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CASE REPORT

Isolated hepatic actinomycosis mimicking hepatocellular carcinoma: Case report and review

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Actinomyces are a rare cause of the intra-abdominal infection that results in chronic suppurative and infectious granulomatous disease. The liver is involved in 15% of cases with abdominal infection and comprises 5% of all cases. Major risk factors include previous surgery, abdominal trauma, gastrointestinal foreign body, gut lesions, and immunosuppression. Due to the insidious course of the disease, symptoms arise several months after onset of the disease. The diagnosis of liver actinomycosis relies on clinical manifestations and imaging findings. Thus, it is often misdiagnosed as a primary liver cancer or metastatic tumor. Here we describe a case of isolated hepatic actinomycosis that mimicked a hepatocellular carcinoma with pretreatment and posttreatment magnetic resonance imaging findings. The patient was cured with long-term antibiotherapy.

KEYWORDS

actinomycosis, hepatocellular carcinoma, liver infection, MRI, solitary hepatic mass

1 | INTRODUCTION

The *Actinomyces* species, which are gram-positive anaerobic or microaerophilic rods, are part of the commensal flora of the mouth, gastrointestinal tract, and female genital tract. They are commonly associated with infections of the mouth and cervicofacial region. In rare cases, these bacteria can form an abscess, termed actinomycosis, in the oral cavity, lungs, or the gastrointestinal tract, which is a chronic, slowly progressive granulomatous infection. Liver involvement has been reported in 15% of cases with an abdominal infection and comprises 5% of all cases of actinomycosis.[1] Diagnosis of hepatic actinomycosis is often difficult because of its indolent clinical course and nonspecific radiological findings, which can be easily misdiagnosed as a primary liver cancer if it is solitary or as a metastatic tumor if it is multiple with imaging features.

Herein we describe a case of isolated hepatic actinomycosis with magnetic resonance imaging (MRI) findings that mimicked a hepatocellular carcinoma (HCC). We also aim to highlight hepatic actinomycosis in the differential diagnosis of HCC with a review of the current literature.

2 | CASE REPORT

A 66-year-old female who had complaints of malaise, poor appetite, and right upper quadrant pain that had been present for one month was admitted to our hospital. She had a history of hypertension, type 2 diabetes mellitus, and myasthenia gravis. In her initial physical examination, the liver was palpated 4 cm below the rib, consistent with hepatomegaly. She did not have a history of alcohol consumption or smoking. Additionally, she had a history of two percutaneous liver biopsies at a different health center, which were performed one and five years ago, due to pruritus and high serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels. Both biopsies revealed mild chronic hepatitis. One year ago, serum anti-HBV IgG, anti-HCV IgG, and autoimmune hepatitis markers (anti-smooth

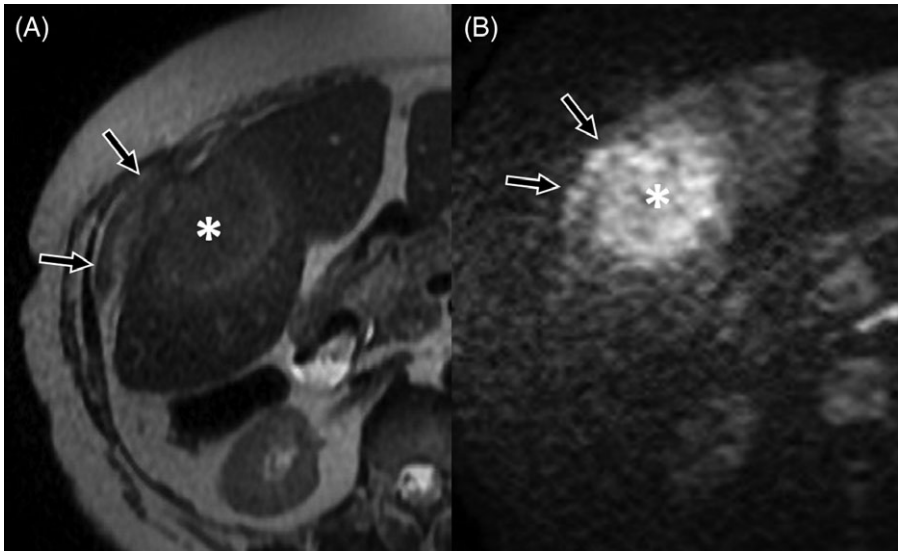

FIGURE 1 Precontrast initial MRI before therapy. A, Lesion (asterisks) is hyperintense on T2W relative to liver parenchyma and invades the adjacent liver capsule (arrows). B, On diffusion-weighted imaging (DWI) sequences, the lesion shows distinctive restriction of diffusion

muscle antibodies [ASMA], antinuclear antibodies [ANA], anti-liver-kidney microsome-1 antibodies [ALKM-1]) were negative, and Antimitochondrial autoantibodies (AMA) was positive in the biopsy specimen. Therefore, the etiology of the chronic hepatitis was not clarified.

In her current laboratory analysis after physical examination, the following values were obtained: serum C-reactive protein level, 13 mg/dL (0–4.9); AST, 47 U/L (0–31); gamma glutamyl transferase (GGT), 235 U/L (0–38); alkaline phosphatase (ALP), 462 U/L (30–120); ALT, 21 U/L (0–38); and total bilirubin 0.34 mg/dL (0–1.2). An abdominal sonography was performed to evaluate the liver morphology and this revealed a 49 × 63 mm sized mass in segment 5 of the liver, mildly heterogeneous liver parenchyma, hepatomegaly (a craniocaudal distance of 19 cm), and splenomegaly (14 cm long axis). Based on these ultrasound results, dynamic contrast enhanced MRI was performed to characterize the liver mass. The mass was hypointense on T1 weighted images, hyperintense on T2 weighted images, and displayed diffuse diffusion restriction on diffusion-weighted imaging (DWI) (Figure 1). After intravenous (IV) gadolinium administration, the lesion was homogeneously enhanced in the early arterial phase (Figure 2). In the venous phase, wash-out and capsular enhancement within the mass were observed (Figure 2). The mass had invaded the liver capsule, and perihepatic free fluid adjacent to the hepatic mass was seen (Figure 2). These imaging features, especially the dynamic contrast enhancement series, fit the diagnosis of HCC, but capsule invasion and pericapsular extension aroused suspicion for exact diagnosis. Besides there was not any predisposing factor that leads to HCC and her alpha-fetoprotein (AFP) level was 1.53 ng/mL (0–9).

Suspicion about malignancy due to imaging findings that was not confirmed by clinical and laboratory findings, directed

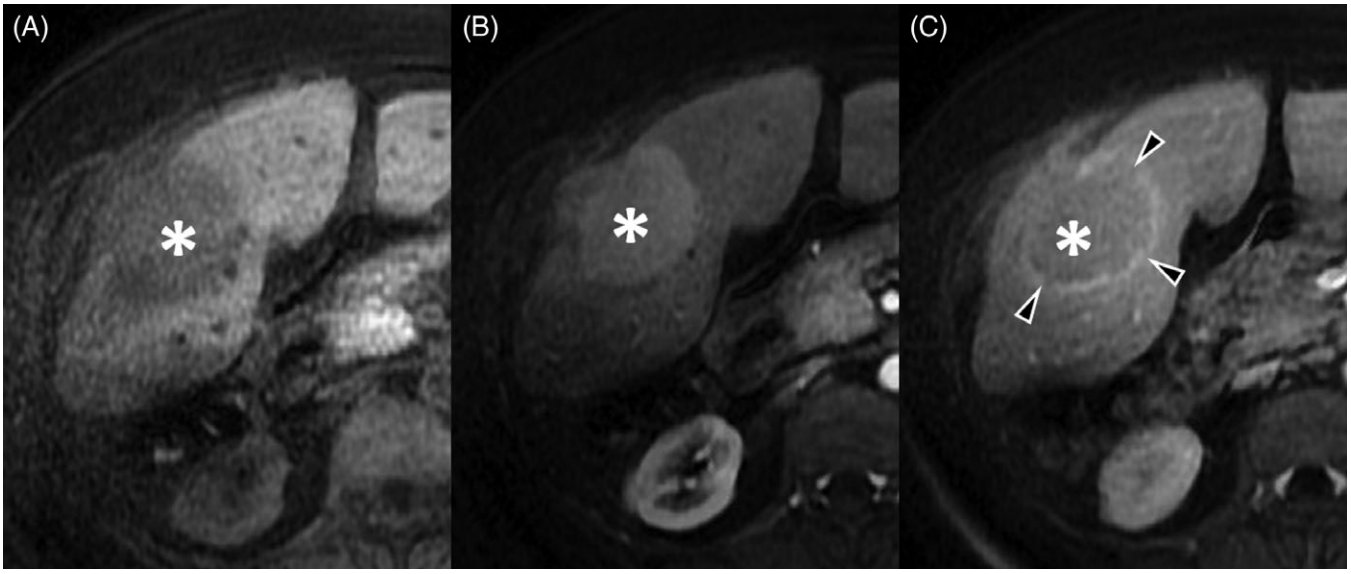

FIGURE 2 Images of the lesion (asterisks). A, Precontrast and B, Postcontrast T1W images show homogeneous prominent contrast enhancement in arterial phase. C, Postcontrast T1W image shows invasion of the adjacent liver capsule and persistence of rim enhancement (arrowheads) in venous phase

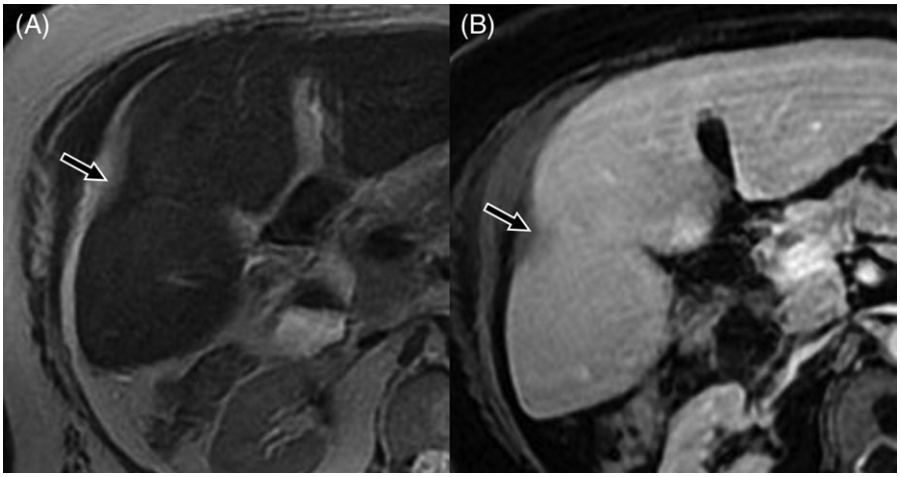

FIGURE 3 Control magnetic resonance imaging (MRI) after six months antibiotic therapy. A, T1W images represent complete resolution of the lesion with minimal sequel and fibrotic changes in the capsule (arrow), adjacent parenchyma and subcutaneous soft tissue. B, After intravenous (IV) gadolinium injection there is minimally fibrotic subcapsular parenchyma, which enhances less than normal liver

us to perform biopsy. Ultrasound-guided percutaneous tru-cut needle biopsy was performed and histopathological evaluation revealed gram-positive branching filaments consistent with actinomycosis. With the diagnosis of actinomycosis, parenteral ampicillin treatment (500 mg every six hours) was started instead of high-dose penicillin G due to the presence of myasthenia gravis. Incidentally, a hematoma had formed in the perihepatic area and the abscess was next to the hematoma. At the end of two weeks, there was no significant change in the size of the lesion and percutaneous drainage of the abscess was attempted. This failed because the lesion was solid and associated with actinomycosis from the liver through the subcutaneous area. Microbiological examination of the biopsy material revealed a proliferation of *Pseudomonas aeruginosa*, in addition to the actinomycosis. After these results, ampicillin treatment was stopped and IV piperacillin–tazobactam (3.375 g every six hours) was started. After two weeks of piperacillin–tazobactam treatment, dynamic contrast-enhanced abdominal MRI was performed and no relevant change was found. The patient's laboratory findings and symptoms improved at the end of three weeks. The IV piperacillin–tazobactam was stopped, and the patient was discharged from the hospital with oral ampicillin treatment (500 mg every six hours) for six to eight weeks. Eventually, a control MRI was ordered two months after her discharge and showed that the liver mass had completely resolved (Figure 3). There was no enhancement or diffusion restriction and only minimal sequela of T1 weighted hypointensity, correlated with fibrosis, remained in the hepatic parenchyma.

3 | DISCUSSION

Actinomyces species are slow growing, gram-positive, nonspore forming bacteria that inhabit microaerophilic and anaerobic conditions. Six of 13 *Actinomyces* species are associated with human disease (israelii, naeslundii, bovis, odontolyticus, viscosus, and arachnia propionica). They are a rare cause of intra-abdominal infection, and by far the most common human pathogen among them is *Actinomyces israelii*, which is a cause of chronic suppurative and granulomatous infectious disease.[2] Liver involvement of actinomycosis usually occurs by hematogenous spread via the portal vein from mucosal injury or infection.[3] Major risk factors include previous surgery, abdominal trauma, gastrointestinal foreign body, gut lesions (ulcer, fistula, tumor), and immunosuppression. Despite the known risk factors, hepatic involvement is cryptogenic in 80%[4] and polymicrobial in 33% of cases.[5] Although our patient was an elderly woman, there is a male predominance for hepatic actinomycosis (70–97%) with 30–50 years being the most common age group.[6] A potential cause for concern in our patient was her history of several percutaneous liver biopsies. It is possible that these repeated biopsies predisposed her to actinomycosis.

Hepatic actinomycosis is reported as a solitary liver abscess in 70% of cases. It is characterized by a single abscess collection occurring more frequently in the right liver lobe. The abscess includes central necrosis that is enveloped by fibrin tissue and granulations.[7] Due to the insidious course of the disease, precise diagnosis may take several weeks or months after presentation.[8] The most frequent symptoms are fever (83.3%), abdominal pain (74.5%), and weight loss (50.9%).[5] Laboratory examinations present with an elevation of serum ALP and GGT levels, as seen in our case.[9] The diagnosis of liver actinomycosis relies on clinical manifestations and imaging findings. Thus, it is often misdiagnosed as a primary liver cancer or metastatic tumor.[10] It is crucial to distinguish it from both malignant and benign (cystic lesions, pyogenic abscess, amebiasis, or echinococcosis) hepatic lesions, regarding characteristics of the lesion.[6] MRI features include a hypointense signal on T1 and hyperintense signal on T2 weighted images.[11] In our case, besides these features on precontrast images, the lesion represented the features of malignancy on contrast-enhanced T1 weighted images as well, which showed enhancement on early phase and washout on post-contrast delayed phases, just as HCC, which is an uncommon finding for actinomycosis and other liver

infectious diseases. Furthermore, according to American Association for the Study of Liver Diseases (AASLD) practice guideline, without any evidence of underlying cirrhosis, imaging is not solely definitive for the diagnosis of HCC and histopathological evaluation is recommended.[12] All these factors entailed us to perform biopsy in this patient.

Definitive diagnosis of hepatic actinomycosis is based on blood cultures and histopathological examination (either percutaneous biopsy or surgical excision) that reveal basophilic filaments and yellow sulfur granules.[5] Blood culture was only positive in 15% of cases.[13] Available therapeutic options are antibiotics, surgical resection, or percutaneous drainage, either alone or in combination.[4] The medical treatment regimen for actinomycosis is using a penicillin derivative.[5] In our case, due to myasthenia gravis diagnosis, instead of penicillin, we applied ampicillin. Duration of therapy is variable, ranging between three to six months.[8] Despite the delay of definitive diagnosis and a corresponding delay in initiating therapy, the outcome is satisfactory with a mortality rate of 7.6%.[6] There were no significant differences in mortality between those that received antibiotics alone and those that combined antibiotics with either percutaneous drainage or surgical intervention.[11] After two weeks of antibiotherapy our patient underwent percutaneous drainage, but because of the solid form of the lesion the procedure failed. She was cured at the end of three months with antibiotic therapy alone, and this recovery was compatible with MRI findings.

4 | CONCLUSION

Solitary hepatic actinomycosis is an uncommon and frequently overlooked etiology for a liver mass. Because of its nonspecific imaging findings and common symptomatology, it can be easily confused with malignancy, especially hepatocellular carcinoma. Physicians should be aware of this differential in the diagnosis and if there is any suspicion, the patient should undergo a biopsy.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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