CASE REPORT

Primary isolated hepatosplenic sarcoidosis mimicking malignancy and causing symptomatic hypercalcaemia

Tarek Haykal,¹ Saira Sundus, Ghassan Bachuwa, Rizwan Danish

Hurley Medical Center, Flint, Michigan, USA

Correspondence to
Dr Ghassan Bachuwa,
gbachuwa2@hurleymc.com

Accepted 10 January 2019

SUMMARY

This is a case of a 67-year-old woman, known to have multiple medical problems, mainly papillary thyroid cancer status post-total thyroidectomy and cervical neck dissection in addition to radioactive iodine currently in remission for 1 year, who presented to the hospital with severe weakness and fatigue. The initial workup showed significant hypercalcaemia and suppressed Parathyroid hormone (PTH). The patient was treated with hydration and pamidronate and her hypercalcaemia and symptoms improved. The differential was wide, however, a CT scan of the chest, abdomen and pelvis did show multiple liver and splenic nodular lesions; therefore, malignancy was the highest possible diagnosis. Biopsy of the splenic lesion confirmed the diagnosis of sarcoidosis. Therefore, the patient was diagnosed with primary isolated nodular hepatosplenic sarcoidosis mimicking malignancy and causing significant symptomatic hypercalcaemia.

BACKGROUND

Sarcoidosis is a granulomatous disease that can affect any organ system.¹ It is of unknown cause so far and it can affect individuals worldwide.¹ It is characterised pathologically by the presence of non-caseating granulomas in involved organs.¹ And while it is known that sarcoidosis most often affects the lung and intrathoracic lymph nodes, it is a multisystem disease that can affect any organ, most frequently the skin, eyes, reticuloendothelial system, musculoskeletal system, exocrine glands, heart, kidney and central nervous system.² Although it is not unusual for sarcoidosis to involve the liver and spleen, it is however usually in the setting of multiorgan involvement.² The presentation of sarcoidosis in one or two organ systems exclusively is quite rare, especially if it does not involve the thorax,² which reflects in our case the rarity of sarcoidosis presenting only in the liver and spleen.

In addition, while it is a classic finding, hypercalcaemia is always an interesting finding for any patient with sarcoidosis.³

Therefore, the rarity of our case ensues in the association of all those findings together, while mimicking malignancy early in the diagnosis.

CASE PRESENTATION

This is a case of a 67-year-old Caucasian woman who presented to the hospital with severe weakness and fatigue. On review of systems, she mentioned having a weight loss of 20 pounds in almost 1 year.

Besides her surgical neck scars, her physical examination was quite unremarkable.

Her medical and surgical history consists of coronary artery disease, diabetes mellitus type 2, dyslipidaemia, hypertension, papillary thyroid cancer status post-thyroidectomy and cervical neck dissection in addition to radioactive iodine and suppressive thyroid replacement therapy.

The patient is married with two children, currently retired and has never used any alcohol, tobacco or illicit substances.

The patient's mother died at the age of 85 from thyroid cancer, her father died at the age of 59 from heart disease. She has two brothers; one died from lung cancer and the other one is alive and healthy.

INVESTIGATIONS

- ▶ On initial laboratory workup, her total calcium was found high at 13.2 mg/dL (normal range: 8.7–10.4 mg/dL), her ionised calcium was high at 1.5 mmol/L (normal range: 1.1–1.3 mmol/L), her 25-vitamin D level was slightly low at 23.6 ng/mL and her 1.25-vitamin D level was normal at 78 pg/mL. In addition, her PTH was low at 1.7 pg/mL and her PTH-related protein was normal at 14 pg/mL (normal range: 14–27 pg/mL).
- ▶ Other routine biochemical tests, including white cell count, liver, pancreatic and renal function tests, serum immunoglobulins, blood and urinary protein electrophoresis and other tumorous markers were within normal ranges.
- ▶ CT scan of the chest, abdomen and pelvis showed multiple nodular liver and splenic lesions ranging from subcentimetric to 3.1 cm; the lung appeared normal (figures 1 and 2).
- ▶ CT-guided biopsy of the biggest splenic lesion showed non-caseating granulomas, with negative fungal stain and acid-fast stain suggesting sarcoidosis (figures 3 and 4).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included:

- ▶ Metastatic malignancy.
- ▶ Primary lymphoma.
- ▶ Multiple myeloma.
- ▶ Granulomatous disease.

TREATMENT

In the hospital, the patient did receive hydration and pamidronate that corrected her calcium level to normal. The patient was not given any form of steroid therapy.

© BMJ Publishing Group Limited 2019. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Haykal T, Sundus S, Bachuwa G, et al. *BMJ Case Rep* 2019;12:e227703. doi:10.1136/bcr-2018-227703

Figure 1 CT-image of the abdomen in axial view, showing multiple splenic lesions, in addition to very tiny hypodense liver lesions.

No further treatments were given, since no clear guidelines or recommendations exist for this specific type of sarcoidosis.

OUTCOME AND FOLLOW-UP

After having all the clinical data with the CT scan and the biopsy result, the patient was diagnosed with primary isolated nodular hepatosplenic sarcoidosis.

After receiving all the treatments in the hospital, she was discharged after 2 days when her calcium level had become

Figure 2 CT image of the abdomen in coronal view, showing multiple splenic lesions, in addition to very tiny hypodense liver lesions.

Figure 3 H&E-stained section (x100): Low-power view of residual splenic parenchyma on the right and non-necrotising granulomatous inflammation on the left characterised by collections of epithelioid histiocytes and multinucleated giant cells (arrows) with background fibrosis.

normal. No steroids were given. She was required to follow up with her primary care physician and her endocrinologist to assess the best treatment approach in her case given that there are no clear guidelines or recommendations as to how to treat this specific type of sarcoidosis. The patient followed up with her endocrinologist where another calcium level taken showed a normal level and the patient was still asymptomatic.

DISCUSSION

Liver and spleen involvement in sarcoidosis has been well described, though it is almost always a part of a multisystem involvement of the illness.⁴ In 2001, a review report did show that 30% of patients with sarcoidosis had two organ involvement, one of which was almost always in the thorax.² An atypical sarcoidosis presentation with uncommon locations to a single organ and no lung involvement is clearly challenging.

Isolated primary hepatosplenic sarcoidosis has been reported, though it is quite rare with only a few cases reported in the

Figure 4 H&E-stained section (x400): High-power view of a multinucleated giant cell demonstrating a stellate, eosinophilic inclusion known as an asteroid body.

literature.¹ Isolated primary hepatosplenic sarcoidosis has also been reported to be mimicking malignancy where sometimes it even causes elevations in tumour markers like CA-125.⁵

In a recent review of sarcoidosis and the multiple organs affected by the disease, it was quite understood that despite all the imaging technologies available, the nodularity of the spleen and liver with sarcoidosis still can mimic malignancies and that is especially true when it is isolated with no other organs involved; therefore, to achieve the diagnosis with liver or spleen involvement, we almost always end up having to do an invasive procedure with either surgery or biopsy or advanced imaging with Positron emission tomography (PET) scan.⁶

Hypercalcaemia is a reported finding in 10% of all patients with sarcoidosis.⁴ One of the most interesting findings in our reported case is the patient's hypercalcaemia that misled the diagnosis further, suggesting malignancy to be high on the differential. Hypercalcaemia in isolated non-lung sarcoidosis has also been reported, but it is still quite a rare finding.⁷

Finally, a few reports have emerged where hypercalcaemia in sarcoidosis was treated with bisphosphonates alone or in combination with steroids,⁸ which encouraged the treatment of our present case with bisphosphonates, especially when all the possibilities to avoid the patient suffering the side effects of steroids were to be considered in view of all her comorbid conditions. Fortunately, the treatment with hydration and pamidronate alone was successful.

A similar reported case of hepatosplenic sarcoidosis was also reported, in which they were able to use antitumour necrosis factor-alpha (anti-TNF- α) as a treatment when the T-cells in the peripheral blood and in the granulomas showed high level of expression of TNF- α which helped in complete remission of sarcoidosis.⁹ Our present case had low levels of T-cells in the granulomas, therefore, that treatment was deferred.

Patient's perspective

I fought thyroid cancer one year ago and have gone through a lot to achieve remission. Once I was having my symptoms I was mainly concerned with recurrence of my thyroid cancer or the appearance of some other type of cancer. However, I have been blessed to learn that it was sarcoidosis only. I will be following up with my doctors to keep all my diseases under control so that I can live a full and healthy life.

Learning points

- Isolated primary hepatosplenic sarcoidosis is a very rare finding.
- While sarcoidosis is known to cause hypercalcaemia, it is unusual for it to present in a non-lung involvement of sarcoidosis.
- An atypical sarcoidosis presentation with uncommon locations to a single organ and no lung involvement is clearly challenging.
- As no clear recommendations or guidelines are given for non-lung sarcoidosis, especially with hypercalcaemia, treatment should be considered based on a case-by-case scenario; our case was treated with hydration and pamidronate without steroids and did well.

Contributors TH: idea creation, data acquisition, data analysis, manuscript writing. SS: data analysis, manuscript writing and editing. GB: data analysis, manuscript editing. RD: primary attending, manuscript editing.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Ungprasert P, Crowson CS, Matteson EL, *et al.* Epidemiology and clinical characteristics of sarcoidosis: an update from a population-based cohort study from Olmsted County, Minnesota. *Rheumatism* 2017;69:16–22.
- 2 Baughman RP, Teirstein AS, Judson MA, *et al.* Clinical characteristics of patients in a case control study of sarcoidosis. *Am J Respir Crit Care Med* 2001;164:1885–9.
- 3 Eklund A, du Bois RM. Approaches to the treatment of some of the troublesome manifestations of sarcoidosis. *J Intern Med* 2014;275:335–49.
- 4 Hamzeh N. Sarcoidosis. *Med Clin North Am* 2011;95:1223–34.
- 5 Herati RS, Koh JM, Gorospe EC. Localized hepatosplenic sarcoidosis with an elevated serum CA-125 level. *ScientificWorldJournal* 2010;10:298–300.
- 6 Tana C, Dietrich CF, Schiavone C. Hepatosplenic sarcoidosis: contrast-enhanced ultrasound findings and implications for clinical practice. *Biomed Res Int* 2014;2014:1–8.
- 7 Mageau A, Rigolet A, Benali K, *et al.* Life-threatening hypercalcemia revealing diffuse and isolated acute sarcoid-like myositis: a new entity? (a case-series). *Medicine* 2016;95:1–6.
- 8 Kuchay MS, Mishra SK, Bansal B, *et al.* Glucocorticoid sparing effect of zoledronic acid in sarcoid hypercalcemia. *Arch Osteoporos* 2017;12:10–14.
- 9 Sebode M, Weidemann S, Wehmeyer M, *et al.* Anti-TNF- α for necrotizing sarcoid granulomatosis of the liver. *Hepatology* 2017;65:1410–2.

Copyright 2018 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <https://www.bmj.com/company/products-services/rights-and-licensing/permissions/>
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow