SHORT REPORT

Unpleasant sweet taste: a symptom of SIADH caused by lung cancer

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A 56 year old woman with large cell lung carcinoma complained of an unpleasant sweet taste (dysgeusia). She developed hyponatraemia caused by the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Dysgeusia disappeared when serum sodium normalised and recurred when hyponatraemia relapsed. Dysgeusia was the initial and only symptom of SIADH in this case.

Dysgeusia is a distortion in the perception of taste. Total dysgeusia is the inability to detect sweet, sour, bitter, or salty tastes. While abnormal taste sensation (dysgeusia) often occurs in cancer,[1–4] partial dysgeusia in which all tastes are interpreted as sweet is rare. We present a case of such a specific taste disorder which occurred in a woman with hyponatraemia and disappeared when serum sodium concentration was normalised. The patient was later confirmed to have lung cancer. We considered the dysgeusia to be related to syndrome of inappropriate antidiuretic hormone (SIADH) secondary to lung cancer.

CASE REPORT

A 56 year old woman, with a seven week history of dysgeusia in which nearly all food was interpreted as sweet was admitted to our hospital seeking treatment for this symptom. She reported that everything apart from eggs had an unpleasant sweet taste, and two weeks before admission, this symptom had gained severity to the point where all other foods induced nausea. Her past medical history included surgical clipping of a subarachnoid haemorrhage in 2003, a sequel of which was right blepharoptosis.

On admission, body temperature was 38.5°C, heart rate 68 beats/min, and blood pressure 130/86 mm Hg. Physical and neurological findings were unremarkable other than the right blepharoptosis.

Her serum sodium concentration was 113 mmol/l, but creatinine, zinc, urea nitrogen, potassium, and liver enzyme levels, as well as blood glucose, were all within normal limits. Serum antidiuretic hormone was normal (0.9 pg/ml). Urinary and serum osmolalities were normal (244 and 254 mmol/kg). Results of thyroid function tests and serum levels of hypothalamic hormones (ACTH, cortisol, growth hormone) were also normal. A 24 hour fluid balance was undertaken on hospital day 2; the patient drank a lot of water (2700 ml) because all food tasted so sweet, and excreted a large amount of urine (3700 ml). Computed tomography (CT) and magnetic resonance imaging (MRI) of the brain revealed no pathological changes in the pituitary gland or other intracranial structures.

Water restriction was begun on the day of admission and serum sodium concentration rose to 124 mmol/l on hospital day 5, at which point nausea and dysgeusia disappeared and the patient regained her appetite. The serum sodium level was maintained at 120 mmol/l or higher. As the symptoms had improved, the patient decided to leave hospital, although the cause of the dysgeusia remained unclear. The dysgeusia and nausea relapsed one week after discharge and she was readmitted. On this admission, her serum sodium concentration was low (109 mmol/l), urinary osmolality was raised (489 mOsm/kg) with serum hypo-osmolality (226 mOsm/kg), but serum creatinine and urea nitrogen levels were normal (0.40 mg/dl and 4.0 mg/dl). On the basis of these laboratory findings, SIADH was diagnosed. Water restriction and saline infusion (1500 ml/day) was begun on the day of admission, and the serum sodium concentration rose to 127 mmol/l within a few days. Dysgeusia again disappeared and the patient was able to resume her normal diet. So long as the serum sodium concentration was maintained at 130 mmol/l or higher, dysgeusia did not recur.

Chest *x* ray findings were normal but CT of the chest revealed a 1.7×1.7 cm mass lesion in the right superior lobe (S1), with multiple periaortic and peribronchial nodules. Biopsy of cervical lymph nodes established the diagnosis of neuroendocrine large cell carcinoma.

DISCUSSION

In this case, the initial and only symptom was an unpleasant sweet taste of nearly all food (dysgeusia), and hyponatraemia was the sole anomaly on biochemical investigation. The dysgeusia disappeared rapidly with normalisation of serum sodium concentration and recurred when hyponatraemia relapsed. The diagnoses of SIADH and large cell lung carcinoma were established on the second admission.

Dysgeusia associated with SIADH is rare.[5] Taste distortion in which tastes are experienced as sweet was first reported to be related to hyponatraemia in 1995[6] and five similar cases have since been reported.[6–8] While the cause of SIADH was lung cancer in all cases, the histological type varied: small cell carcinoma was diagnosed in three cases,[6] oat cell carcinoma in one,[7] and adenocarcinoma in one.[8] Large cell carcinoma was diagnosed in the present case. It is thus clear that as a prerequisite for the development of sweet dysgeusia, lung cancer as well as either hyponatraemia or SIADH must be present.

Animal experiments have demonstrated that the extracellular sodium level may have a modulating effect on the sweet receptor.[9 10] It was suggested that hyponatraemia decreases thresholds in lingual sweetness receptors. However, a low sodium level alone cannot be implicated as the sole cause of taste alteration, as taste thresholds are normal in patients with hyponatraemia from causes other than lung cancer.[11]

Recently, it has become clear that sweet stimuli, such as sugar or artificial sweeteners, bind to a G-protein coupled receptor.[12] We consider that, in addition to hyponatraemia, an unknown taste modifying substance might be produced by the tumour, causing patients with dysgeusia to interpret all foods

Abbreviations: SIADH, syndrome of inappropriate secretion of antidiuretic hormone

as sweet. One such taste modifying substance is miraculin, which is a glycoprotein extracted from the berries of *Richadella dulcifera*, a shrub native to West Africa.[13] After chewing its pulp, all sour substances are experienced as sweet. Miraculin itself does not elicit a sweet response but instead it binds to the receptor membrane near the sweet receptor site. Unless a sour acid is applied, miraculin does not occupy any of the sweet receptor sites; however, receptor membrane bound miraculin changes its structure at the low pH induced by sourness. Altered miraculin fits the sweet receptor site and induces a strong sweet taste.[14] Malignant neoplasms may produce unknown taste modifying substances like miraculin, although they would not cause dysgeusia in individuals with normonatraemia. We thus hypothesise that structural change occurs in the taste receptor membrane only when extracellular sodium levels decrease, which readily allows the taste modifier to attach to the sweet receptor site.

In conclusion, it is necessary to consider SIADH caused by lung cancer when cryptogenic dysgeusia is encountered, particularly if it results in an unpleasant sweet taste.

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REFERENCES

1 **DeWys WD**, Walters K. Abnormalities of taste sensation in cancer patients. *Cancer* 1975;**36**:1888–96.
2 **Markley EJ**, Mattes-Kuling DA, Henkin RI. A classification of dysgeusia. *J Am Diet Assoc* 1983;**83**:578–80.
3 **Schiffman SS**. Taste and smell in disease, part 1. *N Engl J Med* 1983;**308**:1257–79.
4 **Schiffman SS**. Taste and smell in disease, part 2. *N Engl J Med* 1983;**308**:1337–43.
5 **Kovacs L**, Robertson GL. Syndrome of inappropriate antidiuresis. *Endocrinol Metab Clin North Am* 1992;**21**:859–75.
6 **Panayiotou H**, Small SC, Hunter JH, *et al*. Sweet test (dysgeusia): the first symptom of hyponatremia in small cell carcinoma of the lung. *Arch Intern Med* 1995;**155**:1325–8.
7 **Croghan LC**, Salik RM. Undiagnosed lung cancer presenting with dysgeusia. *Am J Emerg Med* 2003;**21**:604–5.
8 **Karthik S**, Roop R, Mediratta NK. Adenocarcinoma of lung presenting with dysgeusia. *Thorax* 2004;**59**:84.
9 **Mierson S**, DeSimone SK, Heck GL, *et al*. Sugar-activated ion transport in canine lingual epithelium. *J Gen Physiol* 1988;**92**:87–111.
10 **Kumazawa T**, Kurihara K. Large enhancement of canine taste responses to sugars by salts. *J Gen Physiol* 1990;**95**:1007–18.
11 **Henkin RI**, Gill JR, Barter FC. Studies on taste thresholds in normal man and in patients with adrenal cortical insufficiency: the role of adrenal cortical steroids and of serum sodium concentration. *J Clin Invest* 1963;**42**:727–35.
12 **Smith DV**, Margolskee RF. Making sense of taste. *Sci Am* 2001;**284**:32–9.
13 **Kurihara K**, Beider LM. Taste-modifying protein from miracle fruit. *Science* 1968;**161**:1241–3.
14 **Kurihara K**, Beider LM. Mechanism of the action of taste-modifying protein. *Nature* 1969;**222**:1176–9.