

CASE REPORT

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Cervical Lymph Node Sarcoidosis Mimicking a Parathyroid Adenoma: A Clinical Case

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Abstract: We report a case of cervical lymph node sarcoidosis misdiagnosed as parathyroid adenoma. This is the second case described in the literature in which lymph node sarcoidosis was misdiagnosed as parathyroid adenoma on Tc-99m sestamibi (MIBI) scan, the first case localized in the neck. A 64-year-old woman presented with a hypercalcemia. Neck ultrasonography revealed a paratracheal hypoechoic mass of 15 mm with peripheral vascularization. MIBI scan and SPECT/CT identified a MIBI-positive area corresponding to the nodule detected by ultrasonography suggestive for a lower right parathyroid adenoma. A mass interpreted as the lower parathyroid was excised associated to a total thyroidectomy. Pathologic examination revealed a granulomatous lymph node consistent with active sarcoidosis. Sarcoidosis should be suspected as a cause of unexplained hypercalcemia and the differential diagnosis of hypercalcemia, even in presence of MIBI uptake, must include sarcoidosis localized in an isolated cervical lymph node.

Keywords: hypercalcemia, sarcoidosis, parathyroid hormone, Tc-99m MIBI, parathyroid imaging, hyperparathyroidism

Clinical Medicine Insights: Case Reports 2013:6 159–163

doi: [10.4137/CCRep.S13026](https://doi.org/10.4137/CCRep.S13026)

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Introduction

The most common causes of hypercalcemia are malignancies, particularly solid tumors, in hospitalized patients¹ and primary hyperparathyroidism in non-hospitalized patients.² The most common cause of primary hyperparathyroidism is a solitary parathyroid adenoma.²

Neck ultrasound and dual-phase Tc-99m sestamibi (MIBI) scan are generally used as first-line tools in the diagnosis of primary hyperparathyroidism.^{3–5} Neck ultrasound is the least invasive and most inexpensive method to accurately localize hyperfunctioning parathyroid, but its efficacy is related to the operator experience and may be reduced in the presence of concomitant nodular goiter.³ MIBI is a lipophilic monovalent cation showing increased uptake in epithelial cells rich in mitochondria such as hyperfunctioning parathyroid cells. MIBI scan shows high sensitivity (71%–93%) and specificity (90%) in localizing hyperfunctioning parathyroid.^{3–5} Reported sensitivity and specificity of MIBI plus SPECT for solitary adenomas vary from 92% to 97% and from 96% to 99%, respectively.^{3–7}

MIBI retention is not parathyroid-specific and is also observed in hypermetabolic thyroid nodules; blood vessels esophagus, longus colli muscle, and enlarged lymph nodes may represent other rare sources of false-positive results.^{3,8,9}

Hypercalcemia occurs in 2%–63% of patients with sarcoidosis; hypercalciuria is about three times more common (30%–50% of cases).^{1,10}

Hypercalcemia in sarcoidosis is due to the uncontrolled synthesis of 1,25-dihydroxyvitamin D₃ by macrophages. 1,25-Dihydroxyvitamin D₃ leads to an increased absorption of calcium in the intestine and to an increased resorption of calcium in the bone.^{1,10,11}

Primary hyperparathyroidism can coexist with sarcoidosis.^{11,12} Less well-recognized is the ability of sarcoidosis itself to masquerade as a parathyroid adenoma.¹³

We report a case of cervical lymph node sarcoidosis misdiagnosed as parathyroid adenoma. Accumulation of MIBI in hilar lymph nodes and in pulmonary interstitial fibrosis in sarcoidosis has been reported previously,^{14–16} other cases of sarcoidosis have been misinterpreted as primary hyperparathyroidism before the MIBI was introduced into clinical practice.^{12,13} A case of active sarcoid mimicking a mediastinal parathyroid

adenoma on MIBI scan was previously described by Klieger.¹⁷ To our knowledge this is the first reported case of neck lymph node misdiagnosed as parathyroid adenoma on MIBI scan and second case described in literature considering other localizations.¹⁷

Case Report

A 64-year-old Caucasian woman presented to our Department with a hypercalcemia. She had no family history of hypercalcemia. She had a history of hypothyroidism caused by Hashimoto's thyroiditis and treated with L-thyroxine. The patient was suffering from hypertension and mild renal insufficiency. Serum investigation revealed increased calcium of 10.5 mg/dL (normal range (nr): 8.6–10.2) and a parathyroid hormone (PTH) of 162 pg/mL (normal range 12–65). Serum phosphorus was 3.5 mg/dL (nr: 2.7–4.5), urinary calcium was 152 mg/24 h (nr: 50–250), and urinary phosphorus was 1298 mg/24 h (nr: 800–3000). Vitamin D 25-OH was 21 ng/mL (nr: 20–100). Serum creatinine was 1.25 mg/dL (nr: 0.6–1.1), the estimated glomerular filtration rate (eGFR) was 90 mL/min/1.73 m (nr: 90–120), creatinine clearance (Ccr) was 85 (85–130 mL/min). Calcium Clearance/creatinine clearance ratio was 0.02 and diagnosis of familial hypocalciuric hypercalcemia (FHH) was excluded. The chest radiograph was normal.

Primary hyperparathyroidism was suspected and a neck ultrasonography was performed, revealing a paratracheal hypoechoic mass of 15 mm of maximum diameter with peripheral vascularization located near the lower pole of the right lobe of the thyroid (compatible with lower right parathyroid). A large hyperplastic multinodular goiter was associated.

MIBI scan and SPECT/CT identified a MIBI-positive area corresponding to the paratracheal nodule detected by ultrasonography (US), suggesting a lower right parathyroid adenoma (Fig. 1).

Being concordant US and MIBI scan, a right inferior parathyroid adenoma was suspected and the patient underwent surgical exploration. A mass suspected to be the lower parathyroid was excised (Fig. 2) associated to a total thyroidectomy. The indication for parathyroidectomy was based on the suspicion of parathyroid adenoma while the indication for thyroidectomy, after informed consent of the patient, was based on the thyroid volume, the volume and the characteristics of the thyroid nodules, and the fact that

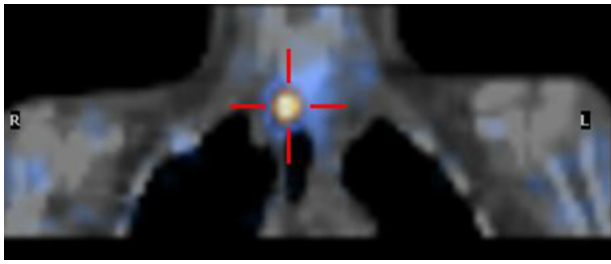


Figure 1. SPECT/CT identified an MIBI-positive area corresponding to the paratracheal nodule detected by US.

the thyroid and the nodules volume were in constant growth. Measurement of intraoperative PTH was made: basal PTH was 152 pg/mL, PTH 10 minutes after excision was 211 pg/mL, while PTH 20 minutes after excision was 152 pg/mL. The bilateral exploration of the neck was negative for the presence of other pathological parathyroid glands.

The patient was discharged on the second post-operative day. Serum calcium was 9.27 mg/dL and phosphorus 3.4 mg/dL.

Pathologic examination confirmed the preoperative diagnosis of Hashimoto's thyroiditis associated with hyperplastic nodular goiter, but did not confirm the diagnosis of parathyroid adenoma, the mass being a granulomatous lymph node consistent with active sarcoidosis (Fig. 3).

No other sarcoidosis lesions or related findings were found, the neck lymph node being the only visible lesion.

The patient has begun therapy for sarcoidosis with corticosteroids and is currently well 5 years after surgery. Serum calcium and phosphorus remained normal (Table 1).

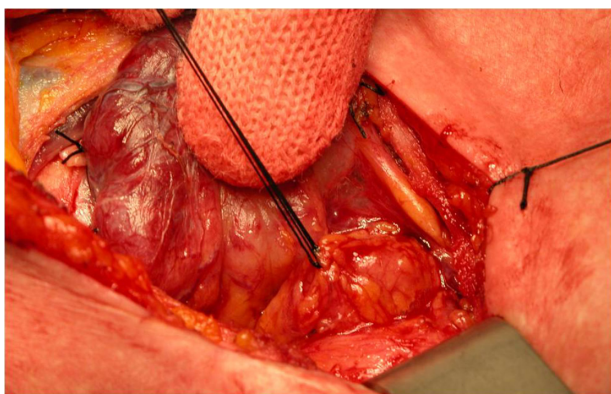


Figure 2. Macroscopic appearance of the MIBI-positive nodule at the neck exploration.

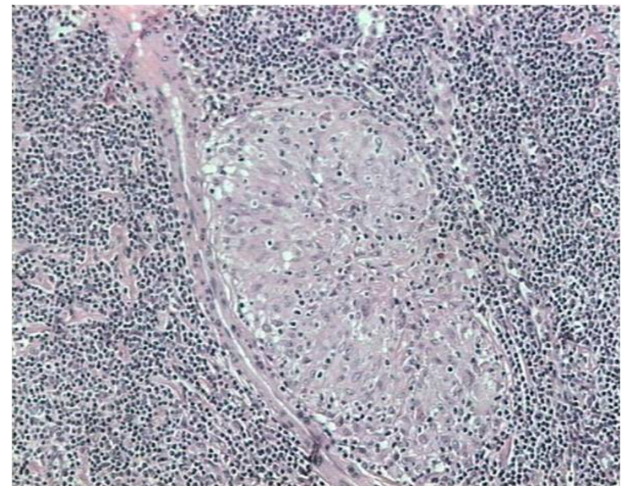


Figure 3. Histologic appearance showing a lymph-node with typical sarcoid granulomata (ematoxylin-eosin).

Discussion

We report a case of cervical lymph node sarcoidosis misdiagnosed as parathyroid adenoma on neck ultrasonography and MIBI scan.

Difficulty in US and MIBI scan interpretation with high rate of false-positive images (15%–20%) has been described in the presence of hypermetabolic thyroid nodules; blood vessels, esophagus, longus colli muscle, and enlarged lymph nodes may represent other rare sources of false-positive results.^{3,8,9}

Hypercalcemia can occur in sarcoidosis, its prevalence being approximately 20%;¹¹ the relation between sarcoidosis and hypercalcemia was first noted in 1939.^{10,18} Risk factors for development of hypercalcemia in patients with sarcoidosis include

Table 1. Clinical course: laboratory data (Calcium, Phosphorus, Creatinine, ACE, PTH) before and after surgery and after corticosteroid treatment.

	Before surgery	After surgery	After corticosteroid treatment
Serum calcium (mg/dL)	10.5	9.27	9.35
Serum phosphorus (mg/dL)	3.5	3.4	3.5
Serum creatinine (mg/dL)	1.25	1.30	1.21
ACE (U/L)	Not carried out	101	75
PTH (pg/mL)	162	152	70



renal insufficiency, increased dietary vitamin D, dehydration, increased uptake of oral calcium and/or decreased calcium excretion, and increased sunlight exposure.^{10,18} Our patient had mild renal insufficiency. In our case, postoperative exams and follow-up allowed to exclude the presence of a primary hyperparathyroidism, sarcoidosis thus being the only cause of hypercalcemia. The presence of a mild renal insufficiency may have been the cause of the increase in PTH.

As with other lipophilic cations, MIBI uptake depends on mitochondrial and plasma membrane potentials. The precise uptake mechanism in sarcoidosis is unknown.¹⁵

Lymph nodes with sarcoid involvement are found in 23% to 37% of patients with sarcoidosis.¹³

Accumulation of MIBI in hilar lymph node and in pulmonary interstitial fibrosis in sarcoidosis has been reported previously.^{14–16} It is a rare to observe other lymph nodes outside the chest showing increased uptake.¹⁴ Before the introduction of MIBI scanning into clinical practice, cases of sarcoidosis misinterpreted as primary hyperparathyroidism have been described.^{12,13} To our knowledge, the only case of active sarcoid mimicking a parathyroid adenoma on MIBI scan was previously described by Klieger,¹⁷ but in that case the disease was localized in the mediastinum. Our case was particularly interesting because it's the second case described in the literature of lymph node sarcoidosis mimicking a parathyroid adenoma on MIBI scan; the first case involved a lymph node localized to the neck. Preoperative imaging studies (US, MIBI, scan and SPECT/CT) were concordant and preoperative diagnosis of parathyroid adenoma was made. Chest radiogram was normal and sarcoidosis was completely unsuspected. Intraoperative measurement of PTH gave discordant results for which it was carried out a bilateral exploration of the neck: no pathological parathyroid was found. Fortunately, the suspicion of parathyroid adenoma was not the only indication for surgery, being present a large multinodular goiter associated with a thyroiditis. Only histological examination revealed the correct diagnosis of sarcoidosis which was subsequently treated.

In conclusion, sarcoidosis should be taken into account as a cause of unexplained hypercalcemia and the differential diagnosis of hypercalcemia, even in

presence of MIBI uptake, must include sarcoidosis localized in an isolated cervical lymph node.

Author Contributions

Wrote the first draft of the manuscript: PGC, AT, GL. Contributed to the writing of the manuscript: GP, AN, SF. Agree with manuscript results and conclusions: PGC, GP, AT. Jointly developed the structure and arguments for the paper: PGC, SF, AN. Made critical revisions and approved final version: PGC, GP, GL, AN. All authors reviewed and approved of the final manuscript.

Funding

Author(s) disclose no funding sources.

Competing Interests

Author(s) disclose no potential conflicts of interest.

Disclosures and Ethics

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests. A written consent was obtained from the patient to reproduce information and photographs appearing in this work.

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