Primary hyperparathyroidism associated with multiple myeloma: a case report

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Abstract

Primary hyperparathyroidism and malignant diseases are the most frequent causes of hypercalcemia. Cases in which hypercalcemia is due to both these diseases have been included in a few reports. Forty six year old woman was admitted for malignant hypercalcemia of 166mg/l, the diagnosis was primary hyperparathyroidism. Multiple myeloma was also suspected given the pancytopenia on the cell blood count associated to hypercalcemia. Urine immunoelectrophoresis indicated Bence Jones protein (L type) and bone marrow biopsy showed mildly hypercellular bone marrow with plasmacytosis (30%). A parathyroidectomy was initially indicated as the first etiological treatment of the hypercalcemia. The patient was referred in a second time to the department of oncology, for a specialized treatment of multiple myeloma. In this paper we have discussed this rare phenomenon. We have also provided a review of the scientific literature published on co-diagnosis of Multiple Myeloma (MM) and Primary Hyperparathyroidism (PHPT).
**Introduction**

Hypercalcemia is a common clinical problem, it occurs in 15% of hospitalized patients [1]. Multiple Myeloma (MM) and Primary Hyperparathyroidism (PHPT) are among the most common causes of hypercalcemia but concomitant diagnosis of the two pathologic processes in one patient has have been included in a few reports. In this article we have discussed a patient presenting with this extremely rare phenomenon and have reviewed the relevant scientific literature.

**Patient and observation**

Forty-six year old woman was admitted for malignant hypercalcemia of 166mg/l, review of symptoms during admission was significant for anorexia, weight loss, general asthenia and polyuropolydipsic syndrome. Vitals at the time of admission were blood pressure 140/58mmhg, pulse 100 BPM, respiratory rate 18c/mn, Laboratory data indicated anemia, leucopenia, trombopenia, concentrations of immunoreactive parathyroid hormone (PTH) were elevated 379,1ng/l, phosphorus was low 27mg/dl, vitamin D was normal 32,48 ng/ml (30-75), albumin was low 21,1g/dl, total protein was hight 100g/dl (66-87), blood urea nitrogen 0,29g/l (0,25-0,48), creatinine 7mg/l (5-9), GFR=168ml\/mn. The dosage of urinary metoxy derivatives was negative, calcitinine was normal 3.6 (<10). X-ray and MRI of the upper left limb showed a brown tumor appearance of proximal radius (Figure 1), Cervical Ultrasound coupled to neck computed tomographic (CT) scans disclosed a mass on the posteroinferior aspect of the right lobe of the thyroid gland, it measures 1,48 * 1,2cm (Figure 2), the diagnosis was primary hyperparathyroidism. Multiple myeloma was also suspected given the pancytopenia on the cell blood count associated to hypercalcemia. X-ray of the skull and lumbar spine showed diffuse bone lytic lesions of various sizes (Figure 3). Serum immunoelectrophoresis revealed only Lambda monoclonal bow, urine immunoelectrophoresis indicated Bence Jones protein (L type) and bone marrow biopsy showed mildly hypercellular bone marrow with plasmacytosis (30%). Hypercalcemia was managed with intravenous hydration, bisphosphonates and furosemide. A parathyroidectomy was initially indicated as the first etiological treatment of the hypercalcemia. The postoperative course following parathyroidectomy was good and serum calcium and phosphorus showed normal values. Serum PTH rapidly fell to the normal level. The patient was referred in a second time to the department of oncology, for a specialized treatment of multiple myeloma.

**Discussion**

Primary Hyperparathyroidism (PHPT) is more common in females, whereas the opposite is true for Multiple Myeloma (MM). Differences in incidence of the two diseases may explain female preponderance cases of concomitant MM and PHPT [2]. A recent review identified a total of 29 case reports describing the association of PHPT and MM, including the first case described by Drezner and Lebovitz in 1978 [3]. The mechanism of this association remains unclear. Given that the diagnosis of PHPT often precedes the diagnosis of MM it has been hypothesized that the high rate of PTH induces MM [4]. Pest et al. hypothesized that elevated PTH may mediate the induction of MM through the downstream biological effects of IL-6 [4]. This hypothesis was supported by the study performed by Pirih et al. who showed that PTH decreases apoptotic cell death of the hematopoietic stemcells via the IL-6 [5]. Arnulf et al. showed that the prevalence of monoclonal gammopathy is higher in patients with PHTP as compared to general population [6]. The above-mentioned pathogenic mechanism gives an insight to how PHPT and MM may be linked. Hypercalcemia in multiple myeloma can be explained by multiple mechanisms. First, plasma cells produce various cytokines, including TNF-α and IL-6, that activate osteoclasts and lead to calcium washout from bones to the
bloodstream [7]. Second, some studies suggest that MM cells may secrete parathyroid hormone-related peptide similarly to other malignancies, such as squamous cell lung carcinoma [8]. Third, serum calcium may be falsely elevated because of a binding to immunoglobulin [9]. PHPT leads to hypercalcemia via direct bone resorption mediated by osteoclasts. Another important mechanism is through an increased calcium absorption in the duodenum and greater reabsorption in the kidneys. In the present case, primary hyperparathyroidism was initially diagnosed as the cause of hypercalcemia and multiple myeloma was suspected concomitantly to HPPT given the associated pancytopenia on cell blood count (CBC). It is interesting that at only 1 month following parathyroidectomy hypercalcemia returned despite of a normal level of PTH. Parathyroidectomy, combination of radiotherapy and chemotherapy had been used for treatment of this coexistent condition with variable success. Rao et al. [10] suggested that parathyroidectomy in patients with coexistent PHPT and MM serves three folds; first, it removes confusion about etiology of hypercalcemia; second, it alters prognosis of myeloma; third, calcium can be used as a tumor marker in cases if there is a recurrence of tumor.

Conclusion

Based on the present experience and the review of the literature hypercalcemia patients should be carefully examined. Diagnoses of primary hyperparathyroidism and multiple myeloma should be discussed in a systematic way and to perform a PTH assay and an immunofixation of serum proteins in the balance of one or the other of these two pathologies; their association is possible and not fortuitous, although their causal link has not yet been identified.

Competing interests

The authors declare no competing interests.

Authors’ contributions

All the authors have read and agreed to the final manuscript.

Figures

Figure 1: brown tumor appearance of proximal right radius on MRI
Figure 2: neck computed tomographic (CT) showing a parathyroid adenoma
Figure 3: bone lytic lesion of the skull

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