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Biopsy for suspected spondylodiscitis

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Abbreviations: **ASA=American Society of Anesthesiologists; ASIA=American Spinal Injury Association; CRP=C-Reactive Protein; CT=Computed Tomography; CTSB=CT-guided Spinal Biopsy; ESR=Erytrocite Sedimentation Rate; FDG=FluoroDeoxyGlucose; FNA=Fine Needle Aspiration. G=Gauge; MRI=Magnetic Resonance Imaging; PCR=Polymerase Chain Reaction; PET=Positron Emission Tomography; SIMP=Spine Infection Multidisciplinary Management Project; SUV=Standard Uptake Value; TB=Tubercolosis.**

Abstract. – *Background:* **Vertebral biopsy is fundamental in determining whether a spinal lesion is of infectious or neoplastic etiology. Accurate diagnosis is critical for proper medical and/or surgical treatment and consequently for the prognosis of the patient. CT-guided percutaneous spinal biopsy (CTSB) may minimize the risk of contamination and complications.**

Aim: **To demonstrate the importance and efficacy of CTSB and subsequent microbiologic/histological examination in the diagnosis of spinal lesions, particularly for those of an infectious nature.**

Materials and Methods: **Two series of spinal infection patients. Prospective series of 69 patients (2009-2011), 24 of whom underwent CTSB. Retrospective series of 130 patients (1999-2008), 65 of whom underwent CTSB. All patients had microbiologic and histological testing of biopsy samples, when possible.**

Results: **For the 2009-2011 patient series, histological examination yielded a diagnosis in 81.8% of cases, microbiologic culture and PCR for Mycobacterium tuberculosis in 45.8%. For the 1999-2008 series, histological examination yielded a diagnosis in 69% of cases, culture in 38.5%. Spinal lesions in 4 patients with previous histories of malignancy were assumed to be metastatic and treated with radiation at outside institutions. After biopsy, all were revealed to be spondylodiscitis.**

Conclusions: **Percutaneous CT-guided needle biopsy is the mainstay of diagnosis for spine lesions of unknown etiology, thus guiding appropriate treatment. Histological diagnosis, when possible, is critical before initiation of therapy and may be helpful in cases where cultures are negative. In the case of a spinal lesion of unknown origin, even in the setting of a previous malignancy, metastasis should not be assumed; infection and new primary lesions should always be considered as part of the differential diagnosis.**

Key words:

Biopsy, Trocar, Spine infections, Vertebral osteomyelitis, Spondylodiscitis.

Introduction

The experience gained in the field of orthopedic oncology during the last 30 years has allowed us to understand the importance of accurate diagnosis prior to the development of a treatment plan. Despite different prognoses, infectious and malignant lesions share the need for specific treatment. The proper treatment for a particular infection or neoplastic process may not be correct, or may even be contraindicated, for another diagnosis. For both orthopedic oncologic conditions and orthopedic infections, procedural and treatment algorithms and guidelines have been adopted; it is only through validation and standardization that errors can best be avoided and optimal results achieved for the patient. A biopsy is the cornerstone of diagnosis and the basis on which subsequent treatment is based, be it medical or surgical. For spine lesions, CTSB is now widely accepted as the standard biopsy proce-

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dure. The purpose of this article is to demonstrate the diagnostic importance and effectiveness of CTSB and of microbiologic and histological examination for spine lesions, with particular attention to infections.

Materials and Methods

Sixty-nine patients with spine infections were treated at our institution from 2009-2011. All were treated according to a recently published diagnostic and therapeutic algorithm[1] (Figure 1). Of the 69 patients, 52 were entirely managed by our Spine Infection Multidisciplinary Management Project (SIMP) and 17 were external consultations. The SIMP patients were studied prospectively with the approval of the hospital Ethic Committee.

There were 37 males (53.6%) and 32 females; average patient age was 60 years (range 5-85). Based on blood, bronchoscopy, urine, and biopsy samples, 18 patients had a diagnosis of tuberculous infection (26%) and 51 had an infection caused by pyogenic bacteria (74%). Seventeen patients (24.6%) were treated surgically; of these, eight had tuberculosis (47%) and nine had another bacterial infection (53%).

Computed tomography-guided spinal biopsies were performed in 24 of the 69 patients. Biopsy was indicated based on the following factors: infection indicated on magnetic resonance imaging (hypointense on T1, hyperintense on T2, morphology consistent with infection), elevation of markers of inflammation (ESR, CRP), a thoracic, lumbar, or sacral lesion (cervical lesions were discussed on a per-case basis given the higher risk of biopsy in that location), the absence of bacterial isolation elsewhere, the absence of indication for emergency surgery (in which case an open biopsy was performed), no antibiotic therapy initiated or outside the therapeutic window of a previously-taken antibiotic.

Each patient was informed of the biopsy risks (the most frequently-reported being neurologic injury and pain) and benefits (etiologic or at least histological diagnosis, resulting in proper treatment) and allowed to choose whether to accept the proposed procedure.

Our guidelines include an F18 FDG-PET/CT prior to the initiation of drug therapy in order to gauge improvement[1,2]. Whenever possible, biopsy was also performed after PET/CT for two reasons: for not to alter the PET signal and to have the benefit of the PET/CT images for adequate sampling of the lesion. If the biopsy was performed first, a minimum of 2 weeks passed before PET/CT was performed.

Description of the procedure

Whenever possible, every attempt was made to have both the interventional radiologist and surgeon present during the procedure. The patient was informed about the importance of their cooperation and of remaining still during the procedure. In most cases, the patient was prone, with a bolster under each anterior superior iliac spine to decompress the abdomen. In rare cases, the biopsy was performed in the lateral decubitus position (obese patients, those intolerant to the prone position for reasons such as severe pain, etc.). However, this position complicates the procedure due to obscuration of anatomical landmarks and difficulty passing through the CT scanner. For selected cervical lesions, an anterior approach may be considered, in which case the patient is placed supine.

Digitized radiograpic images were consulted and the vertebral lesion identified. This was divided into several image slices (four were generally sufficient). Images of the pedicles were usually chosen in order to follow the path of the needle during the biopsy[3-8]. To find the ideal needle trajectory through the pedicle, a line was drawn from the lesion, through the pedicle, to the skin, and measured on the CT. The distance from that point on the skin to the spinous process was then measured. That same distance from the spinous process was then measured on the patient and marked with a dermographic pen. A small metallic marker was secured on the skin over the mark and a scan taken for confirmation. Once the entry point was confirmed and the needle size chosen, the area was prepped and draped in a standard sterile manner. No antibiotic prophylaxis is administered for standard patients. Antibiotic prohylaxis consisted of 2 g of cefazolin administered intravenously for patients characterized by ASA Classification >3. Analgesia was administered according to a protocol developed specifically for these procedures as well as carbocaine-based local anesthesia for the skin and periosteum. Once the local anesthetic was administered, the needle was left in place for use as a landmark for confirmation of correct entry point and trajectory.

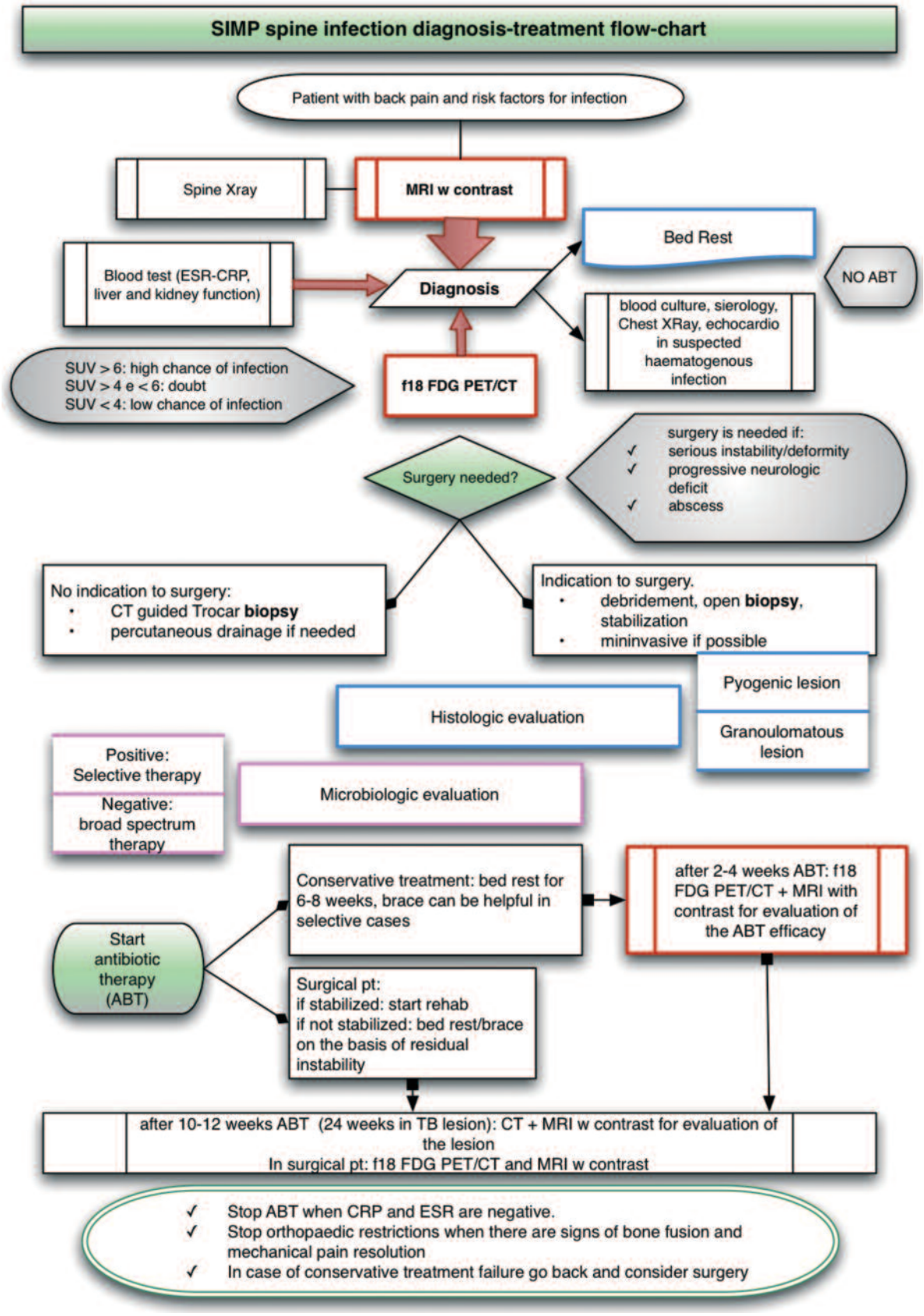

Figure 1. Diagnostic and therapeutic algorithm used at our center[1].

Under CT control, a small incision was made (usually less than 0.5 cm) to facilitate needle entry. Biopsies were performed with 8 gauge bone marrow biopsy needles (either 10 or 15 cm in length) or, less frequently, with 11 gauge needles of the same length, for cases in which only the disc was to be biopsied. With the trocar in place, the needle was inserted into the bone. After verification on CT, the needle was passed through the cortex until it reached the pathologic tissue. The trocar was removed and the needle advanced through the area of interest according to the distance measured beforehand. The needle was then slowly rotated. It was important that the trocar was not removed before arriving at the lesion, so as not to risk filling the needle with healthy bone. Before removing the needle, small lateral motions were made to separate the sample from the remaining portions of the lesion. To collect as large a sample as possible and to avoid leaving any remnants along the needle tract, the needle was connected to a syringe kept under vacuum during extraction. When possible at the end of the procedure, another scan was performed to check for a hematoma secondary to the trauma of the needle.

In all cases, sufficient material was collected for three samples: one for histological examination, one for aerobic/anaerobic culture, and one for both culture and PCR testing for *Mycobacterium tuberculosis*. Whenever possible, samples of both disc and bone were taken. For one patient with a thoracic paravertebral abscess, a drain was placed at the end of the biopsy procedure and maintained until drainage was minimal (Figure 2).

Steril-strips were usually sufficient for skin closure. In cases with slightly more bleeding, a suture was placed, or a steril-strip and dressing. Ice was applied locally at intervals during the first few hours after the procedure.

The case series spanning 1999-2008 was reviewed retrospectively. During this time period, 65 biopsies were performed on a cohort of 130 patients, of which 76 were male (58.5%) and 54 female. The mean age was 55 years (range 1-88). The indications and the procedure were as described above with the following exceptions: all biopsies were performed by a surgeon, PET/CT was not used to choose the portion of the lesion for biopsy, and PCR was not performed. There were 34 granulomatous lesions (26.1%, 33 tuberculous and one brucellar) and 96 pyogenic (73.9%; in 21 cases the bacterium was not identified, but the patients were, nonetheless, treated successfully). Thirty-seven percent of the patients (48/130) were treated surgically; 17 of these had tuberculosis (35.4%) and 31 had other bacterial infections (64.6%). Four patients with paravertebral abscesses were treated with placement of a drain at the end of the biopsy procedure.

Results

For the series of 69 patients spanning 2009-2011, 25 patients met the criteria for biopsy. One patient refused; a total of 24 biopsies were performed. Histological study revealed 14 cases of

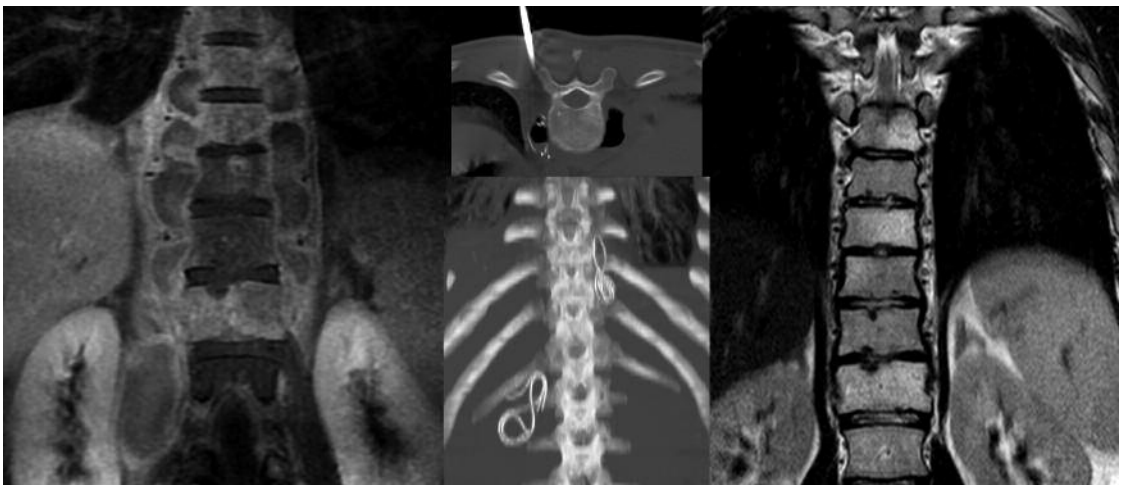

Figure 2. Eighteen year-old male patient with multiple thoracic and thoracolumbar paravertebral abscesses. Treatment consisted of bilateral paravertebral drains placed under CT guidance after biopsy. Pre-procedural, intra-procedural, and 3-month follow-up images revealed resolution of the infection.

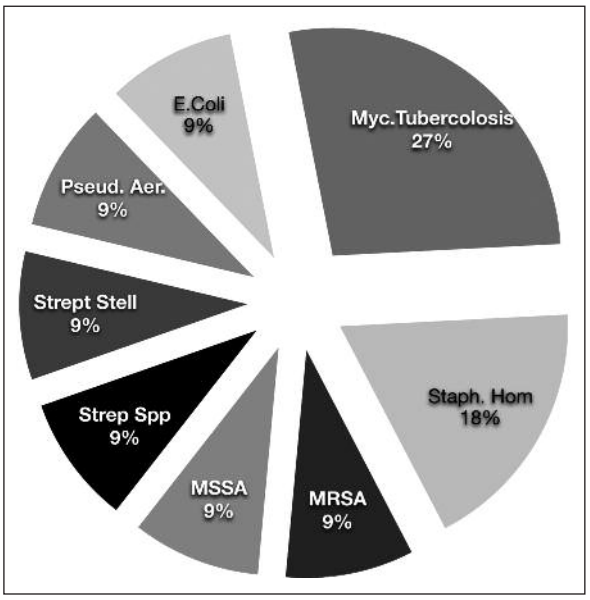

Figure 3. Bacterial culture and PCR results of case series 2009-2011.

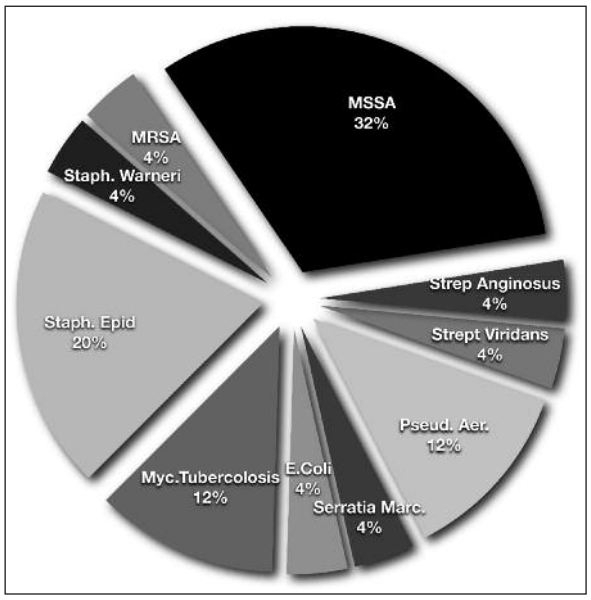

Figure 4. Bacterial culture results of case series 1999-2008.

chronic osteomyelitis and 4 of granulomatous osteomyelitis. In 4 cases the sample was not sufficient for diagnosis or was non-diagnostic. In 2 cases, we were only able to send samples for culture because the material aspirated was fluid, without solid components. Microbiological cultures were positive in 10 cases. For 1 case that was negative by culture, PCR revealed the presence of Mycobacterium Tuberculosis (Figure 3). Histological examination yielded a diagnosis of spinal infection in 81.8% of cases, while bacterial culture and PCR testing provided diagnosis in 45.8% of patients.

The patient treated with a drain after biopsy had rapid clinical improvement with evidence on imaging that the abscess had disappeared within 2 months (Figure 2). All procedures were well tolerated and there were no complications. In 2 of the cases that were non-diagnostic histologically, the biopsy was repeated with subsequent detection of acute-on-chronic spondylodiscitis, but with persistently negative cultures. One case initially diagnosed as chronic spondylodiscitis was refractory to medical therapy; this was revised to granulomatous spondylodiscitis after the second biopsy. The patient who refused a biopsy was treated on the presumed diagnosis of pyogenic spondylodiscitis with success.

With regard to the 65 biopsies performed in the 1999-2008 series, histological examination revealed 24 cases of chronic osteomyelitis and 16 granulomatous lesions, of which 1 was Brucella. In 7 cases the sample taken was liquid only, therefore histological study was not possible. In the remaining 18 cases the sample was not sufficient for diagnosis or was non-diagnostic. Cultures were positive in 25 cases (Figure 4). Therefore, histological examination yielded a diagnosis of spinal infection in 69% of cases, while bacterial culture provided etiologic diagnosis in 38.5%. The abscesses treated with drains were all successful except for one which required subsequent surgical decompression.

Three complications occurred. A 27 year-old male with a tuberculous lesion at L3-L4 developed a caseous subcutaneous collection drained along the biopsy tract from the deep infection. Incision and drainage of the subcutaneous abscess led to rapid resolution of both the superficial and deep infections. A 69 year-old male patient with a lesion at T3-T4 developed progressive neurological deterioration with incomplete paralysis and signs of upper motor neuron compression due to extension of the abscess into the spinal canal (ASIA C). Transpedicular passage of the biopsy needle had been too medial, providing a means of communication between the spinal canal and the needle tract. Urgent surgical decompression and stabilization allowed functional recovery (ASIA E) and the patient fully recovered after appropriate antibiotic therapy for a *Staphylococcus aureus* infection. The third complication occurred in a 54 year-old male who complained of longstanding fever and fatigue

with elevation of ESR and CRP. The specimen taken from the vertebrae was initially diagnosed histologically as spondylodiscitis. The patient did not respond to therapy and a second biopsy of the associated abscess in the paravertebral soft tissues revealed a diagnosis of non-Hodgkin's lymphoma. This case was then excluded from the cohort.

Particular mention should be made of 4 cases with a similar story in the retrospective series. All patients had a previous history of malignancy. They were evaluated in other centers for spine complaints and demonstrated radiographic evidence of a spinal lesion. All were treated with radiotherapy on the assumption that these were vertebral metastases from the previous primary tumor. Lack of resolution of symptoms led these patients to our attention, at which point CT-guided spinal biopsies were performed. Two patients had pyogenic spondylodiscitis and 2 had tuberculous vertebral osteomyelitis (Table I).

Discussion

Spinal diseases of various etiologies (e.g. benign/malignant tumors, pyogenic/granulomatous infections, insufficiency/pathological fractures) may result in similar clinical and radiologic findings. Thus, obtaining a tissue sample becomes the mainstay of diagnosis and treatment of spinal malignancies and infections.

Few clinical or radiologic presentations are so obvious as to allow a diagnosis without biopsy. Even in the setting of a pre-existing disease such as a known primary tumor, a spinal lesion is not necessarily a metastasis. When faced with even the slightest doubt one must make the diagnosis histologically. An accurate diagnosis prior to initiation of specific therapies is the cornerstone of the treatment plan.

Vertebral biopsy can be performed with different techniques: open (incisional) or percutaneous under radiologic control. Image guidance is fundamental for spine biopsies. Ultrasound has been used in the past but is presently restricted to large soft tissue masses in the cervical spine. Fluoroscopy is a readily available technique; it is fast, inexpensive, can be performed in the operating room, allows for real-time visualization of the needle, and surgeons are widely familiarized with its use. However, CT-guided procedures possess several advantages that made it the technique of

Table I. Summary of patients treated with radiation for suspected metastases, later found to have spondylodiscitis.

Pt number	Gender	Age	Primitive tumor	Yrs after primitive tumor diagnosis	Spine level lesion	Therapy after supposed diagnosis of spine mets	Real diagnosis after CTSB	Therapy after diagnosis of spd	Follow up
1	Male	41	Clear cell ca kidney	9	T7-T8	Chemo + Radio TP	Staph Aureus spd	Conservative +ABT	Healed after 3 months
2	Male	66	Lung cancer	2	T10-T11	Radio TP	TB spd	Surgery+ABT	Deceased after 13 months for cancer progression
3	Female	77	Breast cancer	12	T7-T10	Radio TP	TB spd	Conservative +ABT	Healed after 12 months
4	Male	77	Bladder cancer	4	L3-L4	Radio TP	Pyogenic spd	Conservative +ABT	Healed after 3 months

choice when available: it offers multiplanar visualization of complex areas of the spine, especially in locations where other structures may obscure the vertebrae, when soft-tissue masses are involved, or when it is necessary to distinguish between necrotic bone and solid lesions. CT scan is extremely useful for accurate planning of the biopsy trajectory and for pinpointing of small lesions that are difficult to see under fluoroscopy, thereby minimizing the risk of contamination and of accidental damage of important structures[5,9,10]. In addition, the person performing the biopsy is not exposed to ionizing radiation. A good working relationship between the operators executing the biopsy is necessary to reduce the exposure of the patient to superfluous radiation. The need to maintain the patient in the prone position is a disadvantage and may be a limiting factor for the severely debilitated, elderly, or for those with diminished ventilatory capacities.

Needle biopsy has substantial advantages over incisional biopsy, particularly in the spine. The removal of tissue via an open procedure may require a surgery with significant morbidity (e.g. a costotransversectomy for involvement of a thoracic vertebrae or an anterior approach for an osteolytic lesion of the lumbar spine). These patients are often of advanced age with suspected metastatic lesions, which, if confirmed as such histologically, may necessitate palliative treatment. Therefore, it is preferable to avoid unnecessary surgery in which the risks outweigh the benefits.

Percutaneous spinal biopsy under CT guidance is a minimally invasive method that allows precise sampling at a specific location. A fine needle aspirate (FNA) may be performed, however, rarely in orthopaedic oncology does this provide a specific diagnosis[5-8,11]. Another option is to use a very large gauge needle (trocar)[4,7,8]. This is the Authors' preferred technique as it yields a "carrot" of tissue for analysis. In the prospective series, trocar-derived tissue samples for microscopic interpretation resulted in a precise diagnosis more frequently than traditional cultures and PCR amplification for mycobacteria (81.8% vs. 45.8%).

The probability of success is related to the acquisition of a representative sample of lesional tissue, therefore, attempts should be made to avoid reactive or necrotic areas. For this purpose, it is crucial to choose the best area from which to sample. 18FDG PET/CT indicates the metabolic activity of the lesion and may provide useful information about the most significant portion of the vertebra for diagnostic purposes. Although there is no current evidence, it seems plausible that the maximum Standard Uptake Value (SUV) corresponds to the most infected area. More samples may be taken to increase the probability of obtaining good lesional tissue. However, the morbidity of each additional needle passage should be taken into account.

Spondylodiscitis is a disease that usually requires therapy for several months. Empiric therapy must consider a wide range of microorganisms. Therefore, accurate pathogen isolation is essential for proper antibiotic choice. In a series of 55 patients with pyogenic spinal infections, Urrutia et al[12] obtained positive cultures in 52% of blood samples, 65% of CT-guided biopsies, and 80% of open biopsies.

A recent review by Heyer et al[13] reported 95% positive microscopic identification of osteomyelitis but only 31% of the cultures were positive. Other studies reviewed needle biopsies in general, but not for suspected spondylodiscitis; Hao et al[14] reported 90.5% diagnostic accuracy for CTSB in a series of 158 thoracic spinal lesions and Rimondi et al[15] reported an accuracy of 93% for 430 biopsies of the spine, with only nine complications, all of which were transient.

Complication rates of 1-3% have been reported in the literature[9,16]. They are more common in the thoracic spine and include bleeding, neurologic injury, pneumothorax, dural puncture, infection, and tumor seeding along the needle tract. They underscore the importance of careful planning of the biopsy approach and good communication between the radiologist and surgeon. The most important and frequent complications are neurological because in both transpedicular and extrapedicular trajectories the needle passes very close to the medullary canal. Vascular complications are less frequent. The great vessels (aorta and vena cava) and peridural plexuses are at risk. For these reasons, this procedure should be performed in specialized centers with equipped and available operating rooms, should the need for emergent neurologic decompression and/or vascular repair arise. In our series, only 3 complications directly related to the biopsy occurred: 1 of neurologic deterioration, 1 infection, and 1 false-positive (misdiagnosis) which was revealed to be lymphoma after repeat biopsy.

Prior to biopsy, one must always consider that the lesion could be a new primary tumor, which might necessitate en bloc resection of the lesion and biopsy tract. Therefore, whenever possible, it

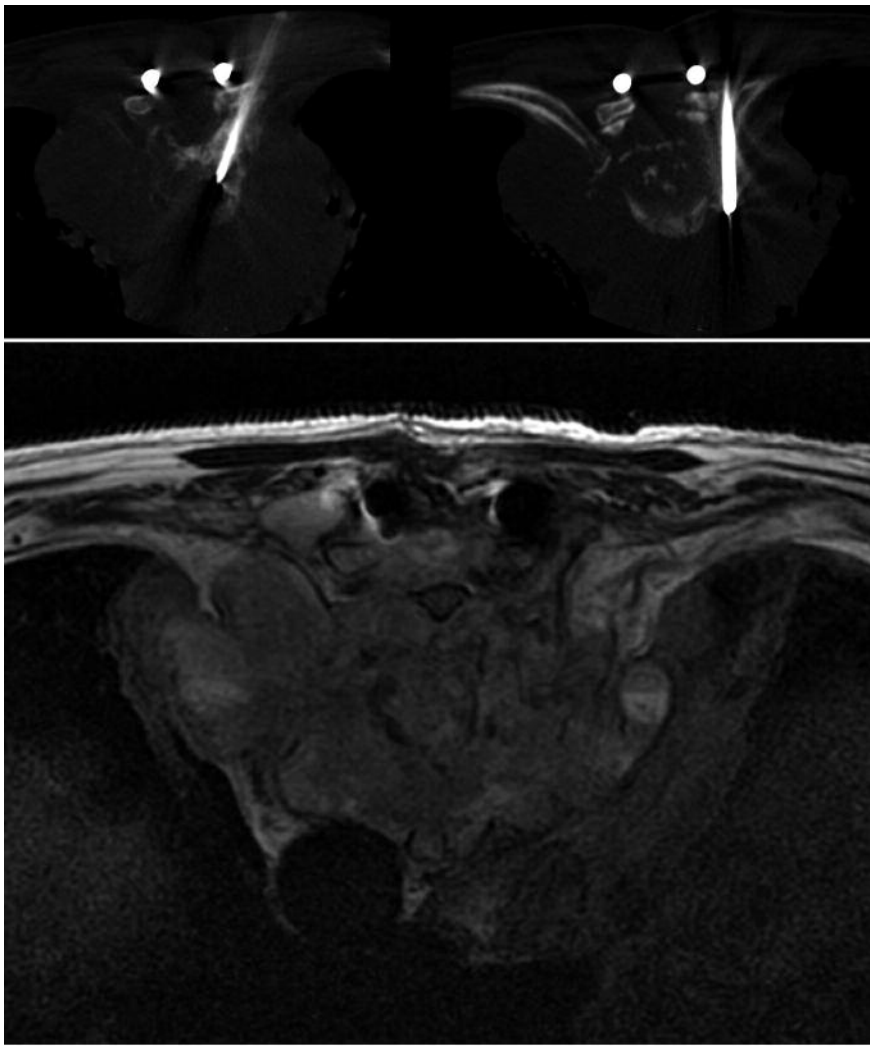

Figure 5. Forty-six year old male patient with multifocal tuberculous spondylodiscitis at T7-T8 and L4, stabilized for the thoracic lesion at an outside center without biopsy or decompression. Visual Analog Scale 10/10. Axial CT and MR scans at T8 revealed evidence of the lesion. Transpedicular bone biopsy as well as paravertebral/costotransvere biopsy of the soft tissues were performed.

is preferable to biopsy through the pedicle[3,4,6-8]. In the case of pathologic fracture with flattening of the vertebral body, the needle can be directed inferiorly through the pedicle to obtain a useful sample. Even in cases of known spondylodiscitis, one may pass through the pedicle of the vertebra below the disc involved and direct the needle proximally to reach the lesion for sampling.

When the diagnosis is discitis and it is necessary to drain an abscess, paravertebral access through the costotransverse junction may be considered. When in doubt as to the nature of a bony lesion, biopsy of an associated soft tissue mass/abscess may lead to a definitive diagnosis (Figure 5). Differential diagnosis is of paramount importance, especially of certain diseases such as lymphoma, the imaging features and histological appearance of which can easily be confused with an infection.

In our series, 4 patients with prior history of malignancy had their spine lesions misinterpreted as metastases at an outside institution. They underwent radiotherapy, which compromised their outcomes and delayed the diagnosis of spondylodiscitis once a proper biopsy was obtained. In another case, both the clinical picture and microscopy suggested an infection. It was only the failure to respond to empiric treatment that lead us to do a second biopsy, at which time sampling of an associated soft tissue abscess lead to a final diagnosis of lymphoma.

Our study is not without limitations. Only a portion of the patients were able to be studied prospectively, yielding 2 separate case series. There was no comparison between the results for the patients who had a CT-guided biopsy and those who had other forms of biopsies. In addition, statistical evaluation was limited.

Conclusions

In summary, vertebral spondylodiscitis is an uncommon but severe disease that can mimic other conditions and for which treatment is highly dependent on proper diagnosis and characterization. CT-guided spinal biopsy is a safe and reliable technique for diagnosis, and is a critical part of the management of vertebral spondylodiscitis patients. Pathologic evaluation and microbiological testing must be performed whenever possible to improve diagnostic accuracy. In spinal lesions of unknown origin, infection must always be considered in the differential diagnosis, even if the patient has a history of a primitive neoplastic lesion elsewhere.

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