An unusual case of hypercalcaemia

Introduction

Squamous cell carcinoma is an aggressive malignant tumour of squamous epithelium and can therefore be diagnosed in locations such as the skin, oral cavity, lung, urinary bladder and cervix. It is difficult to treat and has a poor survival rate. Lesions are often asymptomatic in their early stage and clinical presentation can vary significantly.

Most cancers of the oral cavity are squamous cell carcinoma in origin. Symptoms vary, but a persistent mouth ulcer or an unrelenting hoarse voice is a classical red flag. Well-established risk factors include smoking and excess alcohol consumption. However, the Center for Disease Control and Prevention in the USA states that up to 25% of oral squamous cell carcinoma are caused by human papillomavirus (Gillison et al, 2000).

For patients who present with oral squamous cell carcinoma without evidence of metastases, surgical resection of the tumour along with regional lymph node dissection is the preferred treatment. Postoperative radiotherapy has been used to improve local control although there are no conclusive trials yet documenting its efficacy. Metastatic disease is managed with systemic chemotherapy (Oliver et al, 2007).

Discussion

Isolated metastasis to the liver from a primary squamous cell carcinoma of the palate is rare. There have been a few case reports of primary oropalatal squamous cell carcinoma with distant hepatic metastasis (Shukla et al, 2003).

Parathyroid hormone-related protein is closely related in its function to parathyroid hormone and therefore if a tumour secretes parathyroid hormone-related protein, hypercalcaemia may result (Broadus et al, 1988). Parathyroid hormone-related protein is responsible for most cases of humoral hypercalcaemia in cases of malignancy. There have been occasional reports of clinically significant hypercalcaemia secondary to parathyroid hormone-related protein (Dunne et al, 1995; Fujikawa et al, 2002; Iwase et al, 2003).

The aim of initial treatment for hypercalcaemia is to restore intravascular volume depletion and to promote hypercalciuria. In patients with adequate cardiovascular and renal function this is usually accomplished with 0.9% normal saline infusions at 300–500 ml/h until the fluid deficit is restored.

If cancer therapy is not able to be started immediately, then drugs like bisphosphonates must be used to lower calcium levels and control the hypercalcaemia. The standard daily infusion dose of disodium pamidronate for the treatment of hypercalcaemia in patients with normal renal function is 60–90 mg over 2–4 hours.

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Case Report

A 54-year-old male Caucasian was admitted to North Manchester General Hospital with a 5-day history of confusion and hallucinations. A history taken from his family revealed a prior 4-week history of decreased appetite and weight loss coupled with episodes of urinary incontinence.

Three months before this the patient had been diagnosed with squamous cell carcinoma of the soft palate, confirmed to be locally invasive by computed tomography scan. He had been booked for radical resection of the tumour in the coming week. Past medical history included coeliac disease and hypertension. He was a current heavy smoker and a heavy consumer of alcohol until 1 month ago. He was not taking any regular medications.

On examination the patient appeared agitated and confused. He was apyrexial, with a heart rate of 103 beats per minute, blood pressure 128/75 mmHg and low pulse oximetry at 93%. Systemic clinical examination was otherwise unremarkable. Initial blood investigations including full blood count, urea and electrolytes and liver function tests were normal except for raised inflammatory markers and markedly raised corrected calcium of 4.08 mmol/litre. His parathyroid hormone level was 6 ng/litre. Other investigations included a normal mid-stream urine sample, electrocardiogram and chest X-ray; computed tomography of the head and neck did not show any change from a previous scan showing soft palate lesion with local invasion. The differential diagnosis at this point was sepsis of unknown origin, hypercalcaemia secondary to bony metastasis or confusion secondary to hypercalcaemia or infection.

He was treated with aggressive intravenous fluids (4 litres in the first 24 hours) and intravenous pamidronate for his hypercalcaemia, intravenous broad spectrum antibiotics for sepsis and lorazepam for his agitation. His confusion persisted despite corrected calcium coming down to 3.27 mmol/litre over the next few days.

Subsequently computed tomography of the abdomen, pelvis and thorax was performed which showed diffuse liver metastatic deposits. There was no bony metastasis to account for the hypercalcaemia. A bone scan did not show evidence of any lytic or sclerotic metastases. His inflammatory markers remained high but blood and urine cultures revealed no growth. Tumour markers showed normal carcinoembryonic antigen and alpha-fetoprotein levels. CA19-9 was raised at 841 U/ml (normal range <35 U/ml).

He was reviewed by oncology who deemed him unfit for any intervention but suggested liver biopsy to try and get any clues for the primary as oral squamous cell carcinoma was suggested to be unlikely to metastasize to the liver. He started becoming increasingly drowsy and his calcium started to rise again (corrected calcium 5.26 mmol/litre). A further dose of intravenous pamidronate (90 mg course) made little difference to his hypercalcaemia. He continued to deteriorate and eventually died 22 days after admission. His parathyroid hormone-related protein level was high at 13.8 pmol/litre (normal range <1.8 pmol/litre).

The post-mortem examination revealed diffuse infiltration of the liver by a tumour which was squamous cell carcinoma on histology. There were no other sites found to have squamous cell carcinoma.

Conclusions

This patient developed hypercalcaemia secondary to high parathyroid hormone-related protein levels which were resistant to traditional treatment. The case also shows that resistant hypercalcaemia is possibly a sign of poor prognosis or outcome. **BJHM**

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