Case Report:

Chronic Unclassified Polyarthritis: A Rare Presentation of Primary Hyperparathyroidism

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Abstract

Background: Primary Hyperparathyroidism (PHPT) is the predominant cause of hypercalcemia. The commonest cause of PHPT is parathyroid adenoma (85%) along with parathyroid hyperplasia or carcinoma. The asymptomatic disease could manifest with different and protean symptoms including neuromuscular and neuropsychiatric symptoms. The delayed diagnosis allows bony lesions to progress to osteitis fibrosa cystica and brown tumor.

Case Description: An unusual case of PHPT presented with unclassified chronic polyarthritis for 18 months. The condition was associated with history of recurrent renal stones. Due to improper history taking, lack of routine screening for serum calcium and incompliance of the patient, the diagnosis of PHPT was delayed till osteitis fibrosa cystica occurred. Following admission to hospital for assessment of his arthritic illness, diagnosis of PHPT due to parathyroid adenoma was made. Right hemi-thyroidectomy with excision of the right superior and inferior parathyroid glands was done. Two-years follow-up revealed dramatic improvement after surgery.

Conclusion: Proper history taking, high index of suspicion and routine chemistry investigations could enable early diagnosis of PHPT. Patients with unclassified arthritis should be screened for the possibility of PTH excess or hypercalcemia to exclude hyperparathyroidism.

Key Words: Hyperparathyroidism – Osteitis fibrosa cystica – Unclassified arthritis – Parathyroid adenoma.

Introduction

HYPERPARATHYROIDISM is overproduction of Parathyroid Hormone (PTH). It is usually classified into primary, secondary, and tertiary hyperparathyroidism. Primary hyperparathyroidism could be due to adenoma (80-85%), hyperplasia (10-20%) or carcinoma (<0.5%) [1]. It is a relatively common endocrine disorder, affecting one to seven cases per 1000 adults [2]. It is believed to be the most common cause of hypercalcemia, therefore, the presence of multiple endocrine neoplasia type 1, 2a and 2b should be ruled out [3,4]. Primary hyperparathyroidism is usually asymptomatic in 80%, but can be presented with bone pain, abdominal pain, constipation, easy fatigability and polyuria [5]. Renal stones ensue in 10-25% of the cases [6]. There is a female preponderance with 3:1 female-male ratio [7,8]. Initial investigation of parathyroid disease includes checking serum calcium, phosphorus and parathyroid hormone levels. Serum vitamin D helps differentiating primary vs. secondary hyperparathyroidism. Ultrasonography, magnetic resonance imaging and parathyroid nuclear scintigraphy finalize the diagnosis. Delayed diagnosis and PTH excessive stimulation of activity and proliferation of osteoclasts lead to osteitis fibrosa cystica and reparative brown tumor [9]. The latter is a reparative slowly enlarging painful mass that can be locally aggressive, without metastatic potential [10]. Definitive treatment for primary hyperparathyroidism is parathyroidectomy [11,12].

Case Report

A 25-year-old Saudi male patient was admitted to the Rheumatology Unit on 15/4/2013 at King Khalid University Hospital, Riyadh, Saudi Arabia, for evaluation of polyarthritis. The patient had given permission for the anonymous reporting of his case. The patient came with history of swelling and pain in both ankles, wrists, knee joints and small joint of hands for the last 18 months. Swelling and pain started in ankles and wrists then spread to small joints of hands mainly Proximal Interpha-
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Lumbar (PIP) joints. Later, knee joints were affected. The condition was gradually progressive and associated with general body ache and morning stiffness for one hour. The patient denied history of fever, skin rash or weight loss. He recalled having recurrent renal stones during the last 5 years. Further inquiry showed no history of other chronic diseases or similar illness in the family.

After 3 months from the onset of his illness, the patient was examined. Laboratory assay for serum creatinine, blood urea nitrogen, Liver Function Test (LFT), Rheumatoid Factor (RF), anti-ccp, ER, C-Reactive Protein (CRP), HIV, Anti-Nuclear Antibody (ANA), Anti-DNA, Thyroid Function Test (TFT) was normal. Urine analysis showed proteinuria and granular cast. 24-hrs urine showed total protein of 1049mg/day. Renal biopsy showed evidence of sclerosis and focal interstitial fibrosis and tubular atrophy. The nephrologist prescribed him prednisolone 7.5mg and hydroxychloroquine 400mg daily. However, the patient was not compliant to treatment and was missed for follow-up.

On examination, the patient was conscious, oriented, looks well and not in pain. There were mild PIP joints swelling, tenderness and effusion. No skin rash, joint deformity, decreased range of movement or rheumatoid nodules were seen. The right thyroid lobe was palpable and not tender. The other body systems were normal. Investigations showed normal RF, anti-citrullinated peptide (anti-CCP), ESR, CRP, ANA, and anti-DNA. Serum calcium was 2.98mM/L (NR 2.1-2.55), phosphorus was 0.78mM/L (NR 0.87-1.45), PTH was 221 pM/L (NR 1.65-6.9), Alkaline Phosphatase (ALP) was 2318U/L (NR 50-136). X-ray of hands Fig. (1) showed subperiosteal resorption (PIP index finger) and of clavicles Fig. (2) showed distal clavicle subchondral resorption. Abdominal X-ray and CT showed renal stone Fig. (3). Bone mineral density (BMD; Dexa scan) showed a T-score of −4.4 and Z-score of −4.4 for Lumbar spine, T-score of −3.6 and Z-score of −3.7 for right and left femur, and, T-score of −5.8 and Z-score of −5.8 for Radius. Thyroid ultrasound showed large heterogeneous nodule in the right lobe that was 2.7 X 2.8 X 4.7cm size with increased vascularity and extended posteriorly to involve right parathyroid gland. Parathyroid nuclear scintigraphy showed increased activity of focal tracer in the right thyroid lobe that persisted on the delayed 2 hours images Fig. (4). The patient was diagnosed as parathyroid adenoma or carcinoma with suspension of thyroid involvement. Right hemi-thyroidectomy with excision of the right superior and inferior parathyroid glands and exploration of the other two left glands were done. Histopathology confirmed the diagnosis of parathyroid adenoma. On discharge, the patient was given calcium and vitamin D. After two weeks as a follow-up outpatient, he showed normal serum levels of PTH of 3.32pM/L, calcium of 2.26mM/L and phosphorus of 0.98mM/L. All the complaints of polyarthritis had been resolved and radiological findings became normal. The patient did not need any surgical intervention for the bony lesions.
Fig. (3): X-ray and CT of the abdomen. (A) X-ray revealed renal stone in right side (Arrow). (B) CT showed small calcified density projecting over the renal shadow confirmed to be renal stone (arrow).

Fig. (4): Parathyroid nuclear scintigraphy shows focal tracer increased activity in the right thyroid lobe that persisted after two hours (lower panels).

Discussion

The usual presentation of patients with primary hyperparathyroidism was renal stones and skeletal complication like osteitis fibrosa cystica and brown tumor. However, the introduction of routine measurement of blood calcium in the early 1970s, enabled early diagnosis among most cases with asymptomatic hypercalcemia [13]. More elaborate blood chemistry screening and imaging techniques as MRI further facilitated early diagnosis of primary hyperparathyroidism before development of the bony changes [15]. Consequently, manifestations like osteitis fibrosa cystica and brown tumor became rare as late diagnosis [14,15].

In this case, PHPT due to parathyroid adenoma was diagnosed after 18 months of illness. Despite the extensive work up to resolve proteinuria (renal biopsy and histopathology), there was no evidence for checking serum calcium. Recurrent renal stones should have been considered a clue for hyperparathyroidism. The second factor contributed to this delay is the unusual presentation as chronic unclassified polyarthritis. Although joint pain was reported as one of the manifestations of hyperparathyroidism, chronic polyarthritis is rarely described as a manifestation of the disease [17,18]. In this case, manifestations of chronic polyarthritis exceeded one year duration and there was no laboratory evidence of rheumatoid or other classified arthritis. After three months of illness, a renal disease was diagnosed and steroid and anti-inflammatory drugs were given. The patient was lost thereafter and continued to suffer. The present distribution of the bony and joint lesions (wrist, ankles, knees and PIP) is not typical to hyperparathyroidism, where, lesions usually affect the ribs, clavicles, pelvic girdle and facial bones, the lower limb is seldom affected [5,19,20]. Furthermore, during his illness, the patient suffered from swelling, tenderness and painful movement of his joints which is rarely described elsewhere. Despite being late, findings of the laboratory and radiological workup done after admission to the hospital were of great value in finalizing the diagnosis. These findings along with the history of recurrent renal stones increased the probability of a primary hyperparathyroidism diagnosis. Histopathology of removed tissue showed parathyroid adenoma.
**Conclusion:**

This report described a male patient with unclassified polyarthritis for 18 months. Although primary hyperparathyroidism diagnosis is made nowadays by the routine assessment of serum calcium, phosphorus, ALP and PTH before the development of bony changes, the diagnosis of this patient's illness is made at a late stage. Being unusual manifestation of PHPT, it is recommended to screen patients with unclassified arthritis for the possibility of PHT excess or hypercalcemia during their diagnostic workup.

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**References**

المقدمية: زيادة هرمون جارات الغدة الدرقية هو السبب الأول في إرتفاع نسبة الكالسيوم بالدم، وزيادة هذا الهرمون أسباب عدة من أهمها وأكترها شيوعا هو النوم المديد في أحد هذه الأدوات (85٪)، ومن الممكن أن يحدث هذا الإرتفاع بسبب تضخم جارات الغدة الدرقية أو الإصابة بسكتة خبيثة بإعدادها. وغالباً ما يكون المرض من دون أعراض واضحة على المريض، وفي بعض الاحيان تظهر بعض الأعراض العصبية أو النفسية على المريض. التشخيص المبكر يساهم في إختفاء المرض ويسهل علاجه وقائي من المضاعفات، وتأخير التشخيص يؤدي إلى إتلاف العظام الليفية (الورم البني الذي يصيب العظام).

وصف الحالة: ظهر المريض في الحالة الحالية بشكل غير اعتيادي، بعيرة عن إتهاب والألم بمجموعة من المفاصل أدى إلى تأخر التشخيص حتى 18 شهرًا. بدأت حالة هذا المريض بالإعتياد بالمجموعة من المفاصل تزامنت مع حصوات متكررة في الكلى، ظروف المريض بالشكل النادر وغير المعاد. مع عدم تقدم التاريخ المرضي جيداً وكذلك تجاهل تحليل الكالسيوم أدى إلى التشخيص المتاخر والخطير، ومن ثم إلى إتلاف العظم الليفي الذي أصبح نادر الحدوث في هذا العصر. بعد زيارته من المريض المستشفى والتعامل مع كميات يومية زائدة وسبب استمرار شكوى المريض فقد أظهرت الفحوصات وجود ورم حديد في الغدة جارة الدرقية، وذلك بعد فحص الكالسيوم وهرمون الباراثيرومو وإجراء بعض التشخيصات (إشعاعية، أشعاعية، فوتوسيونية، سيوية)، بعد ذلك تم السيطرة على المرض بإزالة الورم واللغة، ويعتبر المريض لمدة ستين بالعادة ثمانية إختفاء الأعراض سالفة الذكر تماماً.

الخلاصات: إن الجلوس مع المريض وتبقي المريض على يمين المريض يقلل فصل ودقيق من المفاصل المهمة في التشخيص المبكر المرض، وكذلك يجب على الطبيب الأخذ بالحسبان أن بعض الأعراض قد تظهر بآلام غير معاداة، ولا تكفي عن عمل التحليل المخبرية الأولية المهمة لتسهيل التشخيص المبكر. عند فحص المريض بالألم غير معاداة بالمفاصل يجب عليه أن ينصح أن زيادة هرمون الباراثيرومو قد يكون هو السبب.

وراء ذلك، فيجب عمل تحقيق مستويات الكالسيوم والهرمون بالدم لتمكين من إستبعاد زيادة إفراز هرمون الباراثيرومو أو تأكيده مبكراً.