Case Report

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# Hepatic and Splenic Sarcoidosis as a Cause of Hypercalcemia: A Case Report

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**ABSTRACT**

Sarcoidosis is an inflammatory disorder characterized by the presence of non-caseating granulomas. Sarcoidosis can affect any organs in the body. As we know, lung is most commonly affected, but other organs such as liver, skin, eye, and spleen could be involved. Here, we report an interesting case of hepatic and splenic sarcoidosis in 55-year-old woman suffered from epigastric pain, weight loss, and constipation due to hypercalcemia

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## Introduction

Sarcoidosis is a systemic disease of unknown etiology which is characterized by the formation of granulomas in various organs, mainly lungs and the lymphatic system. However, any organs could be affected including liver and spleen (1, 2). Symptoms of sarcoidosis vary, depending on the affected organs. It sometimes develops gradually and lasts for years. And so many patients with sarcoidosis have no symptoms (3-6). Sarcoidosis can present with hypercalcemia in 10%-20% of cases which can cause acute renal failure (3-5, 7, 8).

## Case Report

In March 2015, a 55-year-old woman was

admitted to general ward of Imam Khomeini Complex Hospital with complaint of nausea, epigastric pain, constipation, weakness, and significant weight loss (10 kg in 5 months).

Her physical examination was as follow: pulse rate = 80/minutes, respiratory rate = 15/minutes, oral temperature = 37.5 °C, blood pressure = 130/80 mmHg. The only positive findings were moderate symptoms of dehydration and mild splenomegaly.

She did not take any drug and did not have any previous illnesses. Laboratory findings of the patient before her admission are presented in table 1.

Other workups such as upper and lower gastrointestinal endoscopy were done which were normal. In her abdominal sonography, just mild splenomegaly was detected.

In her new laboratory tests, hypercalcemia was reported (12.7 mg/dl, NL: 8.7-10.2) which was the main clue for us to find out her disease. Hypercalcemia could explain most of her symptoms such as dehydration, nausea, constipation, weight loss, and renal failure. We requested further tests to find the etiology of hypercalcemia. Phosphorus 3.5 mg/dl (NL: 2.5-4.3), serum albumin 4.1 mg/dl (NL: 4-5), parathormone hormone (PTH) 11 pg/ml (NL: 11-50), 25 hydroxy vitamin $D_3$ (25 $OHD_3$) 55 ng/ml (NL: 30-100), 24-hour urinary excretion of calcium were 400 mg/day (NL: 100-300), and serum vitamin A level was 150 µg/dl (NL: 50-200).

There was not any reasonable relation between hypercalcemia and PTH. As a result, we should consider some causes such as malignancy especially lymphoma, sarcoidosis, vitamin A and D intoxication, and tuberculosis in the differential diagnosis. Vitamin A and D levels in serum were normal.

Chest computed tomography (CT) scan and mammography were normal. Purified protein derivative test for tuberculosis was negative and also electrocardiogram was normal. In abdomen CT scan, splenomegaly with multiple hypodense lesions and non-homogenous liver was determined (Figure 1).

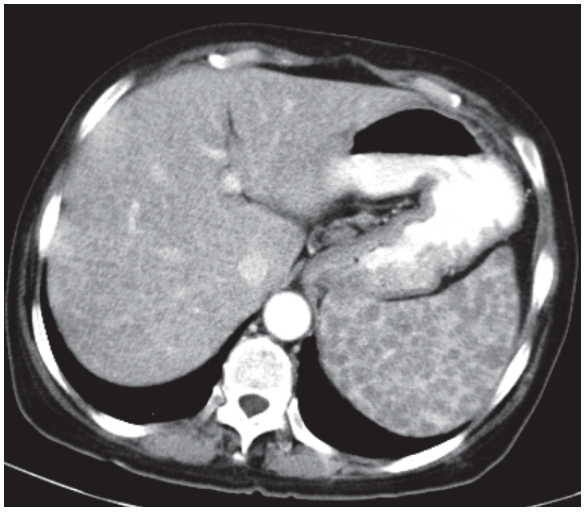

**Figure 1.** Abdomen computed tomography scan showed splenomegaly with multiple hypodense lesions and non-homogenous liver

**Table 1.** Represents the laboratory finding of the patient before her admission

| Laboratory data | Patient | Normal range |
|---|---|---|
| Hb | 11 g/dl | 12.0-15.8 g/dl |
| MCV | 89 fl | 79-93 fl |
| WBC | $8 \times 10^3/mm^3$ | $3.54\text{-}9.06 \times 10^3/mm^3$ |
| PLT | $170 \times 10^3/mm^3$ | $165\text{-}415 \times 10^3/mm^3$ |
| Urea nitrogen | 30 mg/dl | 7-20 mg/dl |
| Creatinine | 2.3 mg/dl | 0.5-0.9 mg/dl |
| ESR 1st | 44 mm/h | 0-20 mm/h |
| ALT | 45 U/l | 7-41 U/l |
| AST | 54 U/l | 12-38 U/l |
| ALP | 150 IU/l | 35-105 IU/l |

Hb: Hemoglobin, MCV: Mean corpuscular volume, WBC: White blood cell, PLT: Platelet count, ESR: Erythrocyte sedimentation rate, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ALP: Alkaline phosphatase

Based on the CT scan findings, liver needle biopsy was performed. In histopathological study, non-necrotizing granulomatous was reported. There was not any evidence of malignancy and lymphoma. Most importantly polymerase chain reaction for acid-fast bacilli and Ziehl–Neelsen stain was negative (Figure 2).

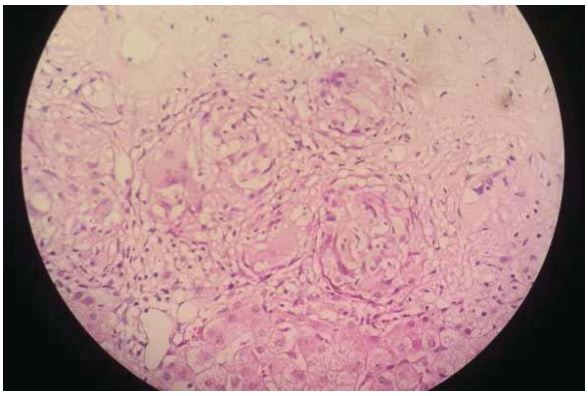

**Figure 2.** Liver histopathological study showed non-necrotizing granulomatous reaction.

We also measured serum angiotensin-converting enzyme (ACE) level, which was 137 IU/l (NL: 9-67). Sarcoidosis was suggested because of the presence of hypercalcemia, histopathological findings of granulomatous reaction, serum ACE and roll out of other causes especially tuberculosis and malignancy.

We treated the patient with serum therapy (normal saline), furosemide (80 mg/day), and prednisolone (30 mg/day). Hypercalcemia and renal function were improved within a week although other symptoms recovered later.

## Discussion

We reported an interesting case of hepatic and splenic sarcoidosis presented by hypercalcemia without pulmonary involvement. Sarcoidosis is an important cause of hypercalcemia which clinicians should consider it in the differential diagnosis.

Overall so many patients with sarcoidosis are asymptomatic, and sometimes, we find hypercalcemia and hypercalciuria during a routine checkup. On the other hand, in symptomatic patients, symptoms that related to hypercalcemia are obvious (3-7, 9). Our patient presented by nausea, epigastric pain, constipation, weakness, and significant weight loss which could be explained by hypercalcemia (3, 5-9).

Hypercalciuria occurs in 40% of patients with sarcoidosis and hypercalcemia in 11%. Therefore, 24-hour urinary excretion of calcium should be measured in all patients suspicious to sarcoidosis. Intrarenal calcium deposition may be so severe and cause renal failure although renal failure due to granulomatous nephritis rarely occurs. In the presented case, we suggest that the acute renal failure has accrued secondary to hypercalcemia and good response to treatment was in favor of it.

Calcium metabolism is disturbed because sarcoidal macrophages possess 25 OHD-1α-hydroxylase, which converts 25 $OHD_3$ to the more active vitamin D metabolite (1, 25 dihydroxy vitamin D), it leads to high calcium absorption in the small intestine and enhanced bone resorption in these patients (3-5, 7, 8).

We should notice that extrathoracic sarcoidosis can occur with or without lung involvement, but isolated extrapulmonary sarcoidosis is so rare, which accounts for < 10% of cases (4, 10).

Most of these lesions are usually asymptomatic. Only 5-30% of patients present with atypical clinical signs and symptoms including nausea, vomiting, jaundice, abdominal pain, and hepatosplenomegaly. Nearly 60% of patients with hepatic manifestations of sarcoidosis have constitutional symptoms such as fever, night sweats, anorexia, and weight loss (6, 7, 9, 11).

Only a small number of hepatic sarcoidosis could be severe, rapidly progressive and lead to cirrhosis, portal hypertension, chronic cholestasis, and Budd-Chiari syndrome (3, 11). Detection of hepatic and splenic lesions on CT is described in 5% and 15% of patients, respectively (5). On the other hand, sarcoidal granulomas produce ACE. ACE level is elevated in 60% of patients with

sarcoidosis and could be helpful for diagnosis (8, 10, 12).

For the diagnosis of sarcoidosis, we need compatible clinical and radiologic findings, histologic evidence of non-caseating epithelioid-cell granulomas in one or more organs, and the absence of organisms, particle, and malignancy (4, 5, 12).

In the presented case, the diagnosis of sarcoidosis was established because of the presence of hypercalcemia, histopathological findings of granulomatous reaction, high serum ACE level, and roll out of other causes especially tuberculosis and malignancy.

A general rule for treatment of sarcoidosis is the presence of organ dysfunction. Detection of granulomatous disease on physical examination, biopsy, imaging studies, or serologic testing is not a mandate to provide treatment (4, 5).

An international expert panel has suggested initiating treatment with oral prednisone at a dose of 20-40 mg/day and evaluating the response to treatment after 1-3 months (4, 5, 7, 9). We treated our patient with prednisolone 30 mg/day. Hypercalcemia and renal function were improved within a week although other symptoms recovered later.

The presented case was a rare case of hepatosplenic sarcoidosis without pulmonary involvement. As we mentioned above, it could be treatable and should be considered in patients comes with symptoms of hypercalcemia.

## Conflict of Interests

Authors have no conflict of interests.

## Acknowledgments

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