Hyperparathyroidism is a complex clinical syndrome characterized by dysfunction in the metabolism of bone, calcium and phosphorus. Rheumatologic manifestations are common amongst patients with hyperparathyroidism. Laboratory evidence of elevated erythrocyte sedimentation rate, positive C-reactive protein (CRP) and high titers of anti-CCP and rheumatoid factor was diagnostic of rheumatoid arthritis (RA) according to European League Against Rheumatism criteria. Eventually, with the concomitant diagnoses of hyperparathyroidism and RA, she was treated with methotrexate and hydroxychloroquine. Hyperparathyroidism may present with rheumatologic manifestations, leading to an initial misdiagnosis. Furthermore, attention to this fact that hypercalcemia is not commonly associated with RA, and rather suggestive of a concomitant disorder, is crucial to the diagnosis of hyperparathyroidism in RA patients with hypercalcemia.

Keywords: Hypercalcemia, hyperparathyroidism, musculoskeletal symptoms, rheumatoid arthritis

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percalcemia is not a typical finding in RA would possibly lower the chances of missing a concomitant diagnosis of hyperparathyroidism.

The following is a patient with the clinical manifestations of hypercalcemia and RA, which eventually led to the concomitant diagnoses of hyperparathyroidism and RA.

Case Report

A 50-year-old woman presented to the emergency department complaining of general malaise, diffuse musculoskeletal pain, and morning joint stiffness of more than one hour duration for a period of approximately one year. The patient had received analgesic treatment with relative improvement in symptoms. However, over the course of her illness, she had experienced increased myalgia and generalized musculoskeletal pain. In addition, the patient gave a several-month history of swelling of the knees, wrists and the metacarpophalangeal (MCP) joints associated with morning stiffness exceeding one hour plus low grade fever. Gradually, she had also developed occasional nausea and vomiting and increased urine volume together with anorexia, constipation, and weight loss of 3–4 kilograms over a two-month period. A significant finding in the patient’s medical history over the few months before admission was that of multiple fractures which had occurred in the
left humerus bone, clavicle, and ribs and the pelvis (Figures 1–3). The patient had received outpatient treatment for epigastric pain and dyspepsia several times. However, the past medical history was unremarkable for diabetes, dyslipidemia, heart disease. She had no history of trauma.

On examination, increased size of the 3rd distal phalanx of the left hand and the 4th of the right hand was noticed. Arthritis was detected in the knee joints and both wrists, and the proximal interphalangeal joints of both hands in a symmetric fashion. No organomegaly or lymphadenopathy was detected.

The laboratory tests were normal for blood sugar levels, serum creatinine, uric acid and liver function tests. However, the finding of hypercalcemia (12.4 mg/dL) and a phosphorus level in the lower normal range (2.7 mg/dL) was followed by a test for serum PTH levels, which was inappropriately high (2347 pg/dL). The serum uric acid and vitamin D levels were in the normal range (41 ng/dL). The patient had an elevated ESR of 56 mm/h and positive CRP.

On bone mineral densitometry, the patient was reported to have osteoporosis in the lumbar vertebrae (T-score = -2) and the femoral neck (T-score = -2.5). A complete abdominal and pelvic ultrasound exam yielded no significant finding.

Considering the elevated PTH levels, a sestamibi scan confirmed the presence of a parathyroid adenoma, which was confirmed on histological examination following surgical resection. Based on the European League Against Rheumatism Criteria, the patient received a score of more than six based on multiple large and small joint involvement, high anti-cyclic citrullinated peptides (anti-CCP) and rheumatoid factor (RF) levels, and abnormal ESR and CRP, which indicates RA diagnosis.11

Ultimately, the patient underwent treatment for RA after parathyroidectomy with 400-mg daily doses of hydroxychloroquine and 10 mg of methotrexate per week with improvement in joint symptoms, musculoskeletal pain and the resolution of the patient’s fever one month after parathyroidectomy.

Discussion

Primary hyperparathyroidism is a common endocrine disorder which is characterized by hypercalcemia, renal stones, and bone disease.1 The diagnosis is made with an inappropriately high serum PTH level in the presence of hypercalcemia. Phosphorus levels are typically low, but may be normal with kidney disease.

In the present case, increased PTH levels, hypercalcemia and hypophosphatemia together with bone involvement in the form of lytic bone lesions called Brown tumor, and multiple fractures in humerus bone, clavicle, rib and pelvis were suggestive of hyperparathyroidism. Secondary hyperparathyroidism due to low serum vitamin D levels was ruled out with a normal serum 25-hydroxyvitamin D concentration (41 ng/dL).10 In this patient, polyarthritis and laboratory data persistent after parathyroidectomy were not justified with the course of hyperparathyroidism.

Rheumatologic manifestations are common amongst patients with hyperparathyroidism. In a study, more than half of the patients (53%) with hyperparathyroidism had musculoskeletal symptoms for twelve months prior to the diagnosis of their disease. Of these, 26% had consulted a rheumatologist or orthopedist, their most common symptom being myalgia followed by arthritis, arthralgia, and erosive synovitis.8 Hyperparathyroidism may also cause osteoporosis and pathologic bone fractures. Biwates reported rheumatoid-like erosions in the metacarpal bones and the styloid process of the ulnar bone in patients with hyperparathyroidism.12 These changes could be the result of acute synovitis and effusion caused by subchondral bone collapse due to hyperparathyroidism.15

However, radiologic evidence of joint space narrowing of the metacarpophalangeal and proximal interphalangeal joints are suggestive of RA. The typical subperiosteal bone resorption on the radial side of fingers is found in a minority of patients with hyperparathyroidism. Bone erosions in hyperparathyroidism are mostly shaggy in appearance and are distributed in the radiocarpal, radioulnar, MCP, and distal interphalangeal joints rather than the PIPs. Other radiologic features in favor of hyperparathyroidism include Brown tumors and cystic changes in bones.15

In this case, symptoms such as myalgia, arthralgia, and arthritis may be observed in patients with hyperparathyroidism, yet laboratory evidence of elevated ESR, positive CRP, and high titers of anti-CCP and RF were diagnostic of rheumatoid arthritis. Also, polyarthritis did not resolve after parathyroidectomy. Therefore, the concomitant diagnoses of hyperparathyroidism and RA were made.

In a study by Kennedy, hyperparathyroidism was reported to be the most common cause of hypercalcemia in RA. This finding was later confirmed by a study conducted between the years 1987 and 1988 on 5000 patients with RA. Other causes of hypercalcemia in patients with RA included the use of thiazide diuretics, cancer, immobility, vitamin D toxicity, and chronic liver disease. These studies demonstrated that the etiologies for hypercalcemia in patients with RA are similar to those of the general population and hypercalcemia in RA was not, as previously thought, a complication of RA.17

Finally, the aim of the present case report with concomitant occurrence of hyperparathyroidism and rheumatoid arthritis was to highlight the fact that hyperparathyroidism may present with rheumatologic manifestations, leading to an initial misdiagnosis. Furthermore, attention to the fact that hypercalcemia is not associated with RA, and rather suggestive of a concomitant disorder, is crucial to the correct diagnosis of hyperparathyroidism in RA patients with hypercalcemia.

References


