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A Case of Sarcoidosis Presenting as Cirrhosis and Portal Hypertension

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Authors' contributions

This work was carried out in collaboration between all authors. Author HY designed the case report. Author CT wrote the case report. Author AS managed the laboratory results. Author NK was the pathology consultant. Author MB managed the literature searches. All authors read and approved the case report.

Case Study

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ABSTRACT

Sarcoidosis is a systemic granulomatous disease of unknown etiology that can involve nearly all organs. Liver is the third most commonly affected organ following the lungs and the lymph nodes. Cases with liver sarcoidosis are usually silent clinically while a few can progress to cirrhosis and portal hypertension in less than 1% of the patients.

A 56 year old female was referred for ecchymosis, protuberant abdomen, bilateral pretibial and ankle edema. Medical history did not reveal any previous disease. Ascites, hepatomegaly, splenomegaly, and facial telengiectasies were present on physical examination. Chest x-ray and CT were normal. Papules and plaques on the knees developed six days after admission. Skin biopsy revealed granulomatous dermatitis. Serum ACE was 250 IU/L. Liver biopsy showed non-caseiting granulomas, severe hepatitis and fibrosis. Sarcoidosis was confirmed based on high serum ACE, histopathologic findings of the skin and liver biopsy samples that revealed non-caseiting granulomas.

We report a case of sarcoidosis complicated by cirrhosis as the initial manifestation of the disease without lung involvement. An extensive literature review of sarcoidosis,

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focusing on case reports, which presented with cirrhosis and portal hypertension without lung involvement, was made.

Keywords: Sarcoidosis; cirrhosis; portal hypertension; liver sarcoidosis.

ABBREVIATIONS

WBC: white blood cell; Hgb: hemoglobin; ESR: erythrocyte sedimentation rate; AST: aspartate aminotranferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; GGT: gamma-glutamyl transferase; PT: prothrombin time; ACE: angiotensin-converting enzyme CT: computed tomography; BAL: bronchoalveolar lavage; ASMA: anti-smooth muscle antibody; HBV: hepatitis B virus; HCV: hepatitis C virus; HDV: hepatitis D virus; LKM: anti-liver microsome type 1 antibody; AMA: antimitochondrial antibody; $FEV_{1:}$ forced expiratory volume in one second; FVC: forced vital capacity; DLCO/VA: diffusion capacity; ANA: antinuclear antibody; RF: rheumatoid factor; Anti-ds-DNA: anti-double-stranded DNA ; Anti-Sm: anti-Smith antibody; Anti-SS-A: anti- SS-A antibody; Anti-SS-B: anti- SS-B antibody; Anti-Scl-70: anti-scleroderma antibody; Anti-Jo-1: antihystidil transferase synthase.

1. INTRODUCTION

Sarcoidosis is a disseminated disease characterized by the presence of non-caseating granulomas [1-3]. It can involve all organ systems to a varying extent and degree [4,5]. Sarcoidosis affects the lungs in approximately 90% to 95% of the patients. Liver is the third most commonly involved organ after the lungs and the lymph nodes [2,3,6]. Sarcoidosis presenting as chronic liver disease is uncommon, although hepatic granulomas can be identified in approximately two thirds of the patients with systemic sarcoidosis. Liver involvement is usually asymptomatic and diagnosis is difficult because no single laboratory test or clinical finding is definitively pathognomonic. Most cases of liver sarcoidosis are clinically silent with only a few patients developing portal hypertension. Cirrhosis is a very rare complication occuring in less than 1% of the patients [1,6-10].

Chronic liver disease associated with sarcoidosis may be challenging. We present a case of sarcoidosis complicated with cirrhosis and portal hypertension along with review of the literature. Manifestations of cirrhosis and portal hypertension were the initial features of the disease without lung involvement.

2. CASE REPORT

A 56 year old woman was admitted for the evaluation of ecchymosis, protuberant abdomen, bilateral pretibial and ankle edema. The patient did not have a previous history of sarcoidosis and any other disease. There was no exposure to drugs or occupational toxic agents. She was a nonsmoker. Physical examination revealed facial telengiectasies, ascites, bilateral lower limb oedema extending till the level of knee, diffuse hepatomegaly of 4 cm below the costal margin, and 2 cm splenomegaly. Blood pressure was 110/70 mmHg. Chest examination was normal with a respiratory rate of 16/minute. Papules and plaques on the knees (Fig. 1) developed on the sixth day of her admission. Initial laboratory data included a normal blood count (WBC: $4.9x10^3$ cells/mm^3, normal: $4.5\text{-}10.5x10^3$ cells/mm^3), normocytic anemia (Hgb: 10.6 g/dL, normal: 12.0-16.0 g/dL), ESR: 42 mm/h (normal: 0-30 mm/hr), AST: 90 U/L (normal: 10-36 U/L), ALT: 28 U/L (normal: 10-40 U/L), ALP: 192 U/L (normal: 25-100

U/L), GGT: 91 U/L (normal: 5-25 U/L), total bilirubin: 3.45 mg/dL (normal: 0.3-1 mg/dL), direct bilirubin: 2.40 mg/dL (normaL: 0.0-0.2 mg/dL), total protein: 6.67 g/dL (normal: 6.5-8.3 g/dL), albumin: 2.34 g/dL (normal: 3.5-5.2 g/dL), and, PT: 16.1 seconds (normal: 11.0-13.0 seconds). Serum ACE was 250 U/L (normal: 8-53 U/L). Tuberculin test was negative. Chest x-ray and thorax CT were normal. Biopsy of the cutaneous lesions showed granulomatous dermatitis. BAL lymphocyte count and CD_4/CD_8 ratio were within normal limits. Transbronchial and bronchial biopies revealed normal lung tissue. BAL culture for bacteria, fungus and mycobacteria was negative. Abdomen CT revealed hepatomegaly, splenomegaly and ascites. The ascites was transudative type with a 1.6 serum-ascites albumin gradient. Liver biopsy revealed loose epitheloid non-caseiting granulomas, severe hepatitis, and hepatic fibrosis compatible with sarcoidosis and cirrhosis (Fig. 2). Serologic markers for HBC, HCV, HDV, ASMA, and, LKM were negative. AMA was <1/100. Pulmonary function tests were within normal limits (FEV_1:112%, FVC:102%, FEV_1/FVC:98%, DLCO:83%, and DLCO/VA:84%). Screening for systemic rheumatologic disease with ANA, RF, Anti-ds-DNA, Anti-Sm, Anti-SSA, Anti-Scl-70, and, Anti-Jo-1 was negative. Endoscopic examination revealed grade II varices in the esophagus. The final diagnosis was sarcoidosis complicated by cirrhosis and portal hypertension. The patient was commenced on 48 mg/day oral methylprednisolone and furosemide 40 mg/day. Steroid treatment was stopped after 12 months. The patient is followed up as an outpatient.

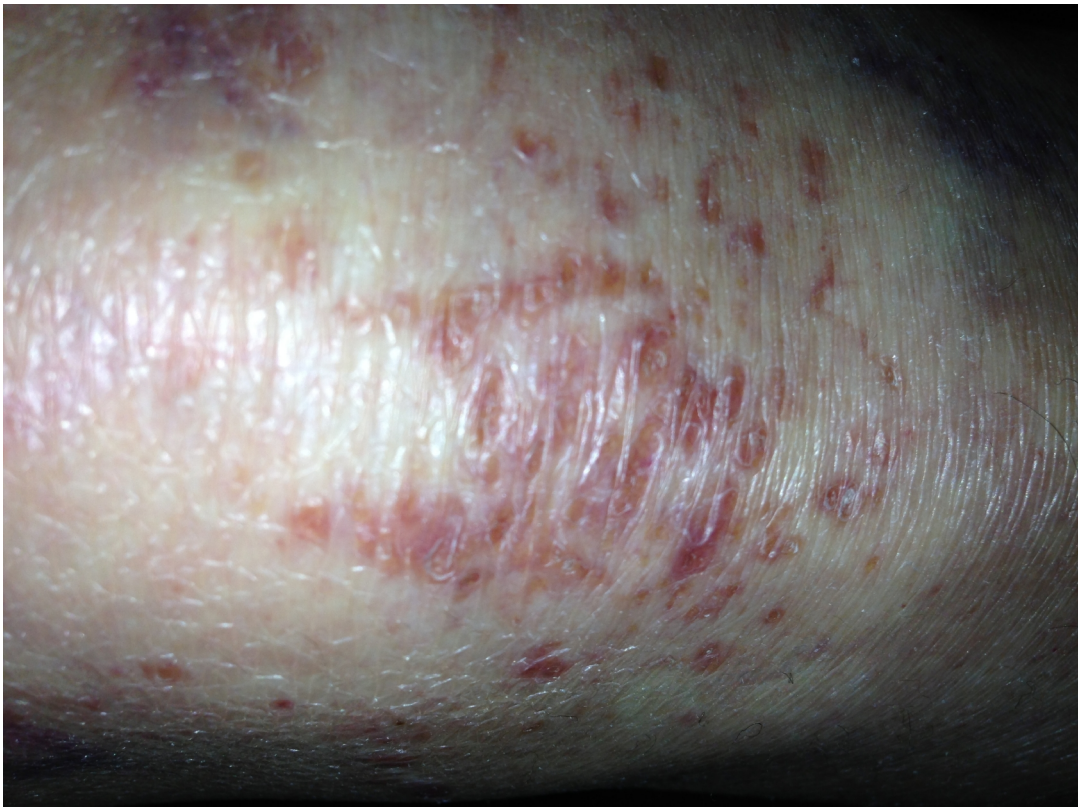

Fig. 1. Plaques and papules on the knees

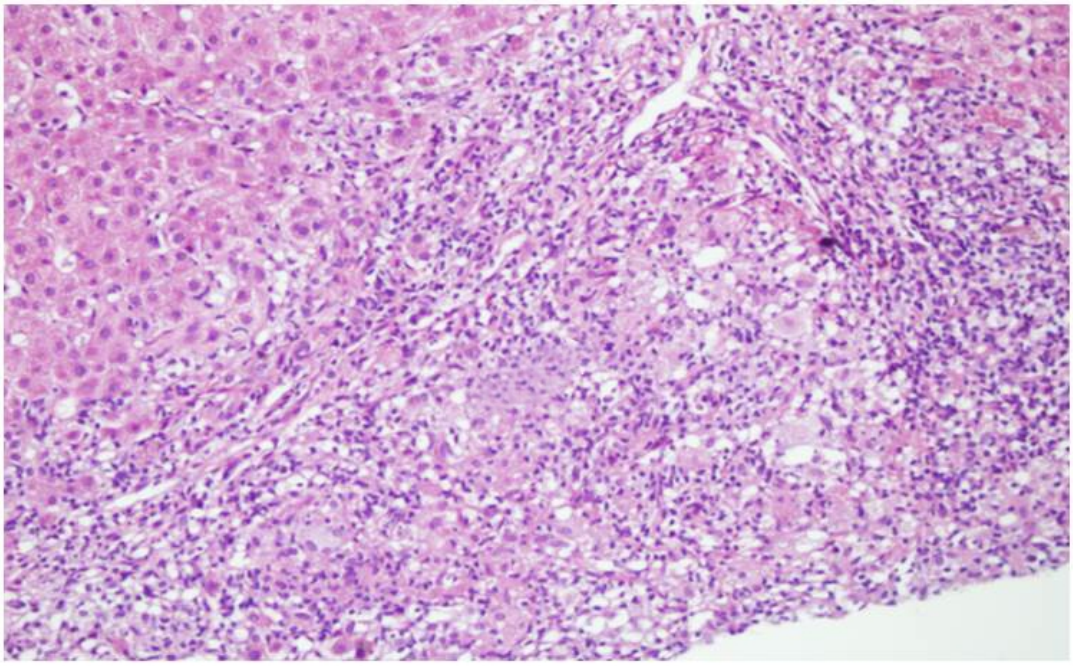

Fig. 2. Loose epitheloid non-caseiting granulomas, severe hepatitis with periportal necrosis, and hepatic fibrosis (HE, X200)

3. DISCUSSION

Sarcoidosis is a systemic granulomatous disease characterized by non-caseating granulomas that may involve any organ to a variable extent. Isolated extrapulmonary disease is rare accounting for less than 10% of cases [8]. Liver involvement is frequent (35%) ranging from asymptomatic incidental hepatic granulomas with mild liver function abnormalities to portal hypertension from granulomas in the portal triad [6,7]. Cirrhosis is a rare complication of sarcoidosis [1,6,7]. The first case was reported in 1949 by Mino et al. [11], followed by Katskin in 1950 [12]. Since then, sarcoidosis with cirrhosis has been increasingly reported [1]. Our patient presented with cirrhosis and portal hypertension with no other manifestations of sarcoidosis at the initial setting with skin involvement developing six days after admission. Medical history did not reveal any previous disease. The high serum ACE supported the diagnosis of sarcoidosis which was confirmed by histopathologic findings revealing the presence of sarcoid granulomas in the skin and liver.

Diseases that may cause cirrhosis were excluded and there was no history of exposure to drugs or occupational toxic agents. Pulmonary symptoms or laboratory findings associated with sarcoidosis were not present. The patient may have had pulmonary sarcoidosis in the past with a spontaneous resolution which is a frequent occurence [2,3]. Symptoms of cirrhosis and portal hypertension were the initial manifestations as the presenting features of sarcoidosis in this patient. The only clue to sarcoidosis was the nonspecific granulomatous skin lesions that may also be encountered in other diseases. High serum ACE may be regarded as an indirect evidence of sarcoidosis since it is well known that cirrhosis and other diseases may also lead to elevated ACE levels. Therefore, the high serum ACE was an equivocal finding from the diagnostic point of view in our patient.

Because sarcoidosis is a systemic disease, diagnosis is based on compatible clinical presentation involving at least two organ systems with supporting evidence of non-caseiting granulomas [13,14]. At presentation, 90% to 95% of sarcoidosis patients have pulmonary disease and up to 50% of the cases have skin, liver, peripheral lymph node or eye involvement. Conversely only 2% of the cases have extrapulmonary disease without pulmonary involvement [4]. There were no clinical or laboratory findings associated with pulmonary sarcoidosis in our patient. Past medical history did not reveal any evidence for the existence of sarcoidosis either.

Cirrhosis is seen in less than 1% of the patients that can further lead to portal hypertension in 3% of the patients [6-10,15]. Liver sarcoidosis is often difficult to diagnose considering the absence of any spesific laboratory or radiologic findings, and its variable manifestations, especially when the lungs are uninvolved. No precise guidelines are available for the diagnosis of hepatic sarcoidosis to date. Diagnosis is achieved by clinical and radiologic findings suggestive of sarcoidosis, supported by the presence of non-caseiting granulomas in the liver biopsy specimens with exclusion of other etiologies for granuloma formation [10]. Histopathologic examination of the liver biopsy samples was compatible with sarcoidosis and cirrhosis leading to final diagnosis in our patient.

After a literature search and as far as we know, this patient appears to be the third case of sarcoidosis complicated by cirrhosis and portal hypertension as the initial manifestations of the disease [10,16]. Lack of lung involvement is another interesting point for this patient. Diagnosis of liver sarcoidosis may pose difficulties considering that it may be asymptomatic, may cause only mild symptoms, or may have a wide spectrum of presentations, and there are no definitively pathognomonic laboratory or radiologic findings. Presence of cirrhosis and portal hypertension presenting as the initial features of sarcoidosis without pulmoary disease is a diagnostic challenge for the pulmonary clinician. This case is extremely rare but not unique. In our patient, biopsy was the most useful diagnostic clue.

4. CONCLUSION

Sarcoidosis presenting with cirrhosis and portal hypertension as the initial manifestation of the disease is rare. Absence of lung involvement is another very rare occurrence. Such a clinical presentation poses great difficulties for diagnosis. Clinicians should bear in mind that sarcoidosis may have extremely unusual presentations.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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