (TB), immunodeficiency, and sources of infective emboli (e.g. infective endocarditis)[1].

It affects around 1 in 40,000-250,000 people depending on geographic region, and is reportedly on the rise, particularly in developing countries[2]. In the United Kingdom it affects around 1 in 50,000 individuals, and typically is associated with higher incidence and mortality in co-morbid patients[3].

Presentation can be late or missed as diagnosis can be challenging due to the few differentiating clinical features from mechanical or degenerative back pain syndromes. Furthermore, laboratory blood test, simple radiographic studies, and blood cultures can be misleading as they yield false-negatives[1-3].

Treatment is typically conservative with antibiotics for uncomplicated cases, but sometimes surgery is required in the presence of neurological deficit or advanced destruction leading to deformity. Additional measures such as orthoses and physical therapy can be used to augment treatment programmes[1-3].

PATHOGENESIS

Infection can be introduced to the disc through direct inoculation (e.g. surgical discectomy, discography), haematogenous spread (e.g. systemic bacteraemia), or directly from neighbouring tissue (e.g. vertebral osteomyelitis)[1,4]. Even though the intervertebral disc has a poor blood supply, protecting it from every episode of bacteraemia; when pathogens do gain access, they will find an immune-privileged

site[5]. This means the intervertebral disc is one area in the body which infections can go undetected by the body's immune system for quite some time, and they do not develop an inflammatory response immediately.

Intervertebral discs are relatively avascular, their cells depend on the blood supply at the margins of the discs for their nutrients. The inner disc is supplied by capillaries that arise in the vertebral bodies, penetrate the endplates, and terminate at the bone-disc junction[6]. This is the route of haematogenous spread, which is second only to direct inoculation as the cause of spondylodiscitis.

Haematogenous spread is caused by septic emboli from a primary source, resulting in a bacteraemia. The most common causes for this are infective endocarditis, infected foreign material (e.g. implanted medical devices or accidental foreign bodies), urinary tract infections, intra-abdominal infections (e.g. gastroenteritis, cholecystitis), or dental infections (e.g. dental abscesses). It is important to consider infective sources, and to screen for them in the initial stages[1,3-9].

The most common cause is *staphylococcus aureus* (28-84%). Various organisms and their frequency are shown in Table 1[1,5-8]. Certain conditions like sickle cell give rise to rare pathogens, such as *salmonella*. Intravenous drug users have a high propensity to grow *pseudomonas*. The Elderly patients are more likely to grown *E.coli* secondary to urinary infections[4,9].

Largely, lumbar (58%) vertebrae are most affected follow by thoracic (30%), and rarely cervical (11%)[10]. This is thought to be because more of the disc is avascular due to its increasing size, and reduction in end capillary termination at the peripheries as previously described[6]. Children, however, have much more vascular intervertebral bodies, meaning discitis is much less common and can indicate underlying immunodeficiency. The vertebral body itself is very vascular, as is therefore thought to be more commonly involved by local spread from the disc. Whilst some argue the primary source is the vertebral body as that is the route of the blood supply, this does not equate to preceding osteomyelitis in all cases[11].

SPINAL TUBERCULOSIS

Tuberculosis of the spine (Pott's disease) is an important differential, particularly in countries where it is endemic and co-exists with HIV (Human Immunodeficiency Virus). Those with known AIDS (Acquired Immunodeficiency Syndrome) caused by HIV are over 20-times more likely to contract TB. Therefore, a high index of suspicion for TB should be held in these patients. These patients tend to have a much slower disease process and will often present much later in the process[12].

The classical appearance of "skip lesions" (multiple sites of infection, with normal levels in between), and "disc-sparing" are driven by its haematogenous spread. Through Baston's vertebral plexus, infective emboli dock onto the vascular vertebral body at various locations. In adults, discs are spared secondary to the poor availability of oxygen in the tissue which TB requires to grow. Destruction of the vertebral body leads to "plana vertebra" as TB affects its entirety. Therefore, multiple sites of infection with these features should trigger investigations for TB[11,12].

Standard blood culture analysis will miss this diagnosis, and prolonged cultures with Ziehl-Neelsen (ZN) staining for acid-fast bacilli will be required to detect *mycobacterium tuberculosis*. However, even this is only 77-85% sensitive, and a negative ZN stain should not exclude TB from the clinician's differential[13].

These patients should receive whole-spine imagine to look for additional leaions, screen for progressive deformity requiring surgical input and "cold abscesses" causing pus to track along fascial planes. A horse voice in a TB patient should trigger the clinician to look for retropharyngeal cold abscesses causing compression[12].

Table 1 Frequency of pathogens in spondylodiscitis[1,5-9].

Pathogen	Frequency	Associated clinical conditions
S. aureus	28-84%	Most common pathogen
Pseudomonas	10-48%	IV drug-users, immunocompromised, diabetic ulcers
Tuberculosis	9-46%	Endemic regions, HIV
Enterobacteriae (e.g. E.coli, Proteus, Klebsiella)	7-33%	Elderly, urinary infections
Coagulase negative staph (e.g. S.epidermidis)	5-16%	Post-operative, endocarditis
Streptococci (e.g. S.viridians)	5-20%	Intravenous drug users, endocarditis, dental work
Salmonella	Rare	Sickle cell
Anaerobes (e.g. P.acnes)	4%	Post-operative or intra-abdominal
Polymicrobial	<10%	Post-operative
Kingella kingae	Rare	Paediatric
Fungal(e.g. candida, aspergillus)	Rare	Immunocompromised, neutropenia
Parasitic (e.g. Echinococcus)	Rare	Endemic areas

DIAGNOSIS

Clinical presentation

Virtually all patients will present with back pain (96-100%) but only 22% will present with neurological deficits due to cord compression, epidural abscesses or phlegmon causing nerve root irritation[3,10]. Such neurological findings due to compression are regarded as a surgical emergency, and must be decompressed urgently to avoid permanent damage and disability. Other factors such as pyrexia (temperature >35.5°C) are present around 70% of the time, and a significant proportion (35%) will have previous evidence of injections or surgery to the spine. Many however, will present later on in the process after previous labelling as mechanical back pain[3].

Extra-spinal extension (infection which extends beyond the intervertebral disc, either as inflammatory masses or abscess formation in surrounding tissues) is common (70%) and may lead to neurological compromise. Therefore, a thorough neurological examination is required to illicit evidence of cord compression (upper motor neurone signs: unsteady gait, hyperreflexia, hypertonicity, and highest normal sensorimotor level) or nerve root irritation (lower motor neurone signs: radiculopathy with/without sensorimotor disturbance). Change in bowel or bladder function could be upper or lower motor neurone. Neurology should be checked regularly for emerging signs.

Other less specific features such as weight-loss, presence of risk factors (elderly, immunocompromised, cardiac disease or symptoms, frequent infections, recent surgery or dental work) may be present, but are more likely to act as an adjunct in determining the source of infection. Spondylodiscitis is rarely the primary diagnosis unless post-operative, and care must be taken to identify the source[3,8,9]. Therefore, a full "systems review" and full-body examination is required for telling clinical signs.

Bloods

It is perhaps reasonable to offer each new presentation of non-traumatic back pain a blood test. C-reactive protein (CRP) is highly

sensitive (94%), closely followed by white-cell count (74%). However, the most sensitive test is erythrocyte sedimentation rate (ESR), and is reportedly present in *all* cases[3]. Therefore, a blood panel indicative of infection with back pain, in the absence of another cause, should prompt the investigation of discitis.

At the same time blood cultures should be obtained prior to any empirical antibiotic commencement. This is because after administration of antimicrobials, the chances of identifying a pathogen in culture significantly drops. This can have huge implications for the patient's long-term treatment plan. Sadly, blood cultures yield poor grown in spondylodiscitis (31-68%), but can be helpful in the diagnostic process for infective endocarditis (Duke's Criteria)[14,15].

Imaging

The gold standard for the investigation of spondylodiscitis is a Magnetic Resonance Imaging (MRI) scan of the whole spine with gadolinium contrast. This will ensure multiple lesions will be identified, and paraspinal abscesses will be detected and differentiated from phlegmon with a sensitivity (93-98%) and good specificity. However, the risk of gadolinium contrast nephropathy is reportedly 0.2-2% (increasing with pre-existing renal disease), and we recognise clinicians may wish to reserve contrast MRIs to those with neurological deficits where identification of abscesses is more clinically important[16,17].

Plain radiographs and Computer Tomography (CT) scans are rarely helpful unless advanced osteomyelitis has caused bony destruction. These are more helpful in osseous deformity and post-operative monitoring. They should not be relied on for diagnosis[18].

Nuclear medicine has a role in identification of sources of infection in scenarios of sepsis of unknown origin (SUO). SPECT CT is by far the most sensitive, but is also expensive and uses large doses of radiation compared to a standard CT. These scans are often only obtained in large centres, and are less available acutely. Whist they will identify spondylodiscitis as the source (or one of), they will not assess the soft tissue envelope in the same detail as an MRI scan[19].

Biopsy

CT-guided biopsy for tissue microbiology is controversial. The reported yields are variable depending on the technique, and is often significantly impacted by the lead time from presentation until the biopsy can occur. It may take several days until the procedure can be undertaken. Usually during this period empirical antibiotics have been given. This coupled with risk of neurological injury often dissuades clinicians from opting for a biopsy[20-22].

Disc material itself yields higher microbiological growth than the adjacent vertebral body, but is more difficult and riskier. Open biopsy yields better growth (74%) than percutaneous needle biopsies (33%). However, in the absence of need for surgical intervention (e.g. decompression of neurological compromise), an open biopsy may add unnecessary surgical morbidity and mortality. The use of rapid diagnostic techniques in culture-negative infections, such as Polymerase Chain Reaction (PCR) for bacteria deoxyribonucleic acid (DNA) or Ribonucleic acid (RNA), is becoming increasingly utilised and important, and should be used if available[20-22].

We recommend that if antibiotics have been withheld, and urgent percutaneous needle biopsy is available, one should endeavour to obtain a sample with the widest gauge needle possible by a suitably qualified radiologist or spinal surgeon under strict aseptic conditions to avoid contaminants. In culture-negative cases, we recommend PCR testing or similar techniques to identify an organism.

Table 2 Comparison of advantages and disadvantages of lumbar interbody fusion techniques in degenerative spinal conditions.

Approach	Advantages	Disadvantages
Anterior (ALIF)	Access to vertebral body	Risk of major vascular injury
	Correcting lumbar lordosis	Implant migration
Posterior (PLIF)	Decompression of cord	No access to anterior
	Posterior instrumentation	More blood loss
Transpedicular (TLIF)	Better pain and functional scores	No access anterior
		Incomplete decompression
Lateral (LLIF)	Access to anterior structures	Can only access L1-L4
	Less invasive than ALIF	Risk of lumbar plexus injury

Other investigations

Work up of the patient should include adjuncts to detect associated conditions and sources of infection, as previously described. One crucial investigation in an echocardiogram (ECHO). A transoesophageal ECHO (TOE) is more accurate in diagnosis infective endocarditis than a transthoracic ECHO (TTE), however is quite uncomfortable for the patient. One study found around 13% of patients with spondylodiscitis had infective endocarditis, and streptococcus or pre-existing valvular disease was a strong predictive factor[23].

CT Thorax, abdomen and pelvis (CT TAP) and nuclear medicine (e.g. white-cell labelled scans) can be effective at identifying primary sources of infection, but carry large radiation doses and expenses. The clinician should always start out with a thorough full-body examination with basic bedside investigations (blood tests, urine culture, electrocardiogram and chest radiographs) before jumping to these studies[17-19].

Treatment

The vast majority of spondylodiscitis cases can be treated non-operatively (90%) with a combination of long-term antibiotics, percutaneous drainage of epidural and paraspinal (e.g. psoas) abscesses. Physical therapy and orthotic devices are often used to maintain skeletal integrity and mobility. However, uncertainty over effectiveness and duration of treatment exists. There are some key indications for urgent surgical intervention, as discussed below[1,4,18,29]. Spondylodiscitis has a mortality of around 2-11% and this increases significantly in the presence of a Spinal Epidural Abscess (SEA), a delayed diagnosis or a delay in treatment[18].

Antimicrobials

For bacterial infections, antibiotics will be required regardless of whether surgery is needed or not. Empirical antibiotics are often required initially, as cultures with sensitivities are not always available, and will take between 24 hours and 5 days to obtain a report. These are usually geographically determined based on the local resistance patterns of the common causative pathogens. In the UK, with *S.aureus* being the most common organism, a broad-spectrum agent such as flucloxacillin is typically first-line[1,4,24].

However, with antibiotic resistance on the rise, it is crucial to identify an antibiotic regime that targets the pathogen without risking side-effects and mutation of resistant organisms. But this isn't always so straight-forward. Blood and tissue biopsies are prone to contaminants. It is estimated that 94% of *S.epidermidis* blood cultures are contaminants; which is concerning considering it is responsible for 5-16% of spondylodiscitis cases[4,9,24].

Antibiotics previously were given for extended periods of time, and controversy remains high. However, the only randomised-controlled study on this topic supports a 6-week course of antibiotics is not

inferior to 12-week courses. However, good evidence exists that a course short of 6-weeks is associated with increased recurrence[25].

There is no specific good data on intravenous versus oral therapy for spondylodiscitis, but in general there is new evidence that many orthopaedic infections can be managed with oral antibiotics providing there is good sensitivity and bioavailability[26]. This is certainly an area which warrants further prospective study in the form of a randomised-controlled trial (RCT).

Orthotics

Many centres historically used Thoraco-Lumbar-Sacral Orthoses (TLSO) to prevent progressive vertebral body collapse and deformity (kyphosis) from the destructive osteomyelitis process. However, there is no good evidence to support the use of TLSO bracing in spondylodiscitis, and they are well-proven to impact patient quality-of-life[26, 27]. We do not recommend the use of TLSO bracing.

Percutaneous screw and rod fixation offers no additional protection against deformity, but is much better tolerated and leads to better pain and functional scores than TLSO bracing[27]. This needs further study before its use in spondylodiscitis can be determined.

CT-GUIDED DRAINAGE VS. SURGERY

Whilst CT-guided biopsy is well recognised in the investigation process, very little evidence exists about using CT-guided drainage as an alternative to surgery. A small number of cases have been identified in the literature of successful CT-guided drainage with complete resolution of infection following non-operative treatment. However, no large comparative studies have ever been undertaken to ascertain the success rate of percutaneous versus surgical decompression in these patients[28]. We advise caution in using CT-guided drainage in cases of epidural collections causing neurological compromise, and is perhaps best reserved for those unable to withstand spinal surgery.

In dealing with paravertebral collections (e.g. psoas abscess) which is commonly caused by discitis, interventional radiological drainage is very successful and produces comparable results to open surgery[29].

SURGICAL INDICATIONS

Surgery has a role in managing spondylodiscitis, despite most (90%) being managed non-operatively. Indications include: (1) Neurological compromise (cord compression, progressive radicular pain, sensorimotor disturbance); (2) Severe ongoing pain (a sign of destruction and progressive instability); (3) Deformity (typically progressive kyphosis, linked to pain and limited function); (4) Instability (due to widespread destruction and concern over risk to the cord); (5) Post-discectomy infections.

Surgical intervention is indicated for those who have neurological deficit secondary to spinal epidural abscess (SEA) formation. Failure of non-operative treatment of SEA is around 42% and urgent surgical decompression and draining is associated with better outcomes and neurological resolution. It also had the added benefit of producing excellent biopsy samples. There is no consensus on timing of surgery however most authors agree < 24-48 hours is best to avoid irreversible damage from expanding collections, and probably < 24 hours in cases of cord compression[30,31].

Severe ongoing pain is typically secondary to degenerative changes or ongoing inflammation at the affected spinal level. Whilst this is not an absolute indication in the absence of deformity or instability; interbody fusion can be considered where conservative measures have failed to show an improvement in pain.

Progressive deformity secondary to collapse of the vertebral body is due to extensive osteomyelitis. The direction of deformity is typically kyphosis at the lumbar or thoracic levels as the anterior vertebral body collapses, however coronal plane deformities can also occur. This can cause mobility issues, pain, stiffness and even increased mortality secondary to reduced lung capacity. Various options depending on the deformity type can be considered. There are no values or measurements which indicate surgical correction in this cohort. Progressive changes over time with follow-up imaging which is symptomatic and debilitating should prompt a referral to a spinal deformity specialist.

There is no official definition or consensus on spinal instability in the literature, and even less so on instability for spinal infection. However extensive and widespread infection, with evidence of spondylolisthesis (translation of one vertebra over another), or progressive deformity can be considered signs of instability. The immediate concern is damage to the cord or nerve roots in this scenario. Instability, however, may require surgical stabilisation before the patient is allowed to ambulate fully.

Decisions around approaches for debridement and stabilisation are very case-specific. Factors such as level of disease, number of affected levels, degree of deformity, derangement of normal osteology, antero-posterior location of infection, and patient factors. Each surgical approach has advantages and disadvantages. For example, debridement of the vertebral body itself can be achieved via all approaches, however anterior and lateral approaches will offer the best exposure for corpectomy and cage insertion/strut grafting for the restoration of lumbar lordosis. However, posterior approaches will allow of debridement of posterior structures around the cord, and insertion of posterior instrumentation[32]. The disadvantages of each type of approach for fusion in degenerative cases is summarised below based on a recent meta-analysis[32] (Table 2).

Due to the rarer and heterogenous data on spondylodiscitis, very few studies comparing approaches exist. Posterior versus anterior approaches for debridement and surgical stabilisation in TB have both been shown to be effective in achieving pain control and stability, with a slight favour towards posterior approaches due better sagittal profile correction and pain/function scores, but at the cost of higher blood loss and increase surgical difficulty and duration[33]. Such decisions should be taken at a tertiary-level with a multidisciplinary team (MDT) approach to dealing with spinal TB. There is little evidence to determine if this can be applied to non-TB spondylodiscitis cases.

Overall, the trend seems to be in favour of combined techniques. These have evolved from combined anterior debridement and strut-grafting with posterior decompression and instrumentation; to percutaneous posterior techniques with or without debridement (anterior or posterior). However, whilst the techniques are becoming less invasive, the earlier decision to stabilise and debride is possibly leading to a lower demand to be as aggressive[34,35].

Post-discectomy is a common cause of spondylodiscitis and some early low-level evidence suggests that surgical debridement in these patients have better resolution, functional outcomes and shorter lengths of hospital-stay compared to non-operative treatment[36].

Full Endoscopic Discectomy (FED) is an emerging technique, and had been shown to be a viable and effective technique in endoscopic debridement of spondylodiscitis. Whilst the data is limited, and the technology is in its infancy in the UK, such minimally-invasive treatment may open up surgery to more patients; reducing hospital

stays and the need for larger open procedures[37].

Rare cases of intramedullary and subdural abscesses have been reported, but no consensus on timing or modality of treatment exists. Timely administration of antibiotics and drainage within 5 days seems to improve outcomes[38,39].

FOLLOW-UP AND MONITORING

Monitoring of antibiotic response is best done using the CRP and ESR, as both will fall as the infection resolves. When compared to MRI appearances, CRP resolves faster than ESR. CRP is more associated with soft tissue resolution, whilst ESR represents bony resolution more closely[40].

MRI scan for monitoring of response and resolution has a very poor correlation with the clinical scenario. Often MRI appearances can look worse initially. MRI should typically only be used in cases of concerning change in status, such as new neurology, or worsening of biochemical markers[41].

Most treatment failures happen early in the process, but ongoing neurological symptoms and pain can represent delayed failure. At 2 years approximately 28% of infections will recur or experience incomplete resolution, and at 5 years 31%. *S.aureus* infection and delayed diagnosis are associated with higher recurrence rates[42].

No single test has been identified as completely trustworthy, and patients should have combined history, examination, blood panel and consideration of imaging. Depending on the factors the clinician is monitoring, a variety of radiological studies can be selected. For simple deformity monitoring, a plain radiograph or dual-planar low-radiation standing radiographic scan may be sufficient, or for soft tissue inflammatory responses and neurological symptoms, an MRI would be better.

Like MRI, a nuclear medicine SPECT is also likely to show high uptake long after infection resolution as a result of bone remodelling, rather than active infection, and should be interpreted with caution[43].

CONCLUSION

Whilst spondylodiscitis is a rare cause of back pain, a thorough history and examination with a simple blood test (including WCC, CRP, ESR) is highly likely to detect the condition and prompt urgent referral. It is also likely to pick up common sources and secondary infections associated with the condition. It is almost inexcusable not to do this considering the lower-costs and long-term superior outcomes of detecting spondylodiscitis early.

Once identified, these patients should undergo urgent whole-spine MRI scan with gadolinium contrast, providing they have good renal function. For those with kidney dysfunction and no neurological concerns, a non-contrast study can be considered.

Blood cultures should be obtained prior to commencing empirical antibiotics as per local guidelines. Thought should be given to less common pathogens based on patient risk factors, and therapy tailored accordingly. Consideration of urgent CT-guided biopsy should take priority, if readily available, prior to treatment and ZN staining should be a standard request. In the likely event of culture-negative infection, PCR for bacterial RNA/DNA should be undertaken.

Neurosurgical or Orthopaedic Spinal Surgeon consultation should be sought immediately, and a low threshold for surgical debridement should be considered in the presence of severe or ongoing pain, instability, neurological compromise or progressive deformity. Mortality is high, and a mantra of "too sick not to operate" should be adopted as opposed to the contrary. CT-guided drainage is unproven.

Follow-up patients in the same way they are investigated, knowing failure rates are high. Complete at least 6 weeks of antibiotics. ESR/CRP should be used in tandem, and imaging should be used with caution, and only where clinically indicated.

Finally, more research into minimally-invasive techniques could open up a doorway to better patient outcomes, lower morbidity/mortality. FED with percutaneous instrumentation warrants our attention.

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