Extensive Visceral Calcification Demonstrated on $^{99m}$Tc-MDP Bone Scan in Patient with Carcinoma Penis and Hypercalcemia of Malignancy

Abstract
Hypercalcemia is a common life-threatening complication associated with several malignancies. Parathyroid-related peptide has been shown to cause hypercalcemia in several solid tumors but rarely in penile cancer. We report a case of penile cancer with hypercalcemia causing metastatic visceral calcification in lungs, liver, and stomach detected on bone scan without significant abnormalities on CT scan.

Key words: Bone scan, carcinoma penis, hypercalcemia of malignancy, metastatic visceral calcification.

A male patient of 34 years is a known case of squamous cell carcinoma penis. He initially presented with ulcer-proliferative growth in penile region, which was proved to be squamous cell carcinoma on biopsy. He underwent penectomy and bilateral inguinal lymph node dissection for the same. He presented with right inguinal lymph nodal recurrence 4 months later. He underwent chemotherapy followed by radiation to right inguinal region. On follow up, he developed severe hypercalcemia. His S. Calcium level was 18 mg/dl (normal range 8.60-10.20 mg/dl). S. Creatinine was 3.79 mg/dl (normal range 0.5-1.5 mg/dl) suggestive of severe renal impairment. He was also having back and chest pain and was referred for bone scan. 20 mCi of Tc $^{99m}$ MDP (Methylene Diphosphonate) was injected IV and after 3 hour whole body swipe images were acquired in anterior and posterior projections on a dual head gamma camera. His whole body bone scan revealed significantly increased diffuse MDP uptake in bilateral lung fields, liver, and stomach. Scan was negative for skeletal metastasis [Figure 1]. Theses findings were suggestive of severe visceral calcification. Correlative CT scan images of thorax and upper abdomen did not show significant abnormality in lungs, liver, or stomach except for minimal bi-basal sub-pleural fibrosis [Figure 2a & 2b]. He underwent MRI scanning of abdomen and pelvis to look for any recurrent malignant disease, as CT scan with contrast was not possible because of severe renal dysfunction. His MRI showed multiple heterogeneous enlarged right inguinal, right internal-external iliac, bilateral common iliac, pre-paraortic, aorto-caval, and retrocaval lymph nodal metastasis.

Discussion
Metastatic calcification was first described by Virchow in 1855. Metastatic calcification is deposition of calcium salts in otherwise normal tissue, because of elevated serum levels of calcium. Causes of metastatic calcification include hyperparathyroidism,
chronic renal disease, sarcoidosis, amyloidosis, myeloma, malignant hypercalcemia of lymphomas, and solid tumors.\cite{1-10}

The exact mechanism of these calcium depositions remains uncertain; however, most accepted mechanism is an increase in the production of ionized calcium (calcium-phosphate complex primarily). The precipitation of ionized calcium is mainly in the alkaline pH tissues: lung, kidneys, myocardium, liver, and stomach walls.\cite{1,3,4-7} Reason for hypercalcemia in malignancy is the release of parathyroid-related peptide by malignant tissues.

Hypercalcemia is a common life-threatening complication associated with several genitourinary malignancies. Parathyroid-related peptide has been shown to cause hypercalcemia in several solid tumors but rarely in penile cancer. Only few cases have been reported.\cite{11-13} Our patient is a case of penile cancer with hypercalcemia causing metastatic visceral calcification detected on bone scan.

Bone scanning is sensitive modality for the detection of metastatic calcification.\cite{14-16} It is more sensitive and can pick up micro-calcification, not detected by conventional imaging modalities. Our case did not show any significant calcification in lungs, liver, or stomach on CT scan. In most cases, these metastatic calcifications are reversible after normalization of calcium metabolism and renal function with disappearance of the increased uptake on bone scan.\cite{1,3,6,7} Unfortunately, we do not have any follow up bone scan of the patient.

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Conflicts of interest

There are no conflicts of interest.

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