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CASE REPORT

Hepatosplenic actinomycosis in an immunocompetent patient

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Hepatosplenic abscess caused by *Actinomyces* is rare and often misdiagnosed as malignancy. Herein, we report a case of hepatosplenic actinomycosis in a 37-year-old immunocompetent man with a 2-month clinical history of intermittent fever and upper left abdominal pain. Physical examination revealed a mildly ill-appearing man with a low-grade fever (38°C) and upper left quadrant abdominal tenderness. Abdominal sonographic examination showed the presence of a 6.3 cm × 6.5 cm heterogeneous abscess with a hypoechoic center and honeycomb appearance in an enlarged spleen (8 cm × 5 cm). Computerized tomography of the abdomen revealed a multiloculated splenic lesion, and laparotomy showed multiple hepatic nodules and a splenic abscess. Histopathological examination of the biopsy revealed filamentous branching bacilli and sulfur granules in the hepatosplenic abscess. The patient successfully underwent splenectomy accompanied by intravenous and oral penicillin treatment. Proper and prompt diagnosis of hepatosplenic actinomycosis is important because the therapeutic plan and prognosis of this pathogen are quite different from other microorganisms and malignancies.

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Introduction

Actinomyces spp. are Gram-positive, microaerobic-to-anaerobic filamentous bacteria that cause actinomycosis and are opportunistic organisms that normally colonize the upper respiratory tract, the gastrointestinal tract, and female genital tract. *Actinomyces israelii* is the most commonly reported pathogenic species. Actinomycosis often masquerades as tumorigenesis, and formulating the proper diagnosis—tumor versus abscess—is often difficult.[1,2] Abdominal actinomycosis has been reported at various locations, including pelvic abscesses in association with intrauterine devices, the abdominal wall, liver, appendicitis, anus with spread to the scrotum, and the rectum.[1–5] Hepatic involvement has been reported in 15% of cases of abdominal actinomycosis and 5% of cases of actinomycosis.[6] Splenic actinomycosis is rare and usually associated with various immunocompromised conditions, such as leukemia, diabetes, autoimmune disease, and alcoholism.[7–10] Here, we report a novel case of hepatosplenic actinomycosis in an immunocompetent patient who recovered after splenectomy and prolonged administration of penicillin.

Case report

A 37-year-old man was admitted to En-Chu-Kong Hospital with a 2-month history of intermittent fever and upper left abdominal pain. He had not undergone prior oral, abdominal, or endoscopic procedures and had no history of surgery, abdominal trauma, foreign body ingestion or aspiration, or typhoid fever. Physical examination revealed a mildly ill-appearing man with a low-grade fever (38°C) and upper left quadrant abdominal tenderness, but no lymphadenopathy was noted in cervical, axillary, or inguinal areas. We did not observe the presence of oropharyngeal ulcers, but we did notice gingival swelling, a few caries, and severe calculi in foul-smelling oral cavities. The chest was clear to auscultation, and the patient's heartbeat was regular without murmurs, rubs, or gallops. Chest radiograph showed no cardiopulmonary disease, and an electrocardiogram (ECG) showed no abnormalities. Initial laboratory values included the following: leukocyte count, 13.2 $\times$ $10^3/\mu L$ (79% neutrophils, 14.4% lymphocytes, 7.1% monocytes, 0.2% eosinophils, 0.3% basophils); hemoglobin, 12.3 g/dL; platelet count, 297 $\times$ $10^3/\mu L$; aspartate aminotransferase (AST), 2 IU/L (normal: <38 IU/L); alanine aminotransferase (ALT), 40 IU/L (normal: <41 IU/L); alkaline phosphatase (ALP), 216 IU/L (normal: <128 IU/L); total bilirubin, 0.3 mg/dL (normal: <1.2 mg/dL); gamma-glutamyltransferase, 132 IU/L (normal: < 63 IU/L); C-reactive protein (CRP), 19.87 mg/dL (normal: <0.44 mg/dL); complement components C3, 109 mg/dL (normal: 90–180 mg/dL); and complement component C4, 22.7 (normal: 10–40 mg/dL). Antinuclear antibody (ANA) testing was negative. Serum protein electrophoresis revealed the following: albumin, 3.0 g/dL (normal: 3.2–5.0 g/dL); α-1

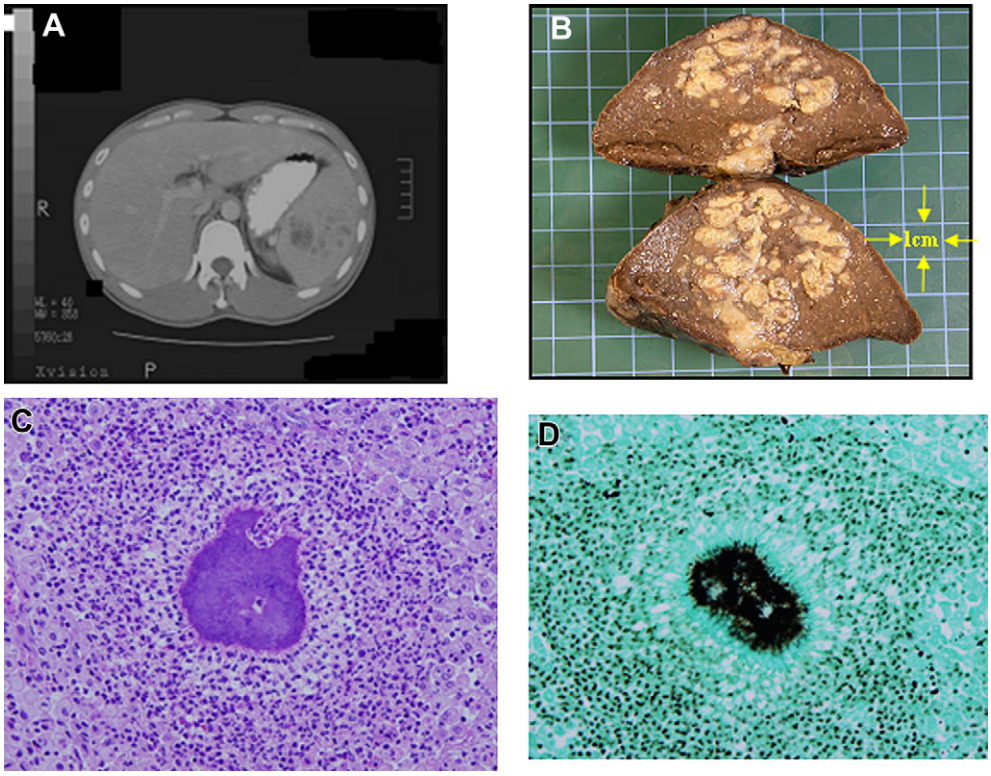

Figure 1 (A) CT radiograph showing ill-defined hypodense lesions with septum in the spleen. (B) Gross pathological specimen. On splenic resection, the spleen exhibited surface nodularity. Multiple pus-filled nodules were sectioned. (C) Filamentous bacteria in a sulfur granule surrounded by inflammatory cells (hematoxylin and eosin stain, 400×). (D) Characteristic filamentous bacteria radiating from the peripheral border (Grocott-Gomori methenamine-silver nitrate stain, 200×).

globulin, 0.4 g/dL (normal: 0.1—0.4 g/dL); α-2 globulin, 0.6 g/dL (normal: 0.6—1.0 g/dL); β-globulin, 0.9 g/dL (normal: 0.6—1.3 g/dL); and γ-globulin 1.7 g/dL (normal: 0.7—1.5 g/dL). He was a carrier of hepatitis B antigen, was negative for anti-hepatitis C antibody. Human immunodeficiency virus (HIV) serology was negative, and his immunocompetency was verified through normal CD 4 and CD 8 counts and normal serum immunoglobulin G, M, and A. Antibody testing for amoeba (indirect hemagglutination assay) was negative. Alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), and carbohydrate antigen 19-9 levels were within the normal ranges. Abdominal sonographic examination revealed a 6.3-cm heterogeneous abscess with a hypoechoic center and honeycomb appearance in the spleen. Contrast-enhanced computed tomography (CT) of the abdomen showed a 6 × 5 cm, ill-defined hypodense lesion in the spleen; however, no liver lesions were found (Fig. 1A). There was no lymph node enlargement and no abnormal fluid collection. Transthoracic echocardiography demonstrated mitral valve prolapse but no valvular vegetation. We empirically administered 1 g ceftriaxone every 12 hours and 500 mg metronidazole every 8 hours. High fever persisted for 6 days of treatment. Then, the patient underwent exploratory laparotomy, which revealed multiple liver nodular lesions (18 nodules measuring 0.5 × 0.5 cm) and a splenic abscess. The resected spleen measured 11 × 7 × 6 cm (Fig. 1B) and weighed 172 g. Frozen sections of the resected spleen and liver nodules showed acute purulent and chronic inflammatory cell infiltration admixed with necrotic substance. Some microorganisms with sulfur granules were observed within hematoxylin and eosin (H&E)-stained necrotic foci (Fig. 1C). These were filamentous Gram-positive and acid-fast negative bacilli. Grocott-Gomori methenamine silver nitrate staining indicated the presence of splenic and hepatic actinomycosis (Fig. 1D). Treatment was changed to intravenous high-dose penicillin G (18 million units per day) for 1 month. Bacteria failed to grow on both blood and tissue culturing. The subject was doing well and shifted to oral penicillin for 3 months. After 4 months of treatment, abdominal MRI demonstrated the total absence of hepatic lesions. On further follow-up after more than 2 years, the patient continued to be asymptomatic.

Discussion

According to the literature, mainly cervicofacial (30—50%), thoracic (20—30%), and abdominal (20—30%) actinomycosis present.[6,11,12] Splenic involvement is very rare. A thorough search of the English literature identified only six cases of splenic actinomycosis that were classified as single-organ involvement (Table 1),[7—10,13,14] and, to date, no cases of actinomycosis have been reported with both splenic and hepatic involvement in an immunocompetent patient. Destruction of the mucosa barrier as a result of surgical trauma, appendicitis, diverticulitis, immunosuppression, typhoid fever, or hematologic malignancy are well-recognized factors that predispose patients to this infection.[12] Multiloculated splenic abscesses may stem from a distant infection, and spread to the liver may directly occur through splenic foci or indirectly via blood from

Table 1 Up-to-date overview of the English-language publications on splenic actinomycosis.

Reference	Age/gender	Co-morbidities	Biopsy confirmed	Culture Report	Lesion Size	Treatment	Antimicrobial, Duration	Outcome
(8)	47/male	Acute myeloid leukemia (AML)	Yes	Negative	2 cm	Splenectomy	Amoxillin/clavulanic acid, 6 months	Died of AML
(9)	72/female	Diabetes type 2	Yes	Negative	Multiple abscesses	Splenectomy	PCG, 6 months	Recovered
(10)	14/female	Autoimmune hepatitis, endocarditis	None	*A. meyeri*	4.4 × 2.6 cm, 1.4 × 1.4 cm	Needle aspiration	Imipenem/cilastin, 58 days	Recovered
(11)	69/male	—	Yes	Negative	6 cm	Splenectomy	PCG, 3 months	Recovered
(12)	18 months/female	—	Yes	*A. naeslundii*	5 × 5 cm	Drainage failure, splenectomy	PCG, 6 months	Recovered
(13)	40/male	Alcoholism	Yes	Negative	Splenic rupture	Splenectomy	PCG, 2 weeks	Recovered

Abbreviation: PCG, penicillin-G.

cryptic foci in distant organs. Dental caries have also been suspected as entry sites in a previously reported case.[15] In this patient, there was no evidence of previous surgical intervention and no cutaneous wounds could be identified. Severe chronic periodontitis and poor oral hygiene may be the port of entry of actinomyces.

Actinomycosis can be accurately diagnosed by isolating *Actinomyces* spp. in culture, but the specimen must be fresh and placed immediately into anaerobic conditions, and the rate of microbiological diagnosis is only 20—40%.[6,11] The presence of granules (sulfur granules) in pus or histological sections is suggestive of actinomycosis. On H&E stains, the bacteria are clumped by the radiating fringe of club-like organisms in the sulfur granules and surrounded by neutrophils and lymphocytes. However, the presence of granules is not pathognomonic of actinomycosis like other organisms, such as *Nocardia* during mycetoma, because *Streptomyces* spp. and staphylococci may also produce such granules. Grocott-Gomori methenamine silver staining can identify branching organisms that are characteristic of the presence of actinomycosis.[12] Both *Actinomyces* and *Nocardia* infections are associated with a similar clinical presentation, but *Nocardia* infections do not form sulfur granules in visceral organs except during mycetoma. Both species are Gram-positive bacilli, but *Actinomyces* spp. are acid-fast negative. While it is difficult to distinguish splenic actinomycosis from other bacterial infections before surgical intervention, the clue might be the actinomycotic chronic presentation characteristic of the former.

Radiological examination is not generally useful. CT findings of a solitary or multiple hypodense lesions in the splenic parenchyma are suggestive of splenic actinomycosis, but do not rule out other microbial infections or malignancies. Moreover, the resolution of the abscess can be followed by CT or magnetic resonance imaging. In this patient, lesions in liver were not detected by the CT scan because they were only approximately 0.5 cm in size, which is beyond the limitations of CT cutting by 1 cm. Bacterial growth was not detected in the blood or tissue cultures, possibly because the growth rates of these organisms are slow because the patient was receiving antibiotics when the samples were obtained.

Most of the reported cases of splenic abscess were caused by actinomyces, received splenectomy due to large abscesses, and failed to respond to treatment with chemotherapy alone. Extirpation surgery (splenectomy) and high-dose penicillin (10—20 million units per day) are recommended for treating splenic abscess. A 3-month course (parenteral penicillin) for 4—8 weeks, following by oral penicillin for 4—8 weeks, should be adequate. The resolution of the abscess should be monitored and tracked by CT or magnetic resonance imaging.

In conclusion, here we demonstrate that hepatosplenic actinomycosis can mimic other infections, including bacterial and fungal infections, tuberculosis, and malignancy. It is important to confirm the diagnosis of actinomycosis using laboratory and pathological testing of clinical specimens because the treatment of other infectious causes of hepatosplenic abscess may be entirely different.

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