

Retroclavicular Parathyroid Adenoma in A Patient with Ankylosing Spondylitis: A Case Report

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Abstract

We report a case of a 38-year-old patient with ankylosing spondylitis who presented with asymptomatic hypercalcemia due to a retroclavicular parathyroid adenoma. Because of the rare location of the parathyroid adenoma, we reviewed 2 similar cases in the literature and further image discussion. (J Intern Med Taiwan 2020; 31: 437-442)

Key Words: Ectopic parathyroid adenoma, Ankylosing spondylitis, Retroclavicular, Hyperparathyroidism

Introduction

Hyperparathyroidism is a status of excess parathyroid hormone secretion. It is a common cause of hypercalcemia. The primary disorder is most commonly due to an autonomously functioning solitary adenoma (80-85%), gland hyperplasia (10-15%), or multiple adenomas (5%)¹. Parathyroid gland (adenomas) are commonly located around the inferior lobes of the thyroid gland². Besides, ectopic locations should also be considered. Persons with hyperparathyroidism are at increased risk for cortical bone loss and fractures. Ankylosing spondylitis (AS) is an inflammatory disease with the main manifestations of low back pain, and they may also experience loss

of bone density and osteoporosis during the disease progression. Although an attempt was made to determine whether a relationship between AS and hyperparathyroidism, the results showed that both AS and hyperparathyroidism are independent entities that have no causative or pathological relationship to each other³. However, the combination of these two diseases increases the risk of osteoporosis and fractures. We report a rare case of a 38-year-old patient with AS who presented with asymptomatic hypercalcemia due to a retroclavicular parathyroid adenoma.

Case Report

A 38-year-old Chinese man was admitted to the Chung Shan Medical University Hospital, with

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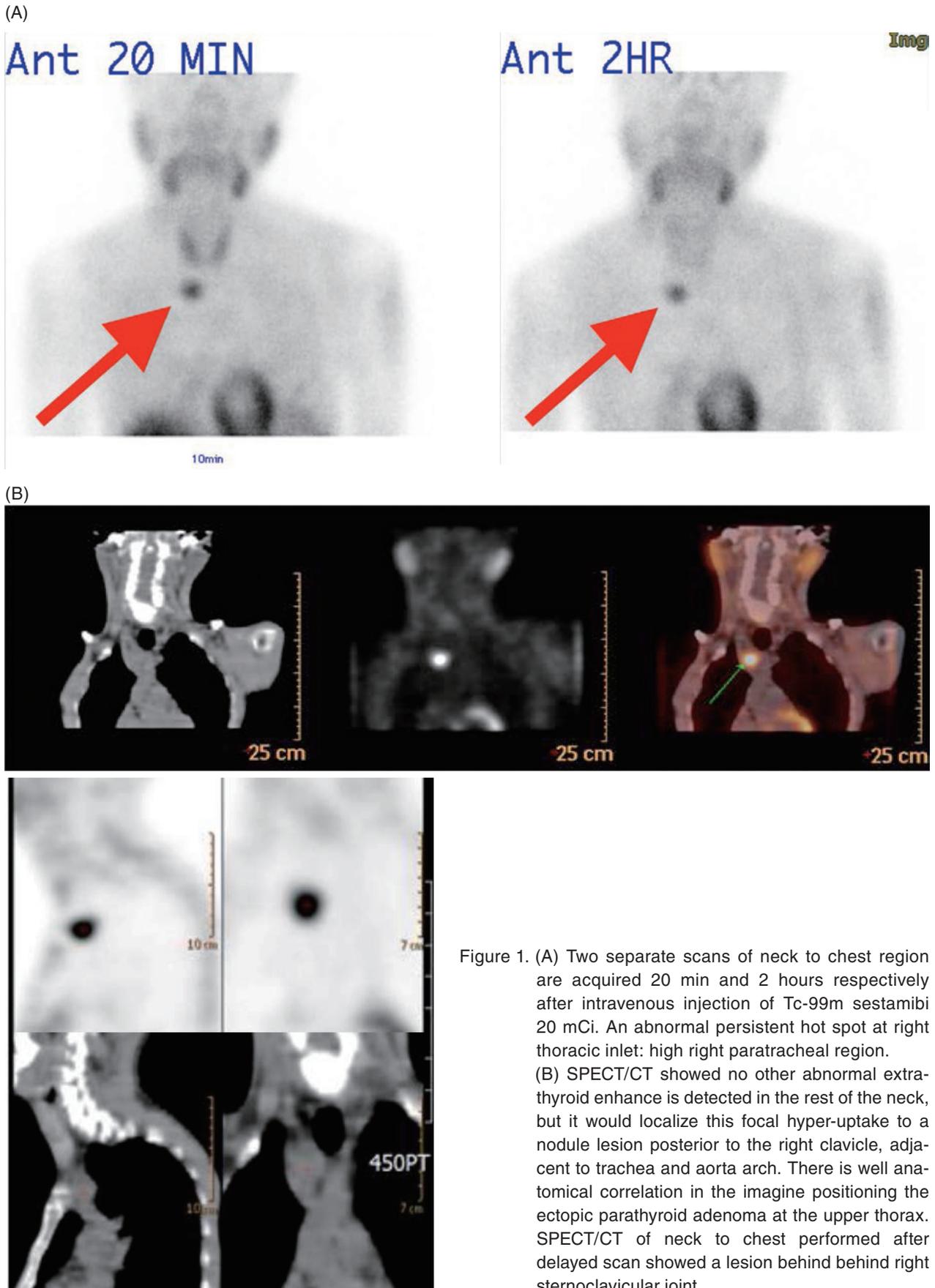


Figure 1. (A) Two separate scans of neck to chest region are acquired 20 min and 2 hours respectively after intravenous injection of Tc-99m sestamibi 20 mCi. An abnormal persistent hot spot at right thoracic inlet: high right paratracheal region. (B) SPECT/CT showed no other abnormal extra-thyroid enhance is detected in the rest of the neck, but it would localize this focal hyper-uptake to a nodule lesion posterior to the right clavicle, adjacent to trachea and aorta arch. There is well anatomical correlation in the imagine positioning the ectopic parathyroid adenoma at the upper thorax. SPECT/CT of neck to chest performed after delayed scan showed a lesion behind behind right sternoclavicular joint.

asymptomatic hypercalcemia during routine follow up for AS. He has AS taking daily therapy with Sulfasalazine, Ixekizumab, and Etoricoxib. His serum calcium level was 13.8 mg/dL (8.9-10.3 mg/dL), phosphorus 2 md/dL (2.4-4.7 mg/dL), magnesium 1.2 mg/dL (1.8-2.5 mg/dL) alkaline phosphatase 316.8 IU/L (20-140 IU/L), and intact parathyroid hormone (iPTH) 1670 pg/mL (12-65 pg/mL).

Anterior planar technetium (99mTc) sestamibi (MIBI) scintigraphy images of the neck and chest showed a focal shadow with intense tracer uptake in the right thoracic inlet: high right paratracheal region at 20 minutes and 2 hours (Figure 1a) following injection of 99mTc-MIBI. Single-photon emission computed tomography/computed tomography (SPECT/CT) scan showed a focal hyper-uptake to a nodule lesion posterior to the right clavicle, adjacent to trachea and aorta arch. (Figure 1b). Neck computed tomography scan demonstrated a heterogeneous contrast-enhancing nodular lesion about 3.1 cm in right retroclavicular region (Figure 2).

A right lower parathyroidectomy was performed. A yellowish-brown mass of 3.3 x 2.5 x 2.0 cm was found in the anatomy area of the right upper paratracheal region and resected (Figure 3). Serum calcium level was 9.5 mg/dL and iPTH 152.3 pg/mL

after surgery immediately. Hypocalcemia occurred 30 days after surgery and gradually improved over a week with calcium carbonate and calcitriol supple-



Figure 2. The non-contrast CT scan revealed an elongated mass in the upper anterior mediastinum in a right para-tracheal location at the T4/5 level, compatible with an ectopic parathyroid adenoma.

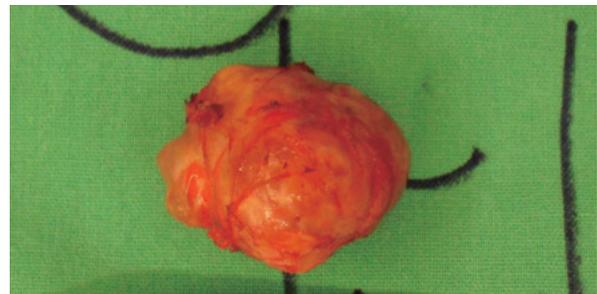


Figure 3. Pathology: 3.3 x 2.5 x 2.0 cm encapsulated yellowish-brown mass.

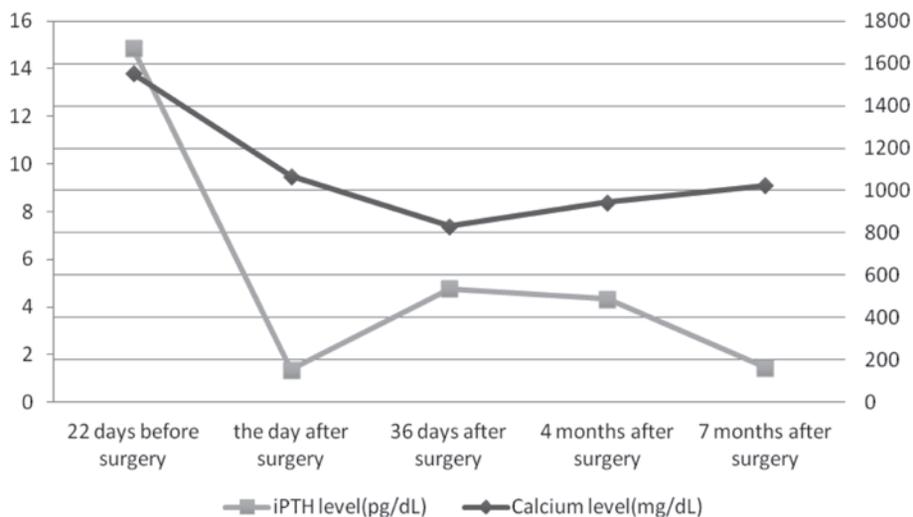


Figure 4. iPTH and calcium level of our patient, data collected from day 22 before surgery to 7 months after surgery.

mentation that was started after surgery and continued thereafter (Figure 4). Serum calcium remained normal after 5 months' follow-up, but iPTH level was about more than 2 fold higher on operation day, become 8 fold higher was found one month after surgery, 7 fold higher was observed 4 months after surgery, declined to 2 fold higher was recorded 7 months after surgery.

Discussion

The prevalence of ectopic parathyroid is about 2-43% in anatomical series and 16% and 14% in patients with primary and secondary hyperparathyroidism, respectively⁴.

Phitayakorn R et al reported a 22% of ectopic parathyroid adenomas in 1562 patients who underwent surgery for hyperparathyroidism⁵. The most common ectopic location was the thymus (38%) followed by the retro/paraesophageal region (31%). The other places include intrathyroidal (18%), mediastinum (6%), undescended (4%), carotid sheath (3%)⁵. Furthermore, some other rare locations has been reported, such as carotid bifurcation, the posterior triangle of the neck, within the vagus nerve, within the hypoglossal nerve, pericardium, right dome of the diaphragm, and even supraclavicular region⁵. Ectopic parathyroid adenomas located in the retroclavicular region are very rarely reported. By reviewing the literature, there were 2 cases reported (Table 1)^{6,7}. Primary hyperparathyroidism (PHPT)

as a result of ectopic parathyroid adenomas can pose diagnostic and management challenges, particularly when imaging studies provide limited sensitivity.

Ultrasonography is a cost-effective image tool and it is commonly used to locate enlarged parathyroid glands, its sensitivity in the localization varies greatly (44%-87%)⁸.

However, ultrasonography usually failed to identify ectopic parathyroid glands. ^{99m}Tc-MIBI scintigraphy combined with SPECT/CT has been proved to have better sensitivity (87%) than sonography (42%) for detecting ectopic parathyroid glands⁹. Other images, such as CT scan may further provide the identification of ectopic parathyroid glands and the differential diagnosis from other lesions. Recently, ¹⁸F-fluorocholine positron emission tomography/X-ray computed tomography (PET-CT) has been used for the assessment of ectopic parathyroid adenoma. It was considered to have better sensitivity and specificity for ectopic active parathyroid gland detection comparing with ^{99m}Tc- MIBI scintigraphy combined with SPECT/CT. However, the accuracy may be interfered with for those with underlying diseases, for example, such as thyroid cancer, metastatic lymph nodes, and inflammatory processes¹⁰⁻¹³. Thus, its use may be limited for patients with small lesions¹⁴, which has less sensitivity in ^{99m}Tc- MIBI scintigraphy combined with SPECT/CT.

As shown in table 1, ^{99m}Tc- MIBI scintigraphy

Table 1. Compare our case with 2 similar cases in published literatures

Patients	Gender	Age	Chief complain	T	S	C	iPTH Before surgery	iPTH After surgery	Ca Before surgery	Ca After surgery
1 ⁶	Male	29	None	V	V	V (SPECT)	60	42	10	9.4
2 ⁷	Female	45	Diffuse bone pain	V	V	V	2000	61	11.8	6.6
3	Male	38	None	V	X	V (SPECT)	1670	152.3	13.8	9.5

T: Tc-^{99m} MIBI scintigraphy planar, S: neck ultrasonography, C: Computed Tomography.

SPECT: single photon emission computed tomography.

Ca: Calcium level, iPTH: intact Parathyroid hormone level.

combined with SPECT scan was performed in case one, while case two received technetium 99mTc-MIBI scintigraphy combined with CT scan, and our case received 99mTc- MIBI scintigraphy combined with SPECT/CT. All lesions were localized by 99mTc- MIBI scintigraphy combined with SPECT/CT scan. This highlights the usefulness of combining multiple imaging techniques to locate an ectopic active parathyroid gland. These combinations might be considered an approach to routine preoperative localization of ectopic parathyroid adenomas¹⁵.

In terms of clinical characteristics, case two presented with diffuse bone pain, case one, and our case were asymptomatic. Our case has the higher calcium level and high iPTH level, compared to case one. Our case has been diagnosed as AS for a long time, it is also possible that bone pain may be masked by etoricoxib. This incidentally finding of hypercalcemia can be attributed to the multichannel biochemical testing assay that includes serum calcium, thus allowing for early identification and treatment. Hypercalcemia, a laboratory finding in hyperparathyroidism, is often the impetus for checking parathyroid hormone levels.

Successful parathyroidectomy was followed by normalization of plasma levels of iPTH and calcium-phosphorus metabolism. Although our patient's calcium have returned to normal range immediately after surgical removal, but iPTH level was about more than 2 fold higher on operation day, become 8 fold higher was found one month after surgery, 7 fold higher was observed 4 months after surgery, declined to 2 fold higher was recorded 7 months after surgery. Normocalcemia with a delay decline of iPTH level can be detected in up to 40% of patients post-parathyroidectomy and may not indicate operative failure, probably related to lower vitamin D concentration, higher concentrations of bone turnover markers, and higher parathyroid hormone concentration¹⁶. We did not checked patients vitamin D level and bone turnover markers,

higher parathyroid hormone is possibly related to elevated parathyroid hormone after surgery. As our patient has both AS and primary hyperparathyroidism which will increase the risk of fracture, normalization of calcium and parathyroid hormone is the only effective method to reduce the risk of bone fractures and loss of bone mineral density.

Conclusion

The diagnosis of PHPT is classical when corrected calcium is high in the presence of elevated iPTH¹⁷. And parathyroidectomy is the only curative therapy for PHPT. We should keep in mind that if we didn't find parathyroid adenomas located at typical location, further image survey ranging from the base of the tongue to mediastinum is recommended, according to the embryological origin of the parathyroid glands. We believe these three cases discussed previously share similar rare ectopic parathyroid location, and non-specific symptoms which also correlate to the diagnosis of PHPT nowadays, even our case with an underlying disease of AS under long term drug used may present only hypercalcemia without bone pain or any other symptoms. Moreover, we found that early Tc-99m plus SPECT/CT investigation may be reliable in such patients with active ectopic parathyroid glands, in particular those more than 3cm in size, located at retroclavicular region.

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一位患有異位性鎖骨後副甲狀腺瘤的 僵直性脊椎炎患者：病例報告

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摘 要

一位38歲男性在接受僵直性脊椎炎的例行門診追蹤時，抽血發現無症狀的高血鈣症，經一系列的影像學檢查，疑似是異位性鎖骨後的副甲狀腺瘤所造成。由於病灶位置特殊，本文針對影像學的檢查、比較兩個類似個案等，來加以討論。