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Metabolic encephalopathy as a cause of mortality in a patient of carcinoma alveolus receiving neo adjuvant chemotherapy

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ABSTRACT

A 45 yrs., old gentleman, with no co morbidities and chronic tobacco chewer, developed a lesion in the left inner cheek, which over a period of 5 months, developed into an ulcero-proliferative growth involving left lower mandible, RMT (retro molar trigone) and buccal mucosa. After clinical history, examination, imaging and histopathology, he was diagnosed as a case of CA (carcinoma) left lower alveolus with secondary lymphadenopathy. He was started on neo-adjuvant chemotherapy (Paclitaxel-Carboplatin). On the 7th day after the first cycle of chemotherapy, patient reported with features of tachycardia, confusion and disorientation. He was admitted in the ward and symptomatic treatment was started. His TLC (total leucocyte count) (2,700/µL) was low and had mild hypokalaemia (3.22 mmol/L). ABG (arterial blood gas) showed partially compensated non-respiratory alkalosis (PCO2 48.3 mmHg, pH 7.47 & HCO3 33.9 mmol / L). In spite of prompt IV (intra venous) fluid support, higher antibiotics administration and comprehensive tertiary care support, patient expired within 36 hours of admission. Dyselectrolytemia and metabolic encephalopathy $\pm$ sepsis can be a sudden cause of death when chemotherapy is being administered in a chemotherapy naive patient. Although it is rare, but prompt IV fluid support, electrolyte management, a holistic approach can prevent such inadvertent mortality.

INTRODUCTION

Cancer is the third commonest cause of mortality and fifth most common cause of morbidity according to recent report of WHO (world health organisation). Head and neck cancers are very common in Indian subcontinent. Treatment of cancer, particularly, chemotherapy is a very toxic treatment and has a lot of effects on the quality of life leading to morbidity and sometimes mortality. Care has to be taken in relation to disease status and health status which includes social, economical and psychological factors during the treatment. It is painful for the treating consultant and patient's attendants to bear the stress regarding the outcome from this deadly disease and utmost care of all the factors combined should be taken, so that the patient can cope up with the morbidity and unnecessary mortality can be avoided.

CASE REPORT

The patient is a 45 years old male working as a construction worker with no comorbidities and no prior history of any drug allergy. He was addicted to chewing tobacco quid for 20 years. He developed a pea-sized swelling in the left inner cheek, which over a 5 months period, increased to engulf the lower part of jaw bone and then it was associated with pain and tenderness, causing a bulge in that part of the cheek externally.

Patient then came to our OPD (outpatient department), with complains of trismus, pain and occasional bleeding from the lesion. Patient's nutritional status was poor and belonged to poor socio-economic background with KPS (Karnofsky performance status) - 70. On examination we found a large 6 x 5 cm ulcero-proliferative lesion, involving the retro-molar trigone, buccal mucosa and the lower alveolus. A 2 x 1.5 cm firm, fixed lymph node was found in the submandibular area. MRI (magnetic resonance imaging) face showed a 6.3 x 5.5 x 5.3 cm T2 hyper-intense lesion involving left half of mandible, infratemporal fossa, medial, lateral pterygoid muscles, RMT and buccal mucosa and a left submandibular lymph node measuring 2.5 x 2.1 cm. FNAC (fine needle aspiration cytology) from the swelling was consistent with squamous cell carcinoma. Chest X-ray, USG

(ultra sonography) whole abdomen, all routine blood investigations and baseline cardiac evaluation were normal.

The patient was diagnosed as advanced CA left alveolus with secondary lymph nodes (c T4N1MO). The surgical oncologist deemed it as inoperable, in view of trismus and the extension of the lesion into pterygoid muscles. We planned to give the patient neo-adjuvant injection Paclitaxel 260 mg (calculated as 175 mg/m2) IV on D1 and injection Carboplatin 450 mg (AUC 5) IV on D2 in view of the advanced nature of the disease. Chemotherapy administration was uneventful.

Patient reported to emergency one week after the administration of chemotherapy with features of fever for 3 days, tachycardia and disorientation. The GCS (Glasgow coma scale) score was E4V2M3. Bilateral pupils were sluggishly reacting to light. On motor examination, patient was moving all four limbs spontaneously. Plantar reflexes were equivocal bilaterally. There was no history of nausea and vomiting. The oxygen saturation was falling rapidly (70% at admission). BP (blood pressure) 106 / 62 mm of Hg, pulse 160 / min and temperature 102° F. RBS (random blood sugar) was within normal limits. Patient was put on oxygen immediately and catheterised. The saturation improved to remain stable around 91 % with oxygen @ 6 L / min. Chest X-ray suggested normal bilateral air entry.

All the routine blood investigations plus culture sensitivity of blood, cough and urine were immediately sent. Broad spectrum antibiotics were started along with continuous monitoring and intra-venous fluid support. ICU (intensive care unit) and neurological opinion was also taken. TLC - 2700/µl, and DLC (differential leucocyte count) showed 68.9 % neutrophils (ANC - 1860/µl) and 20% lymphocytes. Hb (haemoglobin) and total platelets were normal. Serum potassium was 3.22 mmol / L and serum sodium was 137 mmol / L. LFT, KFT and sugar were normal. ABG suggested partially compensated non-respiratory alkalosis (PCO2 48.3 mmHg, pH 7.47 & HCO3 33.9 mmol/L).

Urine output was 1000 ml / 24 hours. Within 30 hours of the admission, the patient's GC (general condition) started deteriorating. Oxygen saturation and blood pressure started falling to around 80 % and 88 / 56 mm of Hg, respectively. Then the patient, suddenly deteriorated. After 2 hours of intensive resuscitation and CPR (cardiopulmonary resuscitation) and with all the emergency medication given continuously, patient could not be revived and expired within 36 hours of admission. In view of the derangements in electrolytes, blood counts and ABG, we concluded the diagnosis of metabolic encephalopathy with component of sepsis following the administration of chemotherapy as the cause of death, although all the precautions, premedications and care was taken during the administration.

DISCUSSION

Chemotherapy has been known to cause side effects [1, 2], acute effects of which are seen most commonly during the first few cycles as the tolerance of the patient to the drug is unknown. Carboplatin should be administered after Paclitaxel when used in combination [3, 4]. Platinum compounds inhibit plasma clearance of paclitaxel[4]. This sequence prevents delayed Paclitaxel excretion, which results in increased paclitaxel drug levels and potentially increased host toxicity. Also, myelosuppression is greater when platinum compound is administered before Paclitaxel[4].

Commonly reported side effects of paclitaxel-carboplatin include: nausea and vomiting[5,6], hypotension, myalgia, arthralgia, hypersensitivity, mucositis, diarrhoea[6,7], skin rash, alopecia, increased serum aspartate aminotransferase[6,8], peripheral neuropathy, SIADH (syndrome of inappropriate anti-diuretic hormone) [5,8,9], infusion site reaction[1], increased serum alkaline phosphatase [6], and flushing, severe myalgia, severe arthralgia [10], and increased serum bilirubin.

Dyselectrolytemia, as such, has not been directly reported as a cause of death in patients receiving paclitaxel, although, electrolyte imbalance, as a consequence of SIADH or as a result of continuous vomiting has been reported. The patient had no associated vomiting, or any hypersensitivity at the time of administration of the drug. Sepsis, followed by septic encephalopathy is a possibility, given the low TLC count, but the absolute count was well above the level of 1500 / dL, ruling out septicemia alone as a cause of death. Also, the negative blood and urine culture tests further foster the fact. The patient had decreased potassium to start with and then the ensuing compensated non-respiratory alkalosis points to the diagnosis of rapid onset metabolic encephalopathy as the best possible cause.

CONCLUSION

Cancer patients suffer from a lot of symptoms apart from cancer, like nutritional deficiency, fatigue, malaise, cachexia, occupational, financial, social constraints and foremost is denial at the time of diagnosis. So, careful administration of chemotherapy, proper post-chemotherapy counselling and prompt management of dyselectrolytemia can avert mortality in these groups of patients from our side. We have to take care of other associated factors into consideration while taking the management decision.

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