Primary hyperparathyroidism (PHPT) and multiple myeloma (MM) are frequently observed in the adult population and can each independently lead to hypercalcemia. Despite the frequency of hypercalcemia secondary to PHPT and MM, these two conditions only rarely concurrently present in patients. We describe the management of PHPT in the setting of poorly differentiated MM in a patient presenting with hypercalcemia and pancytopenia. The patient was deemed at increased risk for surgical removal of the parathyroid gland and refused surgical intervention, so we chronically managed her PHPT and hypercalcemia with Cinacalcet and bisphosphonates. All of the similar cases in the literature are reviewed in this report along with medical management of PHPT. We believe that we describe the first medically managed PHPT in the setting of MM.

Key words: primary hyperparathyroidism, multiple myeloma, hypercalcemia

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Introduction

Hyperparathyroidism and multiple myeloma (MM) are frequently observed in the adult population and each can lead to hypercalcemia. However, the occurrence of these two relatively common conditions in the same patient is rare (1) and has been reported only 17 times in the literature (2-15). In all of the previously reported cases, hypercalcemia was managed by parathyroidectomy along with medical management of the MM. To our knowledge, this is the first case of medical management of multifactorial hypercalcemia secondary to concurrent PHPT and poorly differentiated MM. This approach was pursued because our patient was a high risk surgical candidate with multiple co-morbidities and we wanted to avoid parathyroidectomy.

Case Report

A 59-year-old African American woman with a remote history of breast cancer in remission, hypertension, congestive heart failure (CHF), and normal baseline kidney function was hospitalized for evaluation of shortness of breath related to possible CHF exacerbation and possible pneumonia. The CHF was treated with intravenous furosemide and enalapril and the pneumonia was managed with intravenous antibiotics by a cardiologist prior to our evaluation. At initial evaluation, the patient’s heart rate was 93, blood pressure 112/75 mm Hg, temperature 97.5 degrees Fahrenheit, pulse oximetry 96% on room air. Physical exam showed neck without palpable masses, lungs were clear to auscultation bilaterally, and no focal neurological deficits were found.

On admission, the patient’s laboratory values revealed corrected calcium of 12.7 mg/dl (Table 1-1) and pancytopenia, and parathyroid hormone level of 157 pg/ml, suggesting primary hyperparathyroidism. Further imaging with an ultrasound of the neck revealed a mass suspicious for parathyroid adenoma. Sestamibi scintigraphy was inconclusive for parathyroid adenoma but revealed bone changes (brown tumors) consistent with hyperparathyroidism and increased uptake within the thyroid (Fig. 1). Bone marrow biopsy was done, which showed poorly differentiated malignant cells suspicious of metastatic breast cancer vs. multiple myeloma. Further histochemical evaluation of the malignant cells at M.D. Anderson Cancer Center in Houston, Texas,
Figure 1. Sestamibi scintigraphy of the parathyroid showing multiple osseous lesions which in the left humerus, right proximal humeral head, the scapula bilaterally, the proximal right clavicle, the sternum and in the spine. In addition, there is increased uptake in the thyroid region.

Figure 2. Bone marrow biopsy showing lambda light chain positive cells suggesting multiple myeloma.

Table 1. Patient’s Relevant Laboratory Values

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<tr>
<td>Corrected Calcium mg/dl</td>
<td>12.7</td>
<td>7.8</td>
<td>10.5</td>
<td>7.5</td>
<td>9.8</td>
<td>8.1</td>
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<td>Intact PTH pg/dl</td>
<td>157</td>
<td>383</td>
<td>69</td>
<td>55</td>
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<td>47</td>
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<td>Creatinine mg/dl</td>
<td>1.1</td>
<td>0.9</td>
<td>0.6</td>
<td>0.8</td>
<td>1.6</td>
<td>0.9</td>
</tr>
<tr>
<td>Albumin g/dl</td>
<td>3.8</td>
<td>3.7</td>
<td>3.7</td>
<td>3.2</td>
<td>2.5</td>
<td>2.9</td>
</tr>
<tr>
<td>Magnesium mg/dl</td>
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<td>2.1</td>
<td>2.3</td>
<td>2.2</td>
<td>2.1</td>
<td>1.8</td>
</tr>
<tr>
<td>Phosphorous mg/dl</td>
<td>2.4</td>
<td>2.8</td>
<td>4.5</td>
<td>5.0</td>
<td>3.5</td>
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Discussion

Association of PHPT with MM is a rare clinical event...
and has been previously reported in only 17 instances. In at least one of these cases, no histological study of the parathyroid glands was performed (3), and a second was proven to be due to diffuse hyperplasia of the parathyroid gland, not a parathyroid adenoma (4).

Furthermore only 12 previous cases (1) have provided the details on age, sex and initial diagnosis (Table 2). There were 11 women and 2 men, the former being predominant. The frequency of PHPT is higher in women, while MM is slightly more common in men. Differences in the incidence of the 2 diseases (MM is less frequent than PHPT) were considered to be the basis for woman preponderance.

On the other hand, MM alone was the initial presentation in almost half of the cases (6 out of 13) whereas both causes were reported at presentation 4 times. The more common PHPT was the initial diagnosis in only 3 cases, perhaps because of the subclinical course of the condition.

A second statistical study discussed the management of 13 of these 17 cases. Parathyroidectomy was necessary in 13 cases to achieve the eucalcemic state, and this study concluded that surgical treatment is indicated in these synchronous conditions to correct hypercalcemia (2).

In the present patient, it was crucial to control the PTH level to avoid further bone destruction and worsening hypercalcemia as the malignant disease was advancing and destroying bone. Parathyroidectomy is the current treatment of choice for patients with moderate and severe hyperparathyroidism (16) as defined by the 1991 consensus statement from the NIH (17).

Currently, no approved medical treatment for primary hyperparathyroidism is available. Nonsurgical alternatives would be desirable for patients with primary hyperparathyroidism who failed surgery, have metastatic parathyroid carcinoma, or in whom co-morbidities put them at higher surgical risk (17).

In addition to the patient’s aversion to surgical intervention, our patient had CHF and cervical disease secondary to malignancy, putting her at a higher surgical risk. Therefore, we decided to use Cinacalcet and bisphosphonates to treat hypercalcemia caused by both PHPT and MM, respectively. Cinacalcet, a calcimimetic, is the only medical treatment which is reported to normalize serum calcium and lower PTH concentrations (17). It does so by activating the calcium-sensing receptor (CaSR) on the parathyroid gland (18), and thereby inhibiting PTH secretion by potentiating the inhibitory effects of extracellular calcium on parathyroid cells. They decrease the serum levels of PTH and subsequently calcium, with a leftward shift in the set point for calcium-regulated PTH secretion (Fig. 4) (19-21).

Based on their unique ability to increase the sensitivity of the CaSR to circulating serum calcium and to reduce both PTH and calcium levels, calcimimetics have the potential to provide the most definitive medical alternative to parathyroidectomy (19). Furthermore, bisphosphonates have been shown to increase bone mass in patients with primary hyperparathyroidism (22) as well as to decrease the incidence of hypercalcemia and skeletal bone-related events associated with multiple myeloma by promoting apoptosis of osteoclasts involved in degrading minerals on the surface of bone (23).
Conclusion

Nonsurgical alternatives to PHPT are desirable for patients with primary hyperparathyroidism who failed surgery, have metastatic parathyroid carcinoma, or in whom comorbidities put them at higher surgical risk. This case suggests that a combination of Cinacalcet and bisphosphonates can normalize serum calcium, lower PTH concentrations, and decrease bone demineralization in patients with concurrent PHPT and MM. Further studies are needed to confirm our findings as well as to determine and evaluate long-term non-surgical management of PHPT with Cinacalcet.

References