Case Report

Successful switch to oral therapy with doxycycline in the case of an actinomycotic hepatic abscess

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Abstract

A 72-year-old female was admitted with the symptoms of malaise, loss of appetite, upper right quadrant pain, fever, and sweats, which had been present for last 7 days. CT-scan of the abdomen revealed a hypodense mass in the right liver lobe; histopathological examination of the biopsy specimen yielded a diagnosis of actinomycotic abscess. Treatment with intravenous ampicillin for 8 weeks followed by a course of oral doxicycline for 28 weeks resulted in the complete resolution of the abscess.

Key words: hepatic actinomycosis; medical treatment; doxycycline

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Introduction

Actinomycosis is an indolent, slowly progressive bacterial infection caused by a variety of Gram-positive, non-spore-forming anaerobic germs included in the genus *Actinomyces*. Many *Actinomyces* species are opportunistic pathogens and are included in commensal flora that is found in the oropharynx, gastrointestinal tract, and female genital tract. While cervicofacial infection is the most frequent manifestation of the disease, gastrointestinal involvement occurs in about 13% to 60% of the cases, particularly in the oral cavity [1]. In rare cases, these bacteria can cause disseminated actinomycosis, a disease characterized by the formation of abscesses in the mouth, lungs or the gastrointestinal tract. Pathogenesis of abdominal actinomycosis is presumed to be hematogenous spread through the portal vein from a mucosal injury or other abdominal focus of infection. Hepatic involvement is present in 15% of patients with abdominal infections and represents at least 5% of all cases of actinomycosis [2]. Diagnosis is often difficult because the predominant presenting symptoms are non-specific. Imaging is many times suspicious for neoplasm and positive cultures are notoriously difficult to obtain, making the preoperative rate of diagnosis less than 10%. We report a case of a patient with isolated hepatic actinomycosis cured with medical treatment alone.

Case report

A 72-year-old woman was admitted to the infectious diseases department with seven days' history of fever, chills, malaise and upper right quadrant pain. Her past medical history included hypertension and chronic ischemic heart disease. She was since a week on treatment with prednisone 20 mg per day for a periodontal disease. On admission, her body temperature was 38.6°C. Physical examination showed rebound tenderness at the epigastric region and right upper abdominal quadrant. Laboratory tests showed inflammation (C-reactive protein 128mg/dL and procalcitonin 10ng/ml); leukocytosis (WBC, $13.4x10^9$/L with neutrophils 93%); anemia (hemoglobin 10.7g/dl), elevation of aspartate transaminase, 19.5 upper limit of the normal range (ULN); alanine transaminase 10.2 ULN and alkaline phosphatase, 1.5 ULN; hypoproteinemia, 5.4 g/dL with hypoalbuminemia, 2.4 g/dL. CA 19-9 and alpha-fetoprotein level were normal. We excluded chronic viral hepatitis B or C as AgHBs, anti-HBc, and anti-VHC were negative. Abdominal ultrasound revealed one heterogeneous mass of 10.5 x 8.5 cm in the right liver lobe. It was considered intra-abdominal sepsis, and systemic antibiotic therapy was initiated with meropenem 3 g daily and the patient was transferred to department of surgery for surgical drainage.

A dynamic CT examination with intravenous contrast showed a hypodense mass of 12.4 x 10.5 cm located in the seventh segment of the right liver lobe. No perihepatic fluid was detected. The contour of the liver was smooth and the spleen size was within normal limits. From these findings, liver abscess was highly suspected. A CT-guided fine-needle aspiration and a biopsy of the hepatic mass were both performed. White-yellowish pus was aspirated and histopathological examination of the specimen revealed acute and chronic inflammation, granulation tissue, and Gram-positive branching filamentous rods consistent with an *Actinomyces* species. No pathogen was isolated from the three consecutive blood culture samples obtained. Owing to the typical appearance of the actinomycotic colonies on histopathological examination, other tests were not performed. Drainage was not performed because the lesion compressed the right and middle suprahepatic veins and also the inferior vena cava (Figure). The patient returned to the infectious diseases department and the initial antimicrobial treatment was switched to ampicillin 12 g daily (2 g intravenously every four hours) with complete remission of symptoms. After eight weeks of therapy, a new CT scan showed a reduction in the liver abscess to 5 cm in diameter and inflammation markers normalized. Ampicillin was replaced with oral doxicycline 200 mg daily and the patient was discharged from the hospital the next day. Monthly evaluations indicated good tolerance of therapy without recurrence of symptoms and progressive decrease of the liver mass. A CT scan, performed 139 days after the patient was discharged, showed the complete resolution of the abscess, allowing us to stop the antimicrobial treatment. After three months without antibiotic, the patient exhibited no signs of recurrence.

Discussion

Actinomycotic abscess of the liver is a rare condition. *Actinomyces* species are found as part of the commensal flora in the gastrointestinal tract. They invade the adjacent tissues and bloodstream when normal anatomical barriers are disrupted. Risk factors include previous abdominal or pelvic surgery, poor dentition, alcoholism, biliary tract disease, peptic ulcer, oral neoplasm, immune suppression, long-standing intrauterine contraceptive device, and intravenous drug abuse [3]. In the present case, abdominal CT showed no abnormalities around the hepatobiliary tract. Inflamed gums caused by periodontal disease were thought to be one of the possible entry sites of *Actinomyces* even though the blood culture was negative. Colonoscopy was not performed during hospitalization because the patient refused. Spread to the liver occurs via direct extension from abdominal focus or hematogenously from a distant lesion.

Figure. Dynamic magnetic resonance imaging examination of the liver

The image of the liver shows a solid mass of 14 x 13 cm located in the seventh hepatic segment.

Although our case involves an elderly female, there is a male predominance for hepatic actinomycotic abscess (70% to 97%) with 30 to 50 years being the most common age group [4].

In a review of liver actinomycosis case reports, the most common symptoms were non-specific, including fever (83.3%), abdominal pain (74.5%), and weight loss (50.9%) [5]. Because imaging studies frequently reveal single or multiple lesions, actinomycosis is often misdiagnosed as a primary or metastatic tumor. Definitive diagnosis is based on the demonstration of sulfur granules in the biopsy specimen or aspirated pus and Gram-stained smears and anaerobic cultures.

Treatment of hepatic actinomycosis consists of prolonged antibiotics after surgical debridement and drainage [5]. Penicillin G is the most frequently used antimicrobial to treat actinomycosis, but we chose ampicillin injection as an initial treatment due to a penicillin G shortage. Erythromycin, doxycycline, and clindamycin are other suitable alternatives. Limited *in vitro* data demonstrate that vancomycin, linezolid, and moxifloxacin are active against *Actinomyces*. *In vitro* data also suggest that oxacillin, cephalexin, metronidazole, and aminoglycosides must be avoided [6]. Antimicrobial treatment was switched to doxycycline and not to an oral beta lactam antibiotic because the patient developed a hypersensitivity reaction at the end of the eighth week of treatment with injectable ampicillin. Doxycycline has activity against *Actinomyces* and the selection of resistant bacteria from the normal microflora is low. It is very important to take a sample from the lesion before the start of antimicrobial therapy to identify the etiological agent and if possible to perform antimicrobial susceptibility tests, as support for effective antimicrobial regimens in the initial treatment and also for an oral switch.

The appropriate treatment for liver abscess consists of surgical drainage and antimicrobial therapy. It is necessary to treat this disease with high doses and for a prolonged period of time. As a general rule, a maximum antimicrobial dose for 2 to 6 weeks of parenteral therapy followed by oral therapy for a total duration of 6 to 12 months is required for serious infections, whereas a shorter duration could be sufficient for less extensive diseases, particularly in the oral-cervicofacial region. Monitoring therapeutic effect with imaging tests as computed tomography or magnetic resonance is advisable when appropriate; for our patient, we monitored the hepatic abscess changes with abdominal ultrasonography. Mortality is still high, despite the introduction of guided percutaneous drainage of abscesses and new antibiotics. Although the surgical drainage wasn't performed, the outcome of our patient was favourable with antimicrobial therapy alone.

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