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Severe back pain a cirrhotic patient : a diagnostic challenge

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Abstract
Spondylodiscitis is an infection of the intervertebral disc space, involves the vertebrae, causing vertebral osteomyelitis and spread to adjacent epidural space, causing dural, radicular or spinal cord compression. Appears mainly in adult and immunocompromised patients, mainly by haematogenous inoculation from systemic infections with bacteriemia.
Patients with hepatic cirrhosis have frequent bacteriemias, produced by increased gut permeability, immune dysfunction and frequent need for invasive procedures. Despite high frequency of blood stream infections, discitis and vestebral osteomyelitis are rarely reported.
We present the case of a 53 years old woman, diagnosed with class B Child Pugh cirrhosis, which presents with intense back pain and cauda equina syndrome, without clinical signs of infection. Diagnosis was confirmed by spinal MRI, but very soon after treatment onset, the patient suffered a septic shock with haemodynamic instability, which leads to patient's death.
This case illustrates how an unusual complication of cirrhosis – bacteriemia - could precipitate the unfavorable evolution of the patient by producing a remote septic complication. Persistent back pain in a cirrhotic patient should also raise the hypothesis of an infectious cause, in which early management is essential. Early diagnosis in essential for successful treatment, and good prognosis after long-term antibiotic treatment can be achieved in the majority of patients.
Key words: *spondilodiscitis, vertebral osteomyelitis, bacteriemia, hepatic cirrhosis*

Introduction

Spondylodiscitis refers to an infection of the intervertebral disc space, which in the main of the cases involves the vertebrae, causing vertebral osteomyelitis. Spread to adjacent vertebral bodies may occur rapidly through the rich venous networks in the spine. Discitis and vertebral osteomyelitis usually coexist, sharing the same diagnostic workup and the same treatment [1,2].

Discitis appears mainly in adult patients (> 50 years), its incidence increase with age. It is a rare disorder, affecting 2.2 cases /100,000 persons per year [2].

Risk factors for spondylodiscitis are intravenous drug use, endocarditis, degenerative spine disease, prior spinal surgery, diabetes, corticosteroid therapy, or other immune compromised state [3].

The intervertebral disk has no direct blood supply in adults. Mechanisms of disk infection are: a) direct inoculation following trauma, invasive spinal diagnostic procedures, or spinal surgery; b) hematogenous spread in localized or systemic infections or endocarditis; c) contiguous spread from adjacent soft tissue infection. The most frequent mechanism is hematogenous, which occurs after a bacteremia, although the bacteremia is not apparent in every case [4].

Other pathophysiological mechanism is cirrhosis-associated immune dysfunction which is a dynamic phenomenon, comprised of both increased systemic inflammation and immunodeficiency. Immune paralysis dysfunction is characterized by increase in anti-inflammatory cytokines and suppression of proinflammatory cytokines. Increased gut permeability, reduced gut motility and abnormal gut bacterial colonisation contribute together with immune dysfunction to bacterial translocation, endotoxemia, consequently causing systemic inflammatory response syndrome, sepsis, multiorgan failure and death [5]. It has been also proved that the oxidative stress is increased, and antioxidant mechanisms decreased in toxic hepatic failure [6].

In a large study performed in China on 508 cirrhotic patients, the sources for blood stream infections were

primary infections in 54.33% of cases and spontaneous bacterial peritonitis in 40.16% of patients [7].

Bloodstream infections have a bad prognosis in patients with cirrhosis, being characterized by frequent complications like metastatic infections, infective endocarditis, and endotipsitis (or transjugular intrahepatic portosystemic shunt-related infection) [8].

The aim of this paper is presentation of evolution, diagnostic and therapeuthical challenges in a rare clinical entity: spondylodiscitis in a cirrhotic patient.

Method: case presentation

We present the case of a 53 years old woman, living in rural area, admitted in Neurology Department with a two weeks history of intense pain in the lumbar spine, irradiating in both lower limbs especially on the anterior part of thighs. The pain is exacerbated by movements, had a lancinating character and is so intense that walking has become impossible since one week. The patient also complains of asthenia, bloating and epigastralgia. She denies having any traumatic event, fall or excessive physical effort in the previous days.

The patient was diagnosed 2 years ago with hepatic cirrhosis. Toxic (ethanolic) etiology was presumed in the presence of a recognized chronic alcohol consumption and negative viral markers. Four months ago, she was hospitalized in Gastroenterology Department for an acute exacerbation with hepatoportal encephalopathy; Child-Pugh class B cirrhosis was confirmed.

Clinical examination showed skin and scleral icterus, bulging abdominal wall caused by ascites, with collateral venous circulation. The body temperature was normal. Her blood pressure was 90/60 mmHg, heart rate was 60 b/min. Local examination of the lumbar skin showed no particular lesions. Percussion of L1, L2 and L3 spinal apophysis induced intense pain, and palpation reveals tenderness and stiffness of paravertebral muscles, with important limitation of spine's mobility.

The neurological examination confirms weakness of 2/5 on Medical Research Council (MRC) scale at quadriceps and iliopsoas muscles bilaterally, associated with hypotonia and local muscular atrophy of both quadriceps muscles; the osteotendinous reflexes were absent in both lower limbs, the irradiation of the radicular pain corresponds to L1-L2 territories, where hypoesthesia was present; the elongation manoeuvers were intensely positive.

Sphincterian dysfunction was present (urinary incontinence). The patient was unable to stand or walk.

Blood tests at admission showed anemia (Hemoglobin = 9,5 g/dL) with thrombocytopenia (76.000/mm3) and normal leukocytes count, caused by hypersplenismus, and an increase in inflammation markers: elevated ESR (115 mm/1 h) and C-reactive protein (CRP) (11 mg/dl); the patient also presented hypoglycemia (46 mg/dl) – caused by decrease in hepatic glycogenolysis rate; mildly elevated ASAT values (58 U/L), and a cholestatic syndrome -elevated bilirubin levels (1,17 mg/dl direct bilirubin and 2,46 mg/dl total bilirubin), mildly elevated gamaGT levels (71 U/L), which explained the jaundice. The renal function was normal.

Gastroentrology examination confirms Child Pugh class B cirrhosis, and oeso-gastro-duodenoscopy reveals 2-nd degree varicose oesophageal veins.

Lumbar spine plain radiographies showed vertebral collapse at L2 (20%) and and the L1-L2 intervertebral space appears narrowed with irregularity of vertebral endplates (Figure 1).

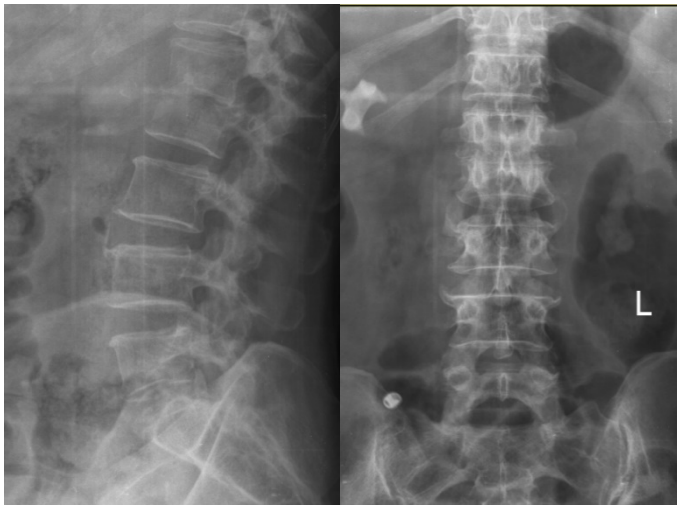

Figure 1: LL (left) and PA (right) radiographies of the lumbar spine

MRI of the lumbar spine (using 1,5 T MRI scanner, with standard protocol for lumbar spine) showed

important inflammatory changes of L1 and L2 vertebrae (low signal T1 and high signal T2 in adjacent vertebral endplate) and of L1-L2 intervertebral disk (low signal in T1, high signal T2 and STIR signal) with contrast enhancement, changes which are extended into the corresponding epidural space, with dural compression (Figure 2), (Figure 3). Abscesses (liquid cavities with enhancing walls) were described in both paravertebral muscles and in the retroperitoneal space; paraaortic limphadenopaties were present (Figure 4).

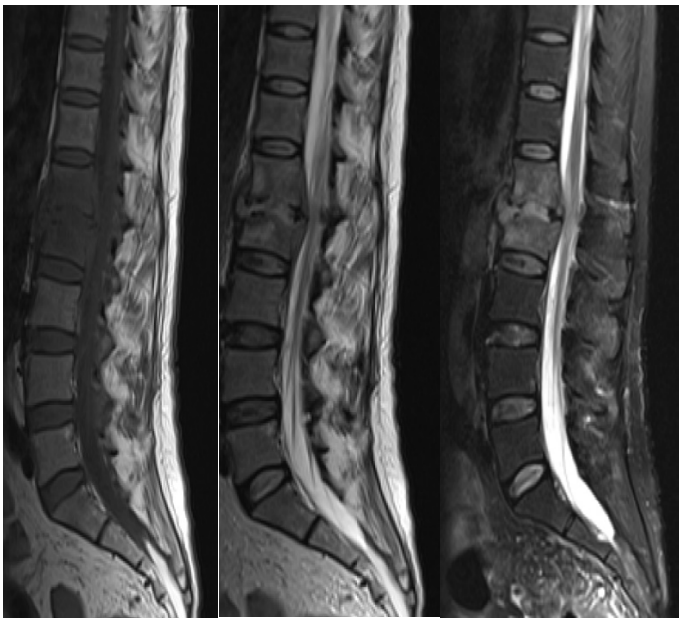

Figure 2: Lumbar MRI in sagital plane: T1 (left), T2 (middle) and STIR (right) showing L1 and L2 osteomyelitis, L1-L2 discitis, epidural abscess and cauda equina compression

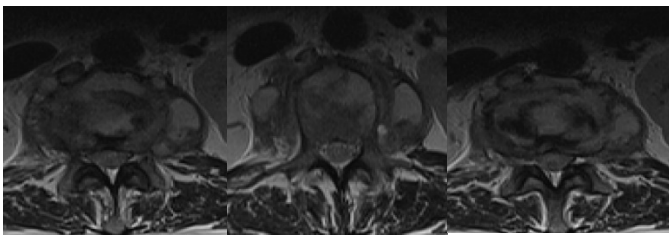

Figure 3: Lumbar MRI , axial T2 sequences, showing inflammatory changes of the vertebra and intervertebral disc with epidural and laterovertebral extension

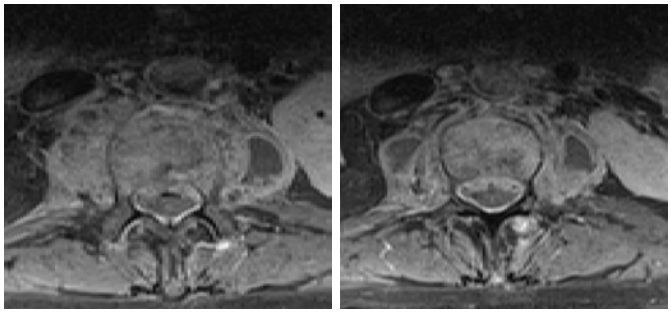

Figure 4: Lumbar MRI, axial T1 with contrast, showing enhancement of the bone, disc and meningeal layers, and enhancing walls of paravertebral abscesses

Empiric antibiotic treatment with Ceftriaxone and Vancomicine was initiated immediately after MRI, and hemocultures were collected. Neurosurgical recommendation was for conservative treatment because of patient's comorbidities, and CT guided vertebral biopsy was scheduled.

The second day after diagnosis, the patient developed haemodynamic instability (blood pressure 70/50 mmHg) and anuria, with alteration of consciousness, possible by septic shock. Cerebral native CT scan was normal, excluding a cerebral hemorrhage. She was transferred to Intensive Care Unit. Despite aggressive treatment and inothropic support, the patient became comatose, and developed an acute hepato-renal syndrome (creatinine 3,42 mg/dl, BUN- 162 mg/dl, Quick time – 27 sec, INR – 2,41, ASAT – 183 U/l, ALAT – 884 U/l), with associated severe anemia (Hb-6,4 g/dl) , thrombopenia (31.000/mm3) and important leucocytosis (16000/mm3). Inflammation markers were highly elevated (CRP – 25 mg/dl and procalcitonin – 12 ng/ml), confirming the septic shock caused by a bacterian infection. Hemocultures were positive for Enterobacter spp. The patient died the third day after diagnosis.

Autopsy was not performed.

For presentation of this case, patient's family consent and Hospital Ethics Committee consent were obtained.

Results:

This patient with known hepatic ethanolic cirrhosis Child Pugh B class was diagnosed with L1 and L2 osteomyelitis, spondilodiscitis and L1-L2 epidural abscess with dural and cauda equina compression, manifested by intense lumbar and radicular pain.

Differential diagnosis in this case was made with tuberculous spondylitis, where the evolution takes a subacute course. A vertebral compression fracture on osteoporosis was excluded on the presence of inflammatory syndrome and lack of traumatic event. Also, a metastatic spinal tumor was excluded on neuroimagistic findings.

Discussion:

In patients with cirrhosis, bacteriemia leading to vertebral discitis is rarely reported [2,9,10]. A series of 39 cases was described in the literature by a group of Korean authors in which 54% of patients had class B Child-Pugh cirrhosis [11].

In our patient, the clinical picture consisted in a upper cauda equina syndrome, associated with vertebral syndrome, back pain being the main symptom. Signs of infection (fever, leukocytosis) were initially missing in our patient. Also, patient denies having any invasive procedures in the month before symptoms onset, and local examination did not find any skin or soft tissue lesions. The etiology of vertebral osteitis and discitis was probable related to hematogenous bacteriemia, and not to spontaneous peritonitis, because the patient has no peritoneal signs.

Patients with hepatic cirrhosis have a high rate of infections, with an occurrence being 10 times higher than in non-cirrhotic individuals [12]. About 20 to 30% of hospital admissions for acute decompensation in cirrhotic patients are related to an infection [8]. Infections are among the most important complications of end-stage liver disease [8], the most common types are respiratory infections and bacterial spontaneous peritonitis [13].

Blood stream infections or bacteriemias are one of the serious complications of cirrhosis, affecting 4–21% of patients [8], being associated with a high mortality rates (30% within 30 days) and representing an important reason for liver failure and death. Compared with non-cirrhotic patients, the occurrence of bacteriemias is significantly higher [7]. Risk factors for bacteriemias in cirrhotic patients are liver failure, long time hospitalisations, history of spontaneous bacterial peritonitis and advanced cirrhosis stage [14,15].

Mechanisms of bacteriemia in cirrhotic patients are [16]:

a) endogenous, explained by dysregulated intestinal bacterial translocation in the blood stream caused by increased gut permeability (exacerbated by slow peristalsis and congestion of the gastrointestinal tract, leading to an excessive growth of the intestinal flora) and by immune dysfunction (loss of the immune surveillance function of the liver)

b) exogenous, explained by frequent hospitalizations, frequent invasive procedures and the use of indwelling devices such as central venous lines or portosystemic shunts.

Spontaneous bacteriemias are generally caused by gram-negative enteric bacilli, anaerobes, and Enterococcus spp [13,16] because the main route of bacteremia in cirrhotic patients is endogenous seeding from the gastrointestinal tract. The gram-negative bacteria such as Escherichia coli and Klebsiella pneumoniae are the leading agents, especially among hospitalized patients [15]. After invasive procedures, staphylococcal bacteriemia is the most frequent [14].

The diagnosis of pyogenic vertebral osteomyelitis in published cases was established by clinical picture, typical MRI findings and isolation of pyogenic microorganisms in blood culture or samples obtained by CT-guided bone biopsy [16]. In our case, MRI aspect was typical for discitis, but rapid deterioration of patient's status made CT-guided biopsy impossible to perform. Hemocultures were positive with Enterobacter spp. . In the literature, bacteriemia was documented in 92% of cases [7], most frequent responsible organisms being Staphylococcus aureus, Streptococci spp., and Enterobacteriaceae [14]. In non-cirrhotic patients, most common isolated germs are gram-negative enteric bacilli [15].

In the published series of cases, 51% developed renal failure [7,11]. In our patient, renal failure was probably related to septic shock with multiorgan failure. Mortality rate is high in literature (38% at 90 days follow-up [7,8].

Conclusion:

The association between hepatic cirrhosis and vertebral discitis is rarely reported, despite the relatively high frequency of infections with bacteriemia in cirrhotic patients. The signs and symptoms of spondilodiscitis are initially non specific (back pain and reduced spinal mobility),

making diagnosis difficult in the absence of signs of systemic infection. Early diagnosis in essential for successful treatment, and good prognosis after long-term antibiotic treatment can be achieved in the majority of patients.

This case illustrates how a rare complication of bacteriemia in cirrhosis could precipitate the unfavorable evolution of the patient. Persistent back pain in a cirrhotic patient should also raise the hypothesis of an infectious cause, in which early management is essential.

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