

Case Report-II

Paraneoplastic Hypercalcaemia in Advanced Carcinoma of Oral Cavity.

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ABSTRACT

Most patients of head and neck cancers in India present in an advanced stage with malnutrition and problems related to chronic alcohol and tobacco consumption. Co-existing metabolic paraneoplastic manifestations make the management of the cancer more challenging. We report a case of advanced carcinoma of oral cavity associated with paraneoplastic hypercalcaemia and multiple life threatening metabolic complications.

INTRODUCTION

Head and neck cancers (HNC) account for approximately 21% of all malignancies. The epidemiological details of head and neck cancer burden in India are given in Table-1.¹ Majority of these patients are in poor general condition with varying degrees of malnutrition. Chronic alcohol and tobacco consumption with their related medical problems have been recognized as additional causal factors of nutritional deficit in HNC patients.

Paraneoplastic syndromes (PS) have occasionally been reported in association with HNC. These syndromes can be more serious than the consequences of the primary tumour itself and can precede, develop in parallel, or follow the manifestations of the tumour. PS that are encountered in HNC can be dermatological, neurological, hematological or endocrine

manifestations.² Hypercalcaemia is the most frequent presentation of paraneoplastic syndrome, in patients with HNC. We report one such case of advanced HNC with multifarious problems of hypercalcaemia, hypernatremia, hypokalemia and hyperglycemia.

CASE: A 41 year old, normotensive diabetic male with history of chronic alcohol intake and tobacco indulgence was diagnosed to have carcinoma of right lateral border of tongue (T4N2cM0); (Squamous cell) in April 2006. Following the diagnosis no treatment was taken and the disease progressed. After a period of 5months, he got admitted with the history of poor oral intake, in a state of drowsiness. He had no history of trauma, epilepsy or thyroid dysfunction in the recent past to account for the drowsiness.

On examination, his general condition was poor. Vitals were normal. He was drowsy with no localizing signs. Examination of cardiovascular, respiratory and abdomen did not reveal any abnormality.

Over the next twenty-four hours, his sensorium further deteriorated and he went into deep coma. Pulse, blood pressure and temperature were recorded as 98/min, 100/70mmHg and 98.4degree F respectively. His respiratory rate was 11/min with slow and shallow breathing. Neurological examination revealed bilateral asterixis. Cardiovascular, respiratory and abdominal examination was unremarkable.

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Table-1: Head Neck Cancers Burden in India

Head and Neck	Male	Female	Total
Cancers	Numbers (%)	Numbers (%)	Numbers (%)
1) Annual Incidence	121385 (70)	51692 (30)	1,73,077*
2) Sub sites			
-Oral cavity	52,008 (30.0)	30,906 (18)	82914 (48)
-Other pharynx	38,542 (22.5)	7,793 (4.5)	46335 (27)
-Larynx	24,216 (14.0)	3,157 (02)	27373 (16)
-Thyroid	4,361 (02)	8,686 (05)	13047 (07)
-Nasopharynx	2,258 (1.3)	1,150 (0.7)	3408 (02)

*HNC constitutes 21% (173,077) of all cancers cases. (Total number of cancers: 8, 51,901; Male: 4, 04,309 (47%); female: 4, 47,592 (53%))

His oxygen saturation was 98%. On investigation TLC, serum electrolytes (Na; K) ionized calcium and random blood sugar was raised (Table 2). Urine was negative for ketones. Chest X-Ray, ECG and CT scan of brain revealed no abnormality and bone scan was normal.

The patient was managed with (a) IV half-isotonic saline hydration (b) infusion of KCl (60-80mEq/L/day) (c) Inj zoledronic acid (4mg over 15 min) (d) Inj calcitonin (100 units S/C every 6 hourly) for three days in succession (e) Insulin according to the sliding scale and (f) parenteral nutrition. He was closely monitored in ICU for his vital parameters, blood sugar, serum sodium, serum potassium, ionized calcium and spO₂.

Gradually over the next 72 hours, he regained complete consciousness and his general condition improved remarkably. The deranged biochemical parameters were restored to normalcy. At present the patient is undergoing treatment with concurrent chemotherapy and radiation. He has no metabolic complications and is on regular follow-up.

DISCUSSION

The most common paraneoplastic syndrome (PS) associated with HNC is parathyroid hormone related-peptide (PTH-rP) induced hypercalcaemia, present in the advanced stage of the disease. It is known as humoral hypercalcaemia of malignancy or HHM. Approximately 4.2% of patients with squamous cell carcinoma of the head and neck have hypercalcaemia mediated by PTH-rP.³

Two distinct forms of hypercalcaemia are encountered in malignancy (4). In the first, serum phosphate is normal or increased. The raised calcium is attributable to the dissolution of bone by tumour metastasis. In second form, hypercalcaemia and low serum phosphate levels mimic primary hyperparathyroidism (Pseudo hyperparathyroidism). This syndrome is seen with non-endocrine tumours and there are no associated bone metastases. In these tumours, PTHrP levels are raised which cross reacts with the PTH receptor. Expression of PTHrP leads to hypercalcaemia by promoting bone resorption

Table-2: Biochemical Parameters of the Patient

Investigations	Values in Patient	Normal Range
Ionized calcium	1.80 mmol/L	1.1-1.4 mmol/L
Serum sodium	168 mEq/L	136-145 mEq/L
Serum potassium	2.3 mEq/L	3.5-5.0 mEq/L
Random blood sugar	251 mg/dl	60-140 mg/dl
Total leucocyte count	35,200/ cu mm	4000-11000/ cu mm

and decreasing calcium excretion by increasing distal renal tubular reabsorption.

Patients of HNC may present with varied signs and symptoms of hypercalcaemia, which include malaise, fatigue, nausea, vomiting, polyuria, dizziness, confusion, lethargy and coma. These are usually present, when the serum calcium levels exceed 3.0mmol/l. If the patient of HNC presents with lethargy and coma, hypercalcaemia as a cause should not be overlooked as early diagnosis and treatment of hypercalcaemia can improve the patient's condition.

Leucocytosis in a cancer patient can be justified as PS, if there is no evidence of acute infection and leukaemia. The occurrence of hypercalcaemia and leucocytosis in combination even though rare has been documented in HNC. A study assessed 225 patients with oral malignancies; of which 11 (4.9%) patients had leucocytosis and five (2.2%) had both hypercalcaemia and leucocytosis.⁵

Altered sensorium, in this patient is multifactorial- cancer related PS (hypercalcemia) and metabolic dysfunction (hyponatremia and hypokalemia) in concurrence with accompanying complicated diabetes; accounting for hyperglycemia. The level of PTH-rP in this patient was not estimated.

Metabolic complications although frequently encountered in HNC patients, have been less extensively studied. As the signs and symptoms with which the patient presents, are difficult to correlate with the primary disease. Combination of increased nutritional demand, decreased oral intake and tumour-induced abnormal metabolism of carbohydrates, lipids and proteins creates a state of metabolic disorder in these patients. In addition alcohol and tobacco aggravate the existing nutritional deficit by providing empty calories without essential vitamins and by acting as an appetite suppressant respectively. Therefore pretreatment metabolic evaluation with appropriate management can avoid additional complications and improve patient's general condition.

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