Case Report

Hypercalcemia Induced by Parathyroid Hormone-Related Peptide After Treatment of Squamous Cell Carcinoma of Oral Cavity


Abstract

Squamous cell carcinoma of the head and neck is a rare cause of humoral hypercalcemia of malignancy. This paraneoplastic syndrome is usually one of the presenting symptoms of the disease. We report a case of squamous cell carcinoma of the oral cavity that presumably elaborated parathyroid hormone-related peptide (PTH-rP) and caused hypercalcemia only after radiotherapy and chemotherapy.

INTRODUCTION

Hypercalcemia was recognized as the most common paraneoplastic syndrome as early as 1924.1 Initial studies implicated parathyroid hormone in the development of hypercalcemia. The exact role of parathyroid hormone in the development of hypercalcemia of malignancy was questioned in the early 1970s.2 The discovery of PTH-rP in 1987 by Mosley et al3 evoked interest in the mechanisms by which certain cancers cause hypercalcemia without necessarily metastasizing to the bone. Hypercalcemia of malignancy is thought to be due to the PTH-rP elaborated by the tumour cells in the advance stage of the disease. We report a case of squamous cell carcinoma of the oral cavity that presumably elaborated PTH-rP and caused hypercalcemia only after radiotherapy and chemotherapy.

CASE REPORT

A 47 years old male, presented with a one month history of swelling in neck with ulceration inside left cheek. He had been a chronic tobacco chewer in the past. Systemic examination did not reveal any significant abnormality. Local examination revealed ulcerating lesion on left cheek. There were multiple enlarged submental and submandibular lymphnodes on left side. CT scan revealed left cheek perimandibular and premaxillary mass consistent with squamous cell carcinoma of the buccal mucosa with involvement of left buccal masticator and parotid space with bilateral neck lymphadenopathy. Histopathology revealed a spindle-shaped squamous cell carcinoma composed of polygonal to spindle shaped cells showing pleomorphic mitotically active nuclei, the supportive stroma being sclerotic. Lymphnodes also showed metastatic deposits close to capsule and in surrounding fat. Investigation revealed Hb 14 gm%, PCV 45.3, platelets 1,40,000/cmm, s. Ca+2 10.5 mg%, s. PO4 3.4 mg%, alkaline phosphatase 110 U/L, total proteins 7.5 gm% with albumin of 3.7 gm%.

He received chemotherapy (2 cycles with paclitaxel, cisplatin and 5-FU. But, despite chemotherapy his pain persisted with an increase in the size of swelling, causing difficulty in speaking, eating, and in opening the jaw. As there was no obvious response to chemotherapy, he underwent left sided commando with wide excision with hemimandibulectomy with left radical neck dissection and excision of maxillary antrum.

After the wound healed, local radiotherapy (25 sittings), along with concurrent chemotherapy with weekly cisplatin was started. In due course of time, patient developed altered sensorium and weakness of left half of body. He required ventilatory support as he was unable to maintain his oxygenation. The investigations showed Hb 12.7 gm%, PCV 41.1, platelets 5,90,000/cmm, s. Ca+2 21.3 mg%, s. PO4 3.4 mg%, alkaline phosphatase 110 U/L, total proteins 7.3 gm% with albumin of 3.3 gm%, s. creatinine 1.4 mg%, parathyroid hormone 51.7 pg/ml (12 to 72 pg/ml). CT scan of brain showed infarct in the right MCA territory.

He was treated with intravenous saline, IV pamidronate and intramuscular calcitonin. His calcium levels came down to normal over next 5 to 7 days, but developed septicemia with multiorgan failure and patient died due to the same.

DISCUSSION

It is now known that PTH-rP is produced by most solid tumours, particularly squamous and renal carcinomas.4 Approximately 4.2% of patients with squamous cell carcinoma of the head and neck have hypercalcemia mediated by PTH-
rP, which is thought to be an ominous prognostic sign.\textsuperscript{5}

Although PTH and PTH-rP are products of different genes, they share many functional and structural similarities and may have evolved from the same ancestral gene as a result of a duplication event.\textsuperscript{6} The amino-terminal portions of PTH-rP and PTH have essentially identical actions through a common receptor. They increase plasma calcium by promoting bone resorption and decreasing calcium excretion. Although PTH-rP is widely distributed in normal tissues such as brain, kidney, skin, uterus, and breast, PTH-rP has little physiologic role in adults. It is involved in local signaling only, and is not released into the general circulation.\textsuperscript{7} On the contrary, in disease states, benign or malignant tumour may overproduce PTH-rP causing hypercalcemia.\textsuperscript{8} The presence of hypercalcemia in malignancy is correlated with the expression of the PTH-rP gene.\textsuperscript{9}

Our patient initially did not have hypercalcemia and presumably did not elaborate PTH-rP despite a large tumour volume. Later, after irradiation and chemotherapy, the tumour tissue then produced PTH-rP, resulting in hypercalcemia. Unfortunately the levels of PTH-rP are not done in our country, therefore, we postulate that radiotherapy or chemotherapy might have caused further cancer cell gene amplification or clonal rearrangement, resulting in overproduction of PTH-rP, though it is possible that this event could have occurred de novo.

\textbf{REFERENCES}


\textbf{Announcement}

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