Vertebral Osteomyelitis In The Adult: A Persistent Diagnostic Challenge
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Abstract
It has been stated in the past that vertebral osteomyelitis (VO) is neither common enough to be readily recognizable, nor rare enough to be a medical curiosity and so represents a diagnostic challenge to the physician (1). The incidence of this condition is on the rise and may be due in part to increases in average life expectancy, risk factors, and medical comorbidities. The clinical picture of VO is rather non-specific. It commonly starts insidiously and follows an indolent course making early diagnosis difficult (2). Consequently, patients often develop highly destructive lesions or disastrous neurological complications related to compression of the spinal cord or its roots (3). Irrespective of the causal agent, VO is a serious infectious disease, which frequently produces long hospital stays therefore, a high clinical suspicion in patients with non-mechanical pain is important in making the correct diagnosis in the early stage of the disease process.

A confirmed case of adult vertebral osteomyelitis is presented and the literature reviewed with emphasis on the diagnostic evaluation and the challenges faced on arriving at such a diagnosis.

CASE REPORT
A sixty-four year old male, diagnosed with Diabetes mellitus, twenty years ago maintained on Metformin and glyburide tablets, presented to the Accident and Emergency Department with worsening back pain over a five month period. He was now having difficulty ambulating because of back pain and weakness to the left lower limb. Three weeks prior to presentation, he was using a cane for assistance with ambulation because of the symptoms experienced. The pain, he described as non-radiating, cramping in nature that was worsen at nights and was aggravated by lying flat. He had no preceding history of trauma. He had seen a total of seven general practitioners and was taking prescribed oral analgesics, which he stated were no longer relieving his symptoms. He was subjected to a six-week course of physiotherapy for mechanical back pain on two occasions within the previous four-month period. Little relief was experienced with physiotherapy.

Plain radiographs done on three occasions resulted in a diagnosis of degenerative lumbar spine disease. There was no history of cough, fever, urinary or gastrointestinal symptoms and no cerebrovascular or cardiovascular events in the past, however he gave a two-week history of anorexia and night sweats prior to presentation. The patient did not have a history of polydipsia or polyuria. There was no history of smoking, alcohol or illicit substance use. On examination, the patient was in moderate painful distress with inability to lie flat in bed. He preferred standing flexed at the waist. His vitals signs were as follows: Temperature 37.9°C, Resp. rate 28bpm, Pulse rate 110bpm BP 160/98mmHg GMR 15. He had no clinical evidence of significant weight loss. Significantly, he had percussion tenderness at the level of L4/5 vertebrae with no gibbus deformity. He had marked limitation in range of movement especially on extension of back and hip joints secondary to pain. Normal bulk and tone to his lower limbs were noted however, there was a positive straight leg raise on the left side with grade 4/5 power to ankle and great toe dorsiflexion. There was decreased sensation in the distribution of L5 nerve root. Deep tendon reflexes were present bilaterally. Normal power and sensation were demonstrated in the upper limbs.

Plain radiographs were done of the lumbosacral spine and chest, which revealed destruction to the inferior endplate of L4 vertebra, the superior endplate of L5 vertebra and the
associated narrowing of L4/L5 intervertebral disc space (figure 1). Blood investigations done included a complete blood count (CBC), blood film, white cell differential, urea, creatinine, Phosphate, Calcium, Alkaline Phosphatase (Alk Phos), and electrolytes, Random blood glucose (RBG), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), blood and urine cultures, HIV test, HbA1c, Protein specific antigen (PSA) (Table1). Given his history and examination with no background of trauma to back, there was a high index of suspicion for vertebral osteomyelitis and so further tests ordered included a Computed tomography scan (CT) and Magnetic resonance imaging (MRI) scan of the lumbar spine, Mantoux test, Sputum for Ziehl Neelsen (ZN) staining, culture and sensitivity.

MRI revealed destructive changes to the intervertebral disc with small collections visualized in the iliopsoas muscles bilaterally. There was no local thecal sac indentation however there was oedematous paraspinous muscles with foraminal stenosis on the left at L4/L5 level. The CT scan showed destruction of the superior endplate of L5 vertebra with involvement of the superior 10% of the vertebral body and destruction of the inferior endplate of the L4 vertebra. CT-guided aspiration of the iliopsoas collections yielded 20cc of thick purulent fluid, from which Staph aureus was isolated. A pyogenic spondylodiscitis was confirmed. Intravenous culture-directed antibiotics were commenced. A Plaster of Paris jacket was used to protect the spine and limb physiotherapy was started. Serial ESR and CRP tests showed a decreasing trend over a six week period and with clinical improvement in symptoms and reducing analgesic requirement, he was discharged after demonstrating unassisted ambulation with no neurological deficits. He was reviewed in the Orthopaedic Outpatient Department with serial radiographs. There was no radiographic progression of destruction of the lumbar spine, and at six months after diagnosis, he demonstrated pain-free unassisted ambulation no longer requiring thoracolumbar bracing.

DISCUSSION

Spinal infections are rare with pyogenic vertebral osteomyelitis (the commonest type) accounting for approximately 1–7% of all bone infections with a male predominance (4-7). An increase in vertebral osteomyelitis has been noted over the past decade and a half, probably as a result of the improving diagnostics. Other factors may include longer survival of high-risk patients with comorbidities, advances in the surgical management of spinal conditions, increasing number of individuals using
intravenous substances, increasing use of immunomodulatory medications, and the resurgence of spinal tuberculosis (TB) partly because of the HIV epidemic (6, 8-14). Diagnosis is based on clinical, laboratory and radiological features and can be difficult. It is often delayed or missed due to the rarity of the disease, the insidious onset of symptoms and the high frequency of low back pain in the general population (15). A delay in diagnosis can range from two to twelve weeks, and on occasions after three months (8, 16).

In the United States, it is estimated that up to 90% of adults will experience an episode of back pain during their lifetime. Of the patients who have acute back pain, 90% to 95% have a non–life-threatening condition. In the remaining patients, acute back pain is a manifestation of more serious pathology (17-19). Because it is such a common complaint and one that is not generally associated with significant pathology, there can be a tendency to overlook the more potentially neurologically or life-threatening conditions. To prevent this, one must approach each patient systematically, specifically looking for those “red flags” in the history and physical examination that raise one's suspicion of potentially significant pathology. The detection of any red flag warrants further investigation.

In more than 90% of patients, unremitting back pain, which is not relieved by rest, is the most common presenting complaint. Back pain that begins or progresses over a period of weeks to months must raise suspicion for infection (20). A new diagnosis of musculoskeletal strain should be a diagnosis of exclusion in the elderly patient and must be made with caution. Though the commonest area of VO is the lumbar spine, the elderly patient who has thoracic back pain alone is a red flag and should be further investigated. Nearly all patients who have musculoskeletal etiologies of back pain recover within four to six weeks (19, 21). Back pain that is persisting beyond six weeks should be a cause for concern especially in those patients whose pain persists despite appropriate conservative management (22). It is pertinent therefore to question the patient regarding the effect of analgesic medication. Patients whose pain is unremitting despite high therapeutic doses of medications must be evaluated for more serious causes of back pain including infection. A history of recent procedures is important as a recent procedure such as those involving the genitourinary or gastrointestinal system is at risk for infectious etiologies. These procedures have a relatively high incidence of bacteremia and can result in hematogenous seeding of the spine (17). Neurologic deficits occur in less that forty percent of patients with VO, however, any presence of associated neurologic symptoms such as parasthesias, motor weakness, urinary or fecal incontinence, or gait abnormalities warrants additional evaluation (2, 7, 23). Butler et al reported that only 29% of patients suffering from infective spondylitis presented with evidence of neurological involvement and the majority of them had incomplete neurological deficit with mild extremity weakness (8). This pain may be accompanied by constitutional symptoms including unintentional loss of weight, fever, night sweats, malaise and a poor appetite. Aggravating factors including lying flat is a red flag for infection. Spinal infection must also be considered in the patient who reports pain that awakens them at night, as this type of pain that is worse at night is atypical for musculoskeletal etiologies. A history of fever or night sweats certainly heightens one’s suspicion however one must also recognize that fever may be absent in the face of spinal infection. Patients with a past medical history of HIV, organ transplantation, diabetes, or prolonged steroid use are at greater risk for an infectious etiology and should raise suspicion for VO. The association of diabetes mellitus has been well documented. Increased age and diabetes mellitus confer an increased risk for the development of pyogenic vertebral osteomyelitis (5, 24).

Physical examination of the patient who has back pain begins with an assessment of vital signs. The patient’s temperature must be interpreted with caution because the sensitivity of fever ranges from 27% to 83% (25). As was mentioned earlier, it is well known that patients who have vertebral osteomyelitis have fever only 60% to 70% of the times the diagnosis is made, making a significant proportion afebrile on presentation (5). Thus, the lack of fever is insufficient evidence to rule out the diagnosis. Cachexia with generalized lymphadenopathy may be suggestive of HIV infection (13). Concern should be raised for the patient who is unable to remain still. Unlike patients who have musculoskeletal strain who prefer to remain immobile because of exacerbation of symptoms with movement, patients who pace about the examining room should be suspected to have renal colic, pyelonephritis, or in the rare cases, spinal infection (22).

When examining the back, the clinician should note any cutaneous findings that suggest infection such as warmth, swelling and/or percussion tenderness of the spinous processes. Physical examination of the back may reveal
localized spinal tenderness with paraspinal muscle spasm and marked limitation in the range of movement of the spine. In advanced disease, patients with infection of the lumbar spine may present with a painful gibbus or a psoas abscess exhibiting exquisite pain on extension of lumbar spine and hips as in the index case. The most important component of the physical examination is the neurologic examination. It is therefore imperative to thoroughly assess motor function, sensation, deep tendon reflexes, gait, and rectal tone.

Laboratory studies frequently obtained in the patient who has suspected osteomyelitis include, CBC, ESR, C-reactive protein and blood cultures. The WBC count may not be elevated in patients with a spinal infection as leukocytosis is present in less than half of patients who have osteomyelitis and is not particularly useful in making a diagnosis of spinal infection (7, 26). However, it should be part of an infection workup as it may provide some general guidance concerning a response to treatment (27). The ESR is a sensitive laboratory indicator of pyogenic infection, which is positive in more than 90% of patients with spinal infections. The average ESR in patients with pyogenic spondylitis ranges from 43–87 mm per hour (28). C-reactive protein (CRP) on the other hand increases within six hours of the onset of a bacterial infection. C-reactive protein is elevated in 90% or more of patients with spinal infection and is more specific than ESR. Elevation in ESR and CRP correlates with the presence of inflammatory response and CRP is more specific that ESR but they are not specific for infection (29).

Therefore an elevation in CRP and/or ESR should not be taken as pathognomonic for an infection. Despite their non-specific nature of an elevation in the ESR, they still provide additional data regarding the possible presence of infection and both serve as good screening and surveillance tests in the diagnosis and treatment of spinal infections.

Blood, urine and sputum cultures and urinalysis should be obtained in patients suspected of having a spinal infection. About 25–59% of positive blood cultures identify the causative agent (5, 29). This rate of successful culture may be higher in patients during a fever spike or lower if the culprit organism is of low virulence (1, 30). Similarly, wound cultures should be obtained on any purulent soft tissue infection because this may be the nidus of infection. It is important to delay the administration of antibiotic therapy until after appropriate cultures have been performed unless the patient is septic or critically ill. It is recommended that specimens for microbial studies be taken from the port of entry and at least three sets of blood cultures should be collected at different times after discontinuation of antipyretic and antibiotic agents. If the patient requires urgent treatment due to sepsis or a fulminant disease course, empirical therapy with a broad-spectrum antibiotic regimen appropriate to treat the most common pathogens for vertebral osteomyelitis (31). Bacterial cultures should be maintained for at least ten days to detect low-virulence organisms.

The definitive diagnosis of spinal pyogenic osteomyelitis can be made only with isolation of the organism from a positive blood culture or biopsy and culture of the infected location. In addition, a biopsy is necessary when a polymicrobial infection is suspected, since blood cultures often yield only one organism (32). Spinal biopsies have popularly been performed using computed tomography (CT) or fluoroscopy for guidance in localizing the site of the suspected infection. In the absence of a positive blood culture in a stable patient it is recommended that antibiotics be withheld until a fluoroscopic or CT-guided percutaneous biopsy is done. Endoscopic biopsy is another option which allows the biopsy to be done under visualization and treatment instituted with debridement of the infected tissues (33, 34). Open biopsies can also be performed if closed biopsy techniques result in negative yields, when the infection is inaccessible to closed techniques and in the presence of a neurological deficit or a painful progressive deformity (35).

In a systematic review of 1008 patients diagnosed with pyogenic vertebral osteomyelitis in fourteen studies, Mylona et al found biopsy, whether open or closed had a positive yield in 79% of cases (5). A core biopsy is preferable to fine needle aspiration (35). For all techniques, identification of the infectious agent is challenging. Aerobic, anaerobic, acid-fast bacilli, and fungal cultures as well as gram stain and histopathology should be included in the minimum laboratory analysis of any biopsy material. Possible explanations for negative results at microbiologic examination include antibiotic treatment initiated before the biopsy, insufficient number of infectious agents in the biopsy material, and biopsy obtained from a location without living infectious agents. Therefore if the initial biopsy is negative and withholding antibiotics is considered safe, a further biopsy can be attempted. If a fluoroscopic or CT-guided percutaneous biopsy is negative, an open biopsy should be performed. Pathology will then aid in distinguishing a neoplastic or metabolic process from an...
infection or help confirm a diagnosis of infection with the
finding of acute inflammation.

Diagnosis is neither always easy nor easily confirmed
bacteriologically. Introduction of the polymerase chain
reaction (PCR) technique allows a more accurate diagnosis.
Sharma et al. studied two target genes that were found to be
specific for Mycobacterium TB in eighty patients; multiple
PCR had a sensitivity of 81.8% in suspected cases of
peripheral TB osteoarthritis (36). This promising test for TB
diagnosis may enhance making the diagnosis of Pott’s
disease in the future with its advantage of being fast,
however, it is still quite an expensive test and it is not readily
available in most medical centres. Most patients can be
successfully treated with antibiotic therapy alone, however,
most investigators recommend obtaining tissue samples
before the initiation of antimicrobial therapy. If the patient
requires urgent treatment due to sepsis or a fulminant disease
course, empirical therapy with a broad spectrum antibiotic
regimen appropriate to treat the most common pathogens for
spondylodiscitis, i.e. Staphylococcus aureus and Escherichia
coli, should be initiated only after collecting blood
cultures.(4) Nevertheless, in one-third of cases the infective
organisms are never identified (37).

We have seen that the symptoms and clinical findings of
patients are often non-specific and may vary widely, thus
making imaging necessary for confirmation and localization
of the infection. Common imaging modalities used for the
diagnosis of osteomyelitis include plain radiography,
radiouclide bone scan, CT, and MRI. Often times the initial
imaging modality is plain radiography. Plain radiography
may reveal abnormalities in up to 89% of cases, a sensitivity
of 82% however a specificity of only 52% (4).
Abnormalities that are consistent with osteomyelitis include
erosion of the vertebral endplate, lytic bony abnormalities,
disc space narrowing, and possibly pre-vertebral soft tissue
swelling (27). Unfortunately, these abnormalities take place
over several weeks thus rendering radiographs unreliable
in the early stages. The plain radiographs may actually appear
normal or only slightly abnormal in the early phases of the
disease, making it rather challenging in differentiating
between infection of the spine and degenerative changes of
the spine. Therefore a high index of suspicion must be
maintained when evaluating plain radiographs for presence
of spinal infection. Pathogens that produce proteolytic
enzymes (S. aureus) spread into the digested disc and the
endplate of the adjacent vertebra, leading to disc herniations
and loss of disc height (1, 38). Pathogens that do not produce
proteolytic enzymes (Mycobacterium tuberculosis) spread
more slowly and tend to make a later clinical presentation.
This more insidious onset allows for more extensive
paravertebral abscess formation and relative preservation of
the disc (39).

Soft tissue extension or origin must be suspected in the
presence of an abnormal psoas shadow, widening of the
mediastinum, or enlargement of the retropharyngeal soft
tissue window. In contrast to pyogenic infections, plain
radiographs in a tuberculous infection often reveal vertebral
bony destruction with relative preservation of the disc spaces
(39). It is recommended therefore that the entire spine with
the addition of the chest should be imaged given the
predilection of tuberculosis for skip lesions at nearby and
distant sites and to assess for active pulmonary disease.

The role of scintigraphy in the detection of bone pathology
before detectable abnormalities on plain radiographs is well
recognized. Radionuclide studies can be much more
sensitive than radiographs in detecting early disease and is
reported to have good sensitivity for detecting infection (40).
The sensitivity of the three-phase bone scan varies between
87 and 98 % with a specificity approaching 100% for the
detection of osteomyelitis in general (41). However, its
specificity falls off for spinal infections, particularly in older
patients with some degree of spondylosis and degenerative
disc disease present (40). Technetium-99m-labelled
methylenediphosphonate (Tc-99 m MDP) bone scintigraphy
reveals areas of involvement as foci of increased activity,
often involving two adjacent vertebrae. Other foci of
increased activity within the axial and peripheral skeleton
may indicate further sites of involvement not clinically
suspected. The infective focus may be cold in very early
osteomyelitis due to sludging and an infarctive process. It
can then become hot as a hyperaemic response occurs (42).
Interpretation of bone scan results therefore must be made
with caution.

In a retrospective study of 100 patients suspected to have
disc space infection, Bruschwein et al found Gallium-67
citrate scan to have a sensitivity of 89%, a specificity of 85%
and an accuracy of 86%, which are quite similar to that of
technetium scans in evaluating pyogenic spinal infections.
Combining these two studies further enhanced the accuracy
of 94% (43). Inflammation scintigraphy with labeled
leukocytes or Tc-99m-labeled antibodies have been used in
the diagnosis of spinal infections as a supplement to
multiphase scintigraphy, in which radioactively labeled
native blood cells or (now preferably) Tc-99m-labeled anti-
granulocyte antibodies are used to detect inflammatory changes in bone tissue. Anti-granulocyte antibodies also label hematopoeisis in the bone marrow, so that the spinal column is subject to physiological enrichment. Indium 111-labeled leukocyte scintigraphy, specificity is improved but sensitivity is very low and is therefore more suitable for the extremities (4). In addition, the high rate of false-negative and false positive results in the presence of spinal infection and the inability to provide anatomic detail make it unsuitable for the routine use in diagnosing spinal infections. The lack of sensitivity may be because by the time patients are studied many infections have progressed beyond the acute stage into a more chronic stage with a relative scarcity of leukocytes (44).

Positron emission tomography with fluorine-18 fluordeoxyglucose (F-18 FDG PET) has been shown as an increasingly useful adjunct to imaging for the diagnosis of spondylodiscitis. Schmitz et al. found that all patients with spinal infection confirmed by histopathology had positive FDG-PET imaging (45). In addition, Stumpe et al. reported the utility of FDG-PET for differentiation of degenerative and infectious endplate abnormalities in the lumbar spine that were detected on MRI. PET did not show FDG uptake in the intervertebral spaces of any patient with degenerative disease (46). There is hardly any physiological enrichment of F-18 FDG in the bone marrow or the spinal column, so that inflammatory processes are imaged as "hot spots" (4). The advantages of F-18 FDG PET include the rapid imaging and the relatively low exposure to radiation. On the other hand, specific differentiation from malignant processes may present a problem (45). Although the sensitivity for FDG-PET approaches 100%, it remains highly non-specific. Among the functional imaging studies, the combination of Ga67-single photon emission computed tomography (SPECT) with bone scintigraphy appears to be a promising combination method for diagnosing spinal osteomyelitis especially when MRI is not available (47). Newer functional imaging modalities for early spinal infections use radiolabeled streptavidin–biotin complex, antimicrobial peptides, and Tc-ubiquicidin-derived peptides with mixed results (47).

CT remains invaluable in performing guided vertebral biopsy. Helical CT can be used in cases in which MRI is not possible or unavailable such as in a patient with a cardiac pacemaker. CT is useful for the detailed assessment of the extent of bone destruction and the detection of the exact position of sequestrum and is helpful in preoperative planning. However, the status of the neural elements cannot be accurately assessed without the use of myelographic dye and the placement of intrathecal contrast, which is contraindicated in suspected infection because it places the patient at risk for intradural spread of the infection thus developing meningitis or arachnoiditis (48). Limitations to CT are a relatively low specificity and a high false-negative rate of detecting complications such as epidural abscesses. It is inferior to MRI in evaluating the disk spaces and the neural elements (27). Early destructive changes of the end plates, an early sign in spondylitis, may be missed by axial CT images because of partial volume averaging. To avoid this, spiral CT with thin slices and multiplanar reconstructions are needed (49). In addition distinction between an abscess and granulation tissue may pose a real challenge.

MRI is currently the diagnostic modality of choice in suspected spinal infections. It is the only imaging procedure that detects early infection and to fully evaluate the extent of disease affecting the spine, delineating soft tissue, neural structures, and formed abscesses. MRI has significantly improved the sensitivity and specificity over simple radiography in the diagnosis of VO. Its sensitivity, specificity, and accuracy rates approach 96, 92, and 94%, respectively (8, 50, 51). The use of gadolinium may enhance changes in equivocal cases and accurately localize and defined from the pattern of uptake of the contrast material. Evidence of involvement of two consecutive vertebrae and the intervening disk is virtually diagnostic of infectious spondylitis. Spinal infections commonly demonstrate typical signal intensity on T1 and T2-weighted images and enhancement within the affected bone marrow after the administration of gadolinium-based contrast material. The signal intensity abnormalities of the vertebral body typically seen on T1 and T2-weighted images in spinal infections are not always observed and awareness of the atypical imaging patterns of spinal infection is important in the appropriate clinical context to avoid a delay in diagnosis (52).

Attempts have been made to define the criteria of differentiation between pyogenic and non-pyogenic vertebral osteomyelitis on the basis of imaging findings. Early in the disease process, MRI demonstrates signs of edema and inflammation. Pyogenic disease is characterized by moderate paraspinal abnormal soft tissue, ill-defined paraspinal signal, erosion or destruction of end plates, and anterior–posterior vertebral involvement (53, 54). In TB, disc enhancement is rare or absent and there is extensive paraspinal abnormal soft
tissue with well-defined abnormal signal (23). In brucellosis, there is moderate paraspinal soft tissue, diffuse but solely anterior part involvement, and no spinal deformity (23). Collapse of a vertebral body occurs with low signal on T1-weighted sequences and high signal on T2-weighted sequences and can provide a diagnostic problem. Bony sclerosis of the vertebral body can alter the signal pattern considerably on MR imaging with low signal on T1-weighted and T2-weighted images. Contrast agents are useful because infection will show contrast enhancement. Although gadolinium-enhanced MRI scans are highly sensitive and specific they often overestimate the presence and extent of the epidural abscess within the spinal canal (55).

CONCLUSION

Vertebral osteomyelitis, a part of a continuum of indolent infection in the relatively immunocompromised patients, is not a very common infection. However evidence suggests that this diagnosis is becoming more and more frequent as there are now increasing populations of susceptible patients. In addition, as our experience and understanding with spinal infections have increased, so has success in its diagnosis. However, the insidious onset of non-specific chronic back pain and paravertebral muscle spasm, the lag in the development of radiographic changes, marked constitutional changes and the frequent absence of fever all confound the diagnosis of vertebral osteomyelitis thus contributing to a significant delay in diagnosis. This leads to increased morbidity and mortality in this population. A heightened awareness of vertebral osteomyelitis and a high clinical suspicion index ought to be fostered when assessing adults especially diabetics with chronic back pain and constitutional signs. Treatment is often times without a microbiological diagnosis in some of these cases, however, identification from blood cultures or eventual biopsies contributes to establishing a diagnosis and guides the specific treatment regime for these patients.

Therefore, it is essential that empirical medical treatment should only be started once blood cultures, and eventually bone biopsy, have been obtained. Fever is not a primary feature in VO and should not be relied on to clinically rule out spinal infection. Non-specific haematological and biochemical parameters are of little value in the diagnosis, however if a neutrophilia with high values of ESR and C-reactive protein are present, they strongly suggest VO. Computed tomography and MRI have significantly improved the sensitivity and specificity of radiographic diagnosis of VO. The prognosis of PVO depends strongly on an early diagnosis, the identification of the causal agent, and the initiation of a specific treatment. Therefore a high suspicion index together with a thorough evaluation of the adult with chronic back pain can result in a shorter time to diagnosis with institution of early intervention thus preventing the debilitating functional sequelae.

References

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