Vertebral Osteomyelitis as a Complication Following Transrectal Biopsy: Case Report and Literature Review

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Abstract: We present a documented case report of lumbar vertebral osteomyelitis after transrectal biopsy (TRUSB) complicated by sepsis due to *Escherichia coli.* The Images and histological examination showed an every day more frequent complication. We review the methods of diagnosis and treatment and compare with the scarce literature.

Keywords: Prostate, transrectal, biopsy, spondylitis, bacteremia.

INTRODUCTION

The increasing incorporation of the prostate-specific antigen (PSA) test as a screening method for prostate cancer has resulted in a significant increase in the number of transrectal ultrasound-guided prostate biopsies (TRUSBs) performed. The TRUSB is typically an outpatient procedure through which a histopathological diagnosis is obtained with a low risk of complications, but complications have been increasing during the last decade due to, among other causes, the increased number of procedures.

The most frequent complications are infection, bleeding, and acute urinary retention (AUR). There are reported cases of tumor seeding, more often associated with transperineal biopsy than with transrectal biopsy [1, 2] but they are rare.

Vertebral osteomyelitis (VO), also called infectious spondylitis or spondylodiscitis, represents 2 to 7% of all forms of osteomyelitis but is an exceptional secondary complication to sepsis produced after a TRUSB, and so far, four cases have been reported, in 1954 [3], 1965 [4], 2010 [5], and 2012 [6].

We present a documented case report of a TRUSB complicated by sepsis due to *Escherichia coli*. The consequence of this infectious complication resulted in a lumbar VO.

CASE REPORT

Male, 71 years old. No relevant medical history. Urological follow-up for a benign prostatic hypertrophy (BPH) treated with tamsulosin (Omnic®). An asymptomatic elevation of the PSA to 5.51 ng/mL was observed. The TRUSB was performed, and pathology showed a prostate adenocarcinoma with a Gleason score of 6 (3+3). He was discharged the same day.

Within two days, he went to the emergency room with a fever over 38°C, without hematuria or rectal bleeding. The physical examination was within normal limits. The CBC highlights were 13,000 leukocytes/μL (neutrophils: 88%), creatinine: 1.5 mg/dL (previous analytics: 1.2), and C-reactive protein (CRP): 27.3 mg/dL. Urine sediment: leukocytes +++. Thoracic Rx: no infiltrates.

Blood and urine cultures were performed, and he was admitted with a diagnosis of urinary tract infection (UTI) and mild acute renal failure following prostate biopsy. He was started on empiric antibiotic therapy treatment (ciprofloxacin 400 mg/12 h IV) and antipyretics. Blood cultures were positive for gram-negative bacilli, and the blood analysis showed hemoglobin: 13.5 g/dL, platelets: 161,000/μL, leukocytes: 9,540/μL (neutrophils: 87.3%), creatinine: 1.3 mg/dL, and CRP: 36.6 mg/dL. The urine culture at admission was negative. The blood culture (2nd extraction) was positive for *E. coli.* The antibiogram showed an *E. coli* strain resistant to ciprofloxacin; therefore, the initial treatment was changed to amoxicillin-clavulanate 1 g/8 h IV. He remained afebrile after admission. In the renal ultrasound, the kidneys presented normal size and morphology with no focal lesions nor dilatation of the tract, the bladder wall was normal, and the prostate was globular with an estimated volume of 81 mL. There were no abnormalities in the seminal vesicles.

The patient reported bilateral lumbar pain that diminished with movement but worsened after admission. He was discharged on the eighth day after admission and recommended for outpatient study for

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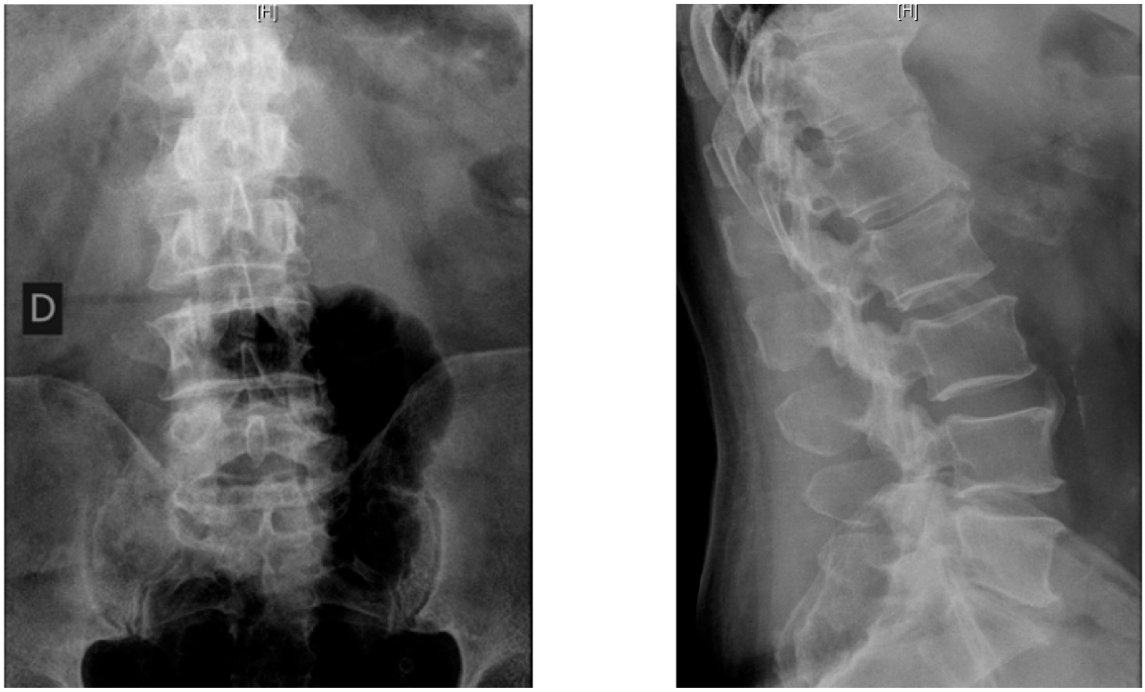

Figure 1: Lumbar spondyloarthrosis.

low back pain. In the first traumatology evaluation, a lumbar Rx was performed (Figure **1**), finding spondyloarthrosis. Physical rehabilitation was recommended.

One month after the biopsy, he underwent a transperitoneal robot-assisted laparoscopic radical prostatectomy. He was discharged without acute complications after three days.

The first outpatient check-up was one week after discharge. Pathology showed a radical prostatectomy specimen with moderately differentiated acinar adenocarcinoma (Gleason 6: 3+3). The neoplasia was limited to the prostatic parenchyma in the peripheral region of both lobes. No images of lymphovascular invasion or seminal vesicle invasion were identified. The tumor volume was estimated to be 9%. The PSA one month after surgery was < 0.04 ng/mL.

The patient continued to have low back pain. He was referred back to traumatology, and an MRI of the lumbar spine was requested (Figure **2**). A marked signal change was identified in the L2 and L1 bodies

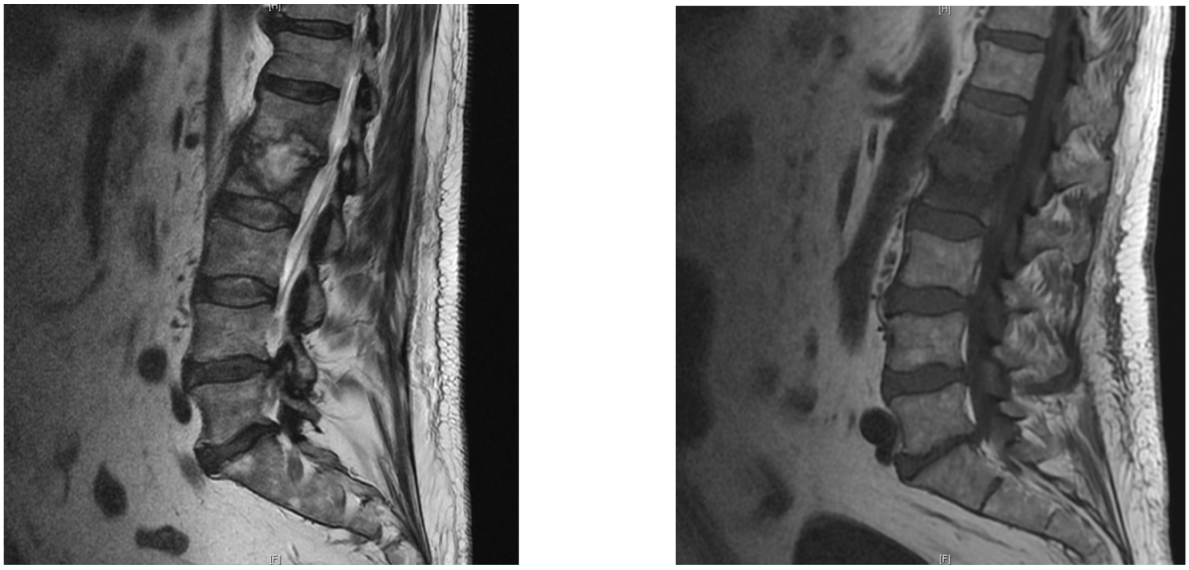

Figure 2: STIR sequence (unenhanced) where alteration of the signal disc L1-L2 and lower and upper plate respectively.

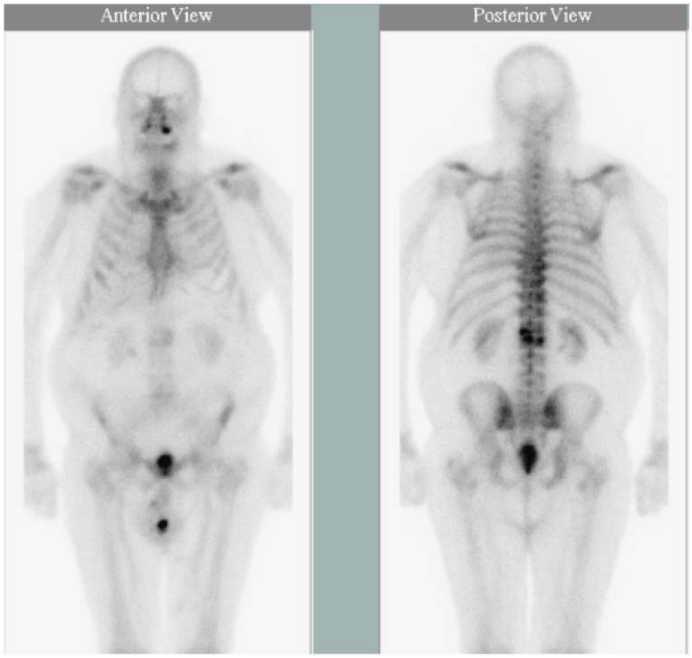

Figure 3: Bone scintigraphy showing a pathological osteoblastic reaction in L1 and L2.

with a pattern suggestive of (infectious?) spondylitis. Metastasis could not be excluded, given the patient's history. A recommendation was made to expand the study with scintigraphy and/or eventual biopsy.

The patient was referred to the oncology service for study and analgesic treatment. Upon physical examination, he presented low back pain non-radiating toward the lower limbs but radiating towards the right gluteus. Lassègue's sign was negative. Fist-percussion on the lumbar spinous processes was positive.

A bone scintigraphy (BS) was requested, and tramadol 50 mg/8 h alternating with metamizol 500 mg/8 h was prescribed. The following week, the pain had improved (reduced from VAS 8 to VAS 3), and the BS (Figure **3**) showed a pathological osteoblastic reaction in L1 and L2 that gave the impression of secondary deposits. There was also increased interapophyseal uptake in the dorsal region joints D9 to D12 of a degenerative nature. In the rest of the skeleton, other pathological deposits were not observed.

The probability of metastatic disease was low because it was a low-risk tumor (by Gleason and PSA level), a pT2c pNx M0 (IIB), and in addition, the PSA after surgery had dropped to almost undetectable levels. Although an extension study was not performed before the surgery, the patient was asymptomatic before starting the process and able to recount very clearly that the onset of symptoms (low back pain) began immediately after the TRUSB. Suspecting VO and considering the history of *E. coli* bacteremia, a vertebral body biopsy was requested for histology and culture.

A core needle biopsy (CNB) of the L2 vertebral body was performed (Figure **4**). The culture was positive for *E. coli,* and the anatomopathological study found no tumor involvement, only fibrin-hematic materials and minimal disintegrated bone tissue fragments, with no evidence of malignancy.

With the diagnosis of osteomyelitis of vertebrae L1/L2 due to *Escherichia coli* producing extended-spectrum β-lactamase (ESBL), he was admitted for parenteral antibiotic therapy combining meropenem 1,000 mg/8 h and gentamicin 240 mg single dose daily. In order to reduce the risk of renal toxicity, gentamicin was replaced with amikacin 1,000 mg/24 h.

DIAGNOSIS OF VO AND CASE DISCUSSION

Infectious complications after a TRUSB are on the rise and show different levels of severity: afebrile symptomatic urinary tract infection (UTI) in 5.2%, febrile UTI in 3.5%, and cases where hospitalization is necessary in 3.1% [22]. Some studies relate this increase in infectious complications to increased mortality (up to 1.3% [7, 8]. However, other studies, such as the PLCO [9] (over 37,000 patients), showed that complications are relatively uncommon after a TRUSB (<2%) with a risk of infection of 0.8%,

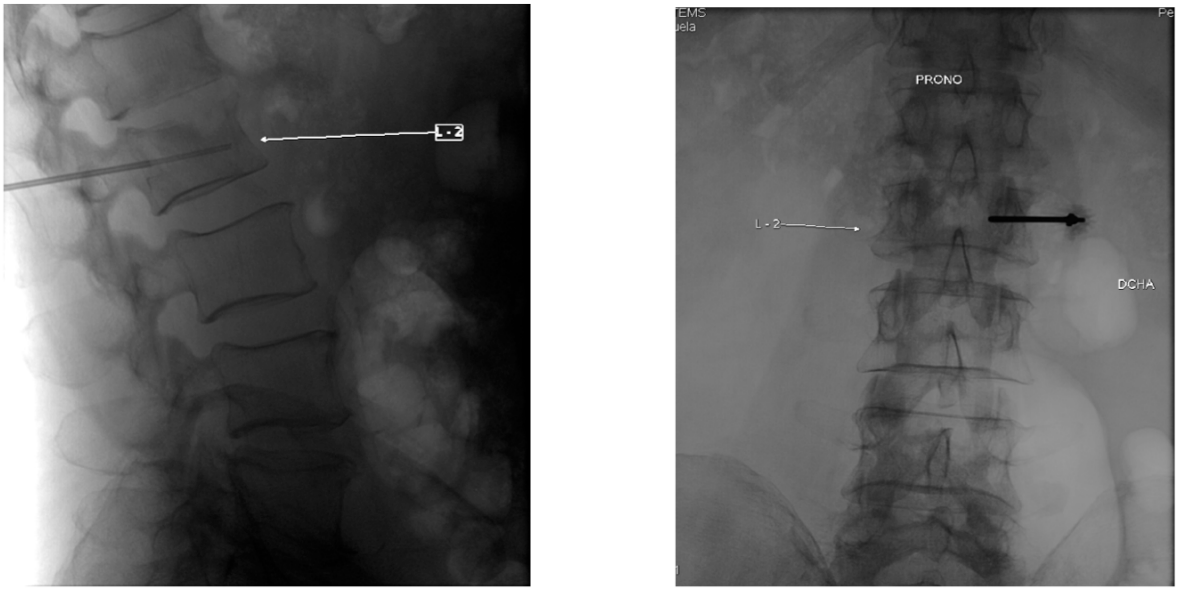

Figure 4: Guided fluoroscopy Core needle biopsy of the L2 vertebral body.

concluding that a TRUSB does not increase mortality (0.095 %) compared to control patients (not subjected to biopsy).

These figures vary compared to other similar studies, such as the Canadian [10] or European ERSPC [11], but both agree on an increase in patient admissions from 1% in 1996 to 4.1% in 2005, attributable to infections and increased antibiotic resistance.

The European study identifies prior prostatitis and benign prostatic hypertrophy among other risk factors related to infections. To these factors, the PLCO study adds the factor of non-Caucasian races for infectious complications.

In a recently published study by Karl-Johan Lundstrom *et al*. [12] the figures are very similar to the studies described above. In the month after the biopsy, 6% of cases presented urinary tract infections, and 1% required hospitalization. In this study, the authors identified having had a urinary tract infection in the previous six months as the most important risk factor along with other comorbidities (as measured by the Charlson index) such as diabetes, urinary symptoms during pharmacological treatment, and antiplatelet treatments. When analyzing the frequency of occurrence of infectious complications over time, they found that complications treated as outpatients declined in recent years, while complications requiring hospitalization increased, especially in patients with high comorbidity. However, they did not observe increased mortality (1%), of which only 0.07% were due to infectious causes (in the remaining 0.93%, the cause was not mentioned).

Infection may clinically present as cystitis, acute prostatitis, or sepsis and, generally, is by gram-negative bacteria *(E. coli* in more than 50% of cases). Proper handling of the biopsy process minimizes these risks [13].

In the work of Adnan Simsir *et al*. In 2010 [14], the possibility of predicting the risk of sepsis (the most serious complication after a TRUSB) was studied, and it was concluded that sepsis was rare (3.06%) but potentially fatal in 0.05% of cases. Although oral antibiotics administered preoperatively and enemas given before the biopsy proved to be effective in reducing the rates of urinary tract infection, patients with urethral catheters or diabetes mellitus and patients who undergo a biopsy of over ten samples per lobe (seven according to other authors [4] should be followed more closely after the biopsy.

VO is a pathology typical of adults, with an incidence of 1/250,000 [15] or 1/450,000 [16], according to the study series consulted. It is twice as common in males as in females [17]. The incidence is increasing mainly due to the increase of nosocomial bacteremia due to the use of intravascular devices, the increasing age of patients, and the use of parenteral drugs.

The infection can reach the bone in three fundamental ways: through the blood, by direct inoculation secondary to trauma or surgery, and from spinal infections in adjacent tissues.

Possible sources of hematogenous dissemination include the urinary tract, skin, subcutaneous tissue (parenteral injections), respiratory tract, intravenous catheters, infected surgical wounds, endocarditis, and dental infections [18]. Other less common causes include infections of heart valves (natural or prosthetic), esophageal rupture, diverticula, and renal abscesses [19]. Hematogenous dissemination rarely occurs after lumbar puncture, myelography, placement of catheters, or epidural injections.

The hematogenous cause is by far the most common. The anatomical characteristics explain the higher incidence and the clinical manifestations of the hematogenous VO in adults. The vertebral tissue has a highly vascularized medulla with a large flow volume, but tortuous, segmental branches come from the posterior spinal artery, which bifurcates to irrigate two adjacent vertebrae. Therefore, bacteria reach the bone tissue of two adjacent vertebrae, establishing the initial focus of the infection, which may extend to the intervertebral disk and other neighboring spaces (epidural or paravertebral). The clinical presentation, therefore, is in the form of spondylodiscitis, with involvement of two adjacent vertebral bodies and the intervertebral disk. The infection may affect only one vertebra (4-8% of cases) and less frequently appears as spondylitis without discitis, discitis without spondylitis, or infection of posterior segments (e.g., vertebral arches, spinous processes [20]. The most common location is the lumbar spine (50-60% of cases), followed by the thoracic and cervical spine.

Most VO is caused by *Staphylococcus aureus,* with more than 50% of cases in most of the study series occurring in developed countries. However, there are other less common but important pathogens, such as gram-negative enteric bacilli (particularly after instrumentation of the urinary tract), *Pseudomonas aeruginosa* and *Candida spp* (frequently associated with sepsis due to intravascular access or use of parenteral drugs), and group B and G hemolytic streptococci (especially in patients with, e.g., diabetes or tuberculosis, [21-23].

The clinical manifestation is back pain of insidious onset, which progressively worsens over time. The pain is often worse at night and may disappear in advanced stages with progressing neurological symptoms such as plegia or paresis. It is usually accompanied by a muscle spasm, increasing the clinical pain.

Fever occurs in 52% of cases [5], frequently masked by taking analgesics.

The differential diagnosis of back pain and fever is broad and includes viral infections, pyelonephritis, or pancreatitis as well as other causes. In the absence of fever, the diagnosis is broader, e.g., osteoporotic or pathologic fractures (metastasis), spondylitis, arthritis, arthrosis, herniated discs, secondary muscle spasms, or spinal cord compression. Because of this wide range of possibilities, there is often a delay in diagnosis (up to 59 days according to studies) [24]. Laboratory studies often show the characteristic features of bacterial infection: leukocytosis with a “left shift” in up to 64% of cases. The elevation of the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) has higher sensitivity, increasing in 98% and 100% of cases, respectively. CRP also more closely correlates than ESR to treatment response.

Hemocultures should be drawn systematically, as they are positive in 25-70% of cases, especially in hematogenous infections. Given that VO is generally a monomicrobial infection, it is usually not necessary to perform more diagnostic tests (biopsies) in patients with positive hemocultures. A post-surgical VO is most frequently a polymicrobial infection, and there may be some discrepancy between the cultures of blood and vertebral tissue, so both techniques should be considered in selected cases. We can also obtain much information from the drainage of collections, such as epidural or paravertebral abscesses, as well as cultures coming from the original focus of the infection (e.g., urinary, skin) in patients in whom there is a clear causal relationship with spondylitis.

If the results of these cultures are negative, the microbiological diagnosis should be confirmed through a vertebral biopsy. A CT-guided percutaneous biopsy, with a sensitivity of 50-75%, is recommended as the first choice. The open surgical biopsy has a sensitivity of 78-86% and is reserved for patients in whom a percutaneous biopsy was negative. If the result of the cultures obtained is negative, a second surgical biopsy is recommended.

High-risk surgical patients should be administered a course of empiric antibiotic therapy for 2-4 weeks while reserving surgery for cases that do not respond to such treatment. All the samples must be processed for culture of aerobes, anaerobes, mycobacteria, and fungi as well as for histological study.

Imaging techniques always start with a plain radiograph, which is the simplest technique. This technique presents changes in the vast majority of

patients but may be normal in the early stages because the characteristic changes take several weeks to appear, thus delaying the diagnosis.

Computed tomography (CT) allows earlier and complete visualization as well as an excellent assessment of cortical bone and adjacent soft tissues. It is especially useful for guiding the vertebral biopsy.

In patients with neurological involvement, magnetic resonance imaging (MRI) is the technique of choice because it has a sensitivity of 90% (even in the first 2 weeks) and facilitates early diagnosis. It is superior to CT in the detection of epidural abscess, so it should be done regularly. However, it cannot be used in patients with certain metal implants and may be normal in patients with linear epidural abscess or meningitis. Both CT and MRI are useful for the diagnosis of psoas abscess, which is a frequent complication of spondylodiscitis.

Bone scintigraphy with technetium-99 is a very useful technique but is less sensitive than MRI (67%).

There are other techniques such as indium-111-labeled leukocyte scintigraphy and Ga-67 SPECT scintigraphy with a sensitivity of 92%. They are rarely utilized and do not detect epidural abscesses as well as MRI.

The FDG-PET scan has a sensitivity similar to MRI and may be the best option if the patient has metal implants, but this technique is not available in most centers, and experience in its use is limited.

CONCLUSION

The need to improve the effectiveness of the TRUSB has led to more samples being obtained in recent years, thereby increasing the risk of complications. Furthermore, increasing antibiotic resistance has resulted in increases in both the number and severity of secondary infections when using this technique, leading to complications such as the one presented in this patient. The risk of death from sepsis after a TRUSB is estimated to be between 0.05 and 0.095%. If we consider the number of biopsies performed worldwide (more than 1 million a year in the USA alone) [25], we can consider it as a significant clinical risk associated with a diagnostic test. We must consider this potential complication and identify clinical conditions that increase the risk of infection to take the necessary preventative measures for each case.

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