



# Extensive Visceral Calcification Demonstrated On Tc-99m MDP Bone Scan In Patient With Sphenoidal Sinus Carcinoma And Hypercalcaemia Of Malignancy: A Bad Prognostic Sign

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## Abstract

Sphenoidal sinus carcinoma is a rare cause of hypercalcemia of malignancy. We report on a 37-year-old male with sphenoidal sinus carcinoma with intracranial extension who developed hypercalcemia of malignancy with progressing disease and demonstrated diffuse metastatic visceral calcifications of lungs, myocardium, stomach, kidneys and thyroid

on follow-up  $^{99m}\text{Tc}$ -methylene diphosphonate bone scan. In the absence of extensive skeletal metastases, bone scan help confirm humoral nature of hypercalcaemia.

## Keywords

*Bone scan, visceral calcification, Humoral hypercalcemia, Sphenoidal Sinus carcinoma.*

## Introduction

Hypercalcemia is a commonly encountered paraneoplastic syndrome present in 10-40% of patients with malignancy. Cancers frequently associated with hypercalcemia are breast, lung, head and neck, kidney and hematologic malignancies particularly malignant myeloma<sup>(1)</sup>. Approximately 6% of patients with squamous cell carcinoma of the head and neck have hypercalcemia<sup>(2)</sup>.

Malignancy associated hypercalcemia can be divided into two syndromes, humoral hypercalcemia of malignancy and local osteolytic hypercalcemia. Humoral hypercalcemia of malignancy is mediated by certain humoral factors secreted into the circulation by tumor cells<sup>(3)</sup>. Local osteolytic hypercalcemia is caused by osteoclastic bone resorption from the release of factors produced by direct skeletal tumor after involvement.<sup>(4)</sup> Parathyroid hormone-related protein (PTHrP) is the most common etiological agent in the setting of humoral hypercalcemia. Approximately 4% of patients with squamous cell carcinoma of the head and neck have

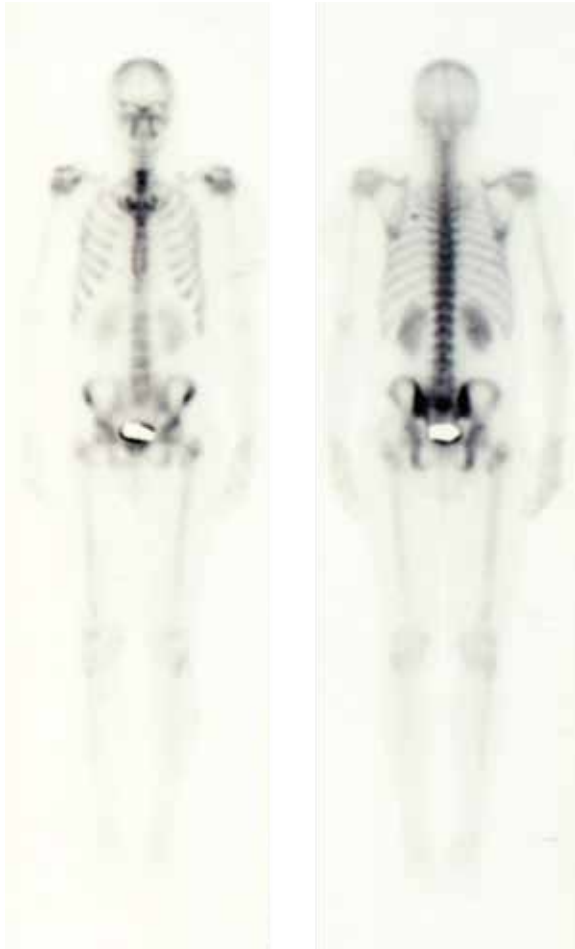
hypercalcemia mediated by PTHrP, which is thought to be an ominous prognostic sign<sup>(5)</sup>. The detection of hypercalcemia in a patient with cancer signifies a very poor prognosis; approximately 50 percent of such patients die within 30 days<sup>(6)</sup>.

## Case Report

A 37-year old gentleman had a long standing nasal sinus complaint. In February 2007 following laser turbinoplasty and nasal polypectomy, he developed ocular pain, diplopia and squint. A CT and MRI scan of nasal sinuses confirmed the presence of an advanced tumour in the sphenoidal sinus with invasion of base of skull and pituitary fossa with temporal lobes extensions. Biopsy confirmed poorly differentiated squamous cell carcinoma. Neck U/S revealed multiple bilateral lymph nodes, positive for metastatic squamous cell carcinoma on FNAC. Other investigations including blood count, biochemistry, CXR and U/S abdomen were normal. Bone scan showed a solitary rib lesion (Figure 1) with no corresponding X-ray abnormality.

The patient received a radical course of locoregional EBRT to the paranasal sinuses and neck nodes starting in July 2007. A total dose of 60 Gy/30 Fr./ 6 weeks was delivered by 3D-

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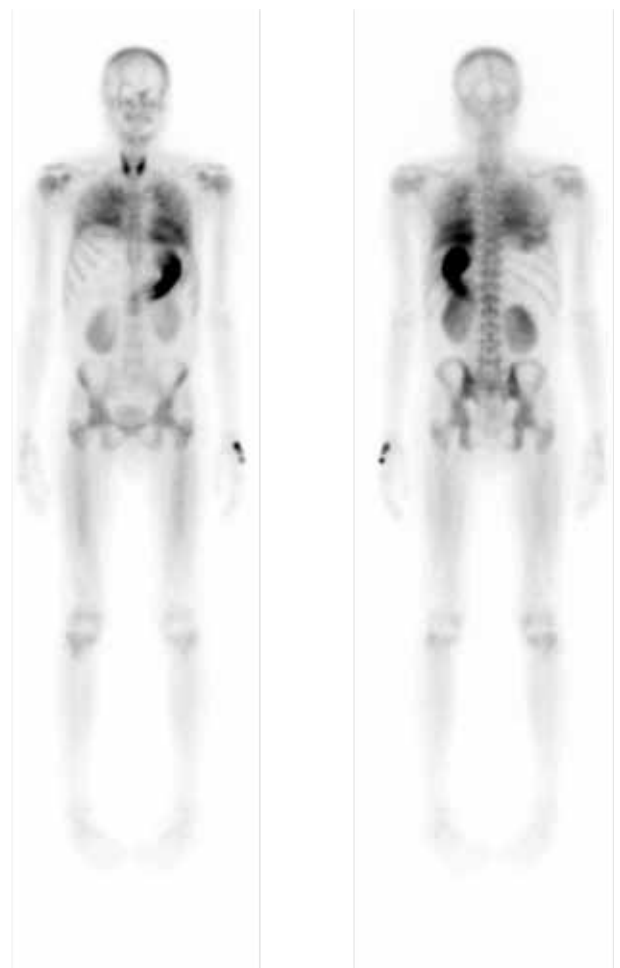
**Fig. 1: Baseline  $^{99m}\text{Tc}$ -methylene diphosphonate bone scan showed a solitary rib lesion with no corresponding X-ray abnormality.**

CRT technique. He also received 4 cycles of concomitant chemotherapy (Carboplatin/ 5 FU), treatment ended on October 2007. He tolerated the treatment well with good subjective response. His diplopia almost completely recovered and he had no further symptoms of nasal obstruction.

In December 2007 the patient presented to oncology casualty in poor general condition. He was confused, disoriented and dehydrated. His lab profile revealed hypercalcaemia with marked deterioration of renal functions and rise of liver enzymes. S. Ca =4.45mmol/L (normal range 2.2-2.6mmol/L), S. PO<sub>4</sub>= 1.68mmol/L (0.81-1.58), alkaline phosphatase 274 U/L, albumin of 24 G/L, parathyroid hormone 51.7 pg/ml (12 to 72 pg/ml), urea 32.6mmol/L and creatinine 534 $\mu$ mol/L.

Abdominal U/S revealed no evidence of obstructive uropathy, however multiple liver

metastasis were detected. The patient was started on hydration and biphosphonates and Calcitonin. A CT scan of the brain, paranasal sinus and neck was performed which revealed an advanced paranasal sinus tumour with extensive brain involvement as well as multiple cervical lymphadenopathy. A bone scan was repeated to assess extent of osseous metastases. Planar whole body imaging was performed 3 hr after injection of 24 mCi of  $^{99m}\text{Tc}$ -methylendiphosphonate (MDP) and showed extensive visceral activity in lungs, the heart, stomach, kidneys and thyroid (Figure 2). The solitary rib lesion reported previously was faintly visualized in the background of lung uptake. Quality control of the reconstituted Tc-MDP kit was normal and bone scans of other patients injected with the



**Fig. 2:  $^{99m}\text{Tc}$ -methylene diphosphonate bone scan show diffuse metastatic visceral calcifications on lungs, myocardium, stomach, kidneys and thyroid. The solitary rib lesion reported previously was faintly visualized in the background of lung uptake.**

same kit showed no evidence of abnormal soft tissue uptake.

The patient remained under supportive care, his renal profile improved but hypercalcaemia persisted and his condition progressively deteriorated as he succumbed to his illness on January 2008.

## Discussion

Paranasal tumors account for 3-4% of head and neck cancer and less than 1% of all malignancies in the body. Primary malignant tumor of sphenoidal sinus represents 1-2% of all paranasal tumors. There is slight male predominance. Mean age is 50 years<sup>(7)</sup>.

Humoral hypercalcemia in the absence of skeletal metastases is rare among sphenoidal sinus carcinoma patients. The usefulness of bone scan in evaluating metastatic calcification is a well-known fact and many case reports and review articles had been published.<sup>(8,9,10)</sup> In our patient, bone scan was instrumental in diagnosing humoral hypercalcemia in the absence of skeletal metastases. Bone scan demonstrated extensive calcification in thyroid, heart, both lung, stomach and kidneys after developing hypercalcemia. The bone scan done 4 months earlier was unremarkable. In addition to evaluate the status of skeletal metastasis, bone scan can detect metastatic calcification and can give supporting evidence of the humoral nature of hypercalcemia.

Humoral hypercalcemia is defined as hypercalcemia found in patients with cancer without extensive bone metastasis and hyperparathyroidism. The fundamental cause

of cancer-induced hypercalcemia is increased bone resorption induced by tumor PTHrp, with calcium mobilization into the extracellular fluid and, secondarily, inadequate renal calcium clearance<sup>(11)</sup>. Other factors playing role in the pathogenesis are IL-1, IL-6, prostaglandins, TGF alpha and -beta, PDGF, TNF-alpha<sup>(12)</sup>. Metastatic calcification occurs in non-osseous, viable tissue in the presence of severe hypercalcemia when the solubility product for calcium and phosphate is exceeded and precipitation of calcium in the extracellular space occurs. Diphosphonates tends to accumulate at such places.

Hypercalcemia and poor prognosis is an important fact with regard to the management of cancer patient, but the diagnosis of hypercalcemia can be done by blood analysis and the role of bone scan is not very high. Metastatic calcification detected by bone scan is a consequence of severe hypercalcemia and not all patients with hypercalcemia have positive bone scans. It has been reported that the average survival time after the occurrence of hypercalcemia in head and neck cancer is approximately 1 or 2 months<sup>(13)</sup>. The appearance of visceral calcification on bone scan thus may have some prognostic significance.

## Conclusions

Hypercalcaemia of malignancy is extremely rare in sphenoidal sinus carcinoma. In this study we have presented an example of humoral hypercalcemia on bone scan. The occurrence of hypercalcemia in these patients apparently implies an extremely poor prognosis, and long-term survival cannot be expected.

## References

1. Grill V & Martin TJ Hypercalcemia of malignancy. *Reviews in Endocrine and Metabolic Disorders* 2000;1: 253–263.
2. Dorman EB, Yang H, Vaughan CW, et al. The incidence of hypercalcemia in squamous cell carcinoma of the head and neck. *Head Neck Surg* 1984;7:95-98.
3. Wysolmerski JJ, Broadus AE. Hypercalcemia of malignancy: the central role of parathyroid hormone-related protein. *Annu Rev Med.* 1994;45:189-200.
4. Waller A, Caroline NL. Hypercalcemia. *Handbook of Palliative Care in Cancer.* 2nd ed. Boston, MA: Butterworth-Heinemann; 2000;367-72.
5. Mundy GR & Martin TJ The hypercalcemia of malignancy: pathogenesis and management. *Metabolism Clinical and Experimental* 1982; 31:1247–1277
6. Ralston SH, Gallagher SJ, Patel U, Campbell J, Boyle IT. Cancer-associated hypercalcemia: morbidity and mortality: clinical experience in 126 treated patients. *Ann Intern Med* 1990;112:499-504.

7. Mendenhall WM, Riggs CE Jr, Cassisi NJ: Treatment of head and neck cancers. In: DeVita VT Jr, Hellman S, Rosenberg SA, eds.: *Cancer: Principles and Practice of Oncology*. 7th ed. Philadelphia, Pa: Lippincott Williams & Wilkins, 2005; 662-732.
8. Padhy AK, Gopinath PG, Amini AC. Myocardial, pulmonaiy, diaphragmatic, gastric, splenic and renal uptake of Tc.99m MDP in a patient with persistent, severe hypercalcemia. *Clin Nucl Med* 1990;15:648-64
9. Peller PJ, Ho VB, Kransdorf MJ. Extraosseous Tc-99m MDP uptake: a pathophysiologic approach. *Radiographics* 1993;13:715-734
10. Loutfi I, Collier BD., Mohammed AM. Nonosseous Abnormalities on Bone Scans. *J Nucl Med Technol* 2003; 31:149-153
11. Stewart AF. Hypercalcemia associated with cancer. *N Engl J Med* 2005;352:373-9.
12. Clines GA, Guise TA. Hypercalcemia of malignancy and basic research on mechanisms responsible for osteolytic and osteoblastic metastasis to bone. *Endocr Relat Cancer* 2005;12:549-83.
13. Iwase M, Takemi T, Manabe M, Nagumo M: Hypercalcemic complication in patients with oral squamous cell carcinoma. *Int J Oral Maxillofac Srg* 2003;32:174-180.