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Severe Hyponatraemia in a Patient with Right Complex Ophthalmoplegia

Abstract — Hyponatraemia is a common electrolyte imbalance in oncology. Rarely has it been reported as a presentation of nasopharyngeal carcinoma (NPC). A 43-year-old gentleman presented with double vision, headache, weight loss, complex ophthalmoplegia and submandibular lymphadenopathy. Computed tomography (CT) scan and nasopharyngeal biopsy confirmed the diagnosis of NPC. Prior to chemotherapy, he developed severe hyponatraemia. Blood investigations failed to pinpoint a clear diagnosis, and he was not responsive to aggressive supportive treatment. Pituitary gland function tests and MRI subsequently was performed, and found a pituitary extension causing hypocortisolism. Finally, his hyponatraemia was successfully optimised with oral hydrocortisone. This case illustrates that ophthalmoplegia and hyponatraemia are important warning signs of NPC or any other aggressive sellar mass that should not be neglected.

Keywords **— nasopharyngeal carcinoma, hyponatraemia, ophthalmoplegia, electrolyte imbalance, oncology**

1 INTRODUCTION

Hyponatraemia is one of the most common electrolyte disorders. It is related to a wide variety of aetiologies and comorbidities. This may sometimes pose challenges for clinicians in timely recognition of the true underlying causes. Clinical signs and symptoms may serve as important hints to the underlying causes of hyponatraemia.

2 CASE REPORT

A 43-year-old gentleman, ex-smoker of 20-packed-year presented with double vision associated with right sided headache for 2 months. He also suffered a loss of appetite and had lost 15 kg of weight over the past 3 months.

Physical examination showed right eye ptosis with complex ophthalmoplegia (Figure 1) and corresponding diplopia. There was failure of abduction of right eye. His right pupil was dilated but visual acuity was normal. There were presence of right eye ptosis and mild facial palsy on the right side with reduced in right nasolabial fold and frontal creases (Figure 1A). Besides, there was reduced sensations over right side of his face. These findings were corresponding to palsies of cranial nerve III, V, VI and VII. Left submandibular lymph nodes were enlarged at 3 cm x 3 cm. Vital signs were normal and he was clinically euvolaemic.

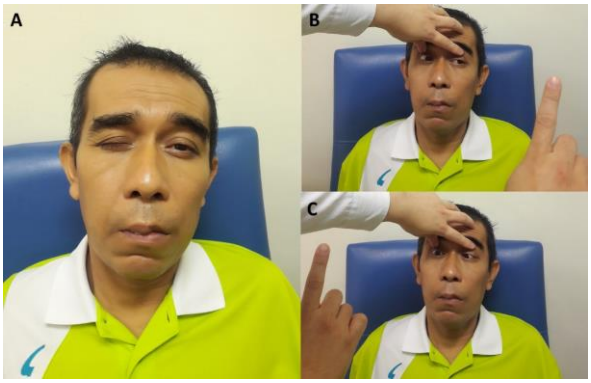

Figure 1 A. Right eye ptosis. Note that there was also mild facial palsy on the right side with reduced in right nasolabial fold and frontal creases. **B.** and **C.** Significant impaired right eye abduction and slight right eye adduction weakness.

Computed tomography (CT) scan showed a right parapharyngeal mass causing obliteration of the right fossa of Rosenmuller with fullness at the right cavernous sinus. Besides, a multinodular

goitre was also noticed from CT scan. He was found to have hyperthyroidism (Table 1) and thyroid malignancy was ruled out by fine needle aspiration cytology. Thyroid scan supported the diagnosis of toxic multinodular goitre and he was treated with Carbimazole 20mg daily. Biopsy of the nasopharynx confirmed the diagnosis of non-keratinizing nasopharyngeal carcinoma (NPC). The patient was subsequently planned for chemotherapy and radiotherapy.

Unfortunately, his blood investigation results prior to the cancer treatments showed severe hyponatraemia with serum sodium of 118mmol/L. (Table 1) Clinically, the patient was normovolaemic, was not on any medications that might contribute to hyponatraemia such as tricyclic antidepressants, selective serotonin reuptake inhibitors, opioids or thiazide diuretics, neither was chemotherapy nor radiotherapy commenced. He had loss of appetite and there were few episodes of vomiting one day before admission. However, the patient was not responding to supportive treatment of hyponatraemia and was referred to our centre for further management.

Table 1: Laboratory results

Test	Result	Reference Ranges
Serum sodium (mmol/L)	118	135 – 145
Serum potassium (mmol/L)	4.1	3.5 – 4.5
Serum chloride (mmol/L)	86	101 – 109
Serum urea (mmol/L)	2.6	2.5 – 6.7
Serum creatinine (mmol/L)	58	45 – 84
Random blood sugar (mmol/L)	7.9	4 – 10
Serum osmolality (mOsm/Kg)	267.5	285 – 295
Urine osmolality (mmol/L)	433	500 – 1400
Urine sodium (mmol/L)	17	40 – 220
TSH (mIU/L)	0.005	0.38 – 5.33
Free T4 (pmol/L)	20.41	7.86 – 14.41
pH	7.36	7.35 – 7.45
pCO2 (mmHg)	35.7	35 – 45
Bicarbonate (mEq/L)	20.4	23 – 30
Base Excess (mEq/L)	-5.1	-2 – +2

Abbreviations: T4, thyroxine; TSH, thyroid-stimulating hormone, pCO2, partial pressure of carbon dioxide

Hyponatraemia from NPC with complex ophthalmoplegia raised the possibility of cranial nerve compression and whether was there any pituitary extension albeit not detected in the initial CT scan. Thus, pituitary gland function tests and Magnetic Resonance Imaging (MRI) were done.

Table 2: Pituitary Function test

	Result	Reference ranges
Plasma cortisol (nmol/L)	Morning: 18	8am to noon: 118 – 618
	Noon: 30	8pm to 8am: 85 – 459
LH (mIU/mL)	0.76	1.24 – 8.62
FSH (mIU/mL)	3.06	1.27 – 19.26
Total testosterone (nmol/L)	<0.35	5 – 26
Prolactin (mIU/L)	637	56 – 279

Abbreviations: FSH, follicle stimulating hormone; LH, luteinizing hormone

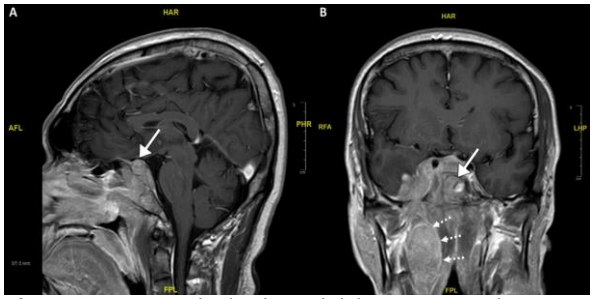

Figure 2 A.-B. MRI brain showed right cavernous sinus mass with intracranial extension, with pituitary gland and sellar involvement (arrows). **B.** Right nasopharynx enhancing mass was seen in the visualized upper neck region (dotted arrows).

The patient's pituitary function test showed high prolactin level of 637 mIU/L, low luteinizing hormone 0.76 nmol/L, low early morning plasma cortisol 18 nmol/L and low total testosterone level <0.35 nmol/L. (Table 2) Vasopressin level was not done due to limited resources. In addition, measuring this analyte is rarely helpful and the result may be misleading since it rapidly degrades in the test tube unless fastidious precautions are taken. MRI result revealed NPC with extension into the pituitary, right medial temporal fossa, right cavernous sinus, right optic canal and superior orbital fissure. (Figure 2)

The patient was then diagnosed as hyponatraemia secondary to hypocortisolism, caused by NPC with pituitary extension. The mild hyperprolactinaemia was likely caused by "stalk effect". His right eye complex ophthalmoplegia was due to cranial nerve compression by the NPC extension as well. His hyponatraemia was successfully treated with oral hydrocortisone and oral sodium chloride.

3 DISCUSSION

Hyponatraemia is a common electrolyte imbalance in oncology. [1, 2] One third of the causes are due to depletional state from reduced

oral intake, gastrointestinal or renal losses. [3] Syndrome of inappropriate antidiuretic hormone secretion (SIADH) contributes around 30% of the causes, especially among patients with small-cell lung cancer [4], followed by head and neck tumours. [1]

Hyponatraemia is often associated with diagnosis challenge. Diagnosis should only be made when salt and water intake is normal. The low urine sodium in this patient was probably due to concomitant dehydration which has not been fully optimised. Multiple retests may be needed before a final diagnosis can be made. In centres with limited laboratory testing, diagnosis and treatment are often delayed. Besides, clinical assessment including volume status in the hyponatraemia algorithm may not be 100% accurate. [5] For example, the gold standard of assessing extracellular volume is radioisotope study, which may be not practical. [6] The SIADH criteria are largely the same as originally proposed by Bartter & Schwartz and it is importantly to remark that SIADH remains a diagnosis of exclusion. [7]

In head and neck tumours, SIADH is a well-recognised form of paraneoplastic syndrome which is associated with hyponatraemia. [1] It can also be an iatrogenic complication of chemotherapy and radiotherapy. [1] This made some clinicians tend to jump into a wrong diagnosis way too early. In fact, SIADH is one of the most frequent reported misdiagnosis in cases of adrenal insufficiency. [8] The diagnosis of SIADH should only be made after ruling out adrenal insufficiency. For hyponatraemia in head and neck tumours, pituitary or hypothalamic involvement needs to be ruled out.

NPC is considered an endemic in Asia especially South China, Hong Kong and Southeast Asia. Due to language barrier, literature is limited on its various presentation. A systematic search was performed in MEDLINE and Google Scholar for literature and case reports describing about “hyponatraemia”, “hypopituitarism” and “nasopharyngeal carcinoma”. The literature is scarce and most of the reported cases were hyponatraemia following treatment of radiotherapy or chemotherapy, [9, 10] as well as a consequence of paraneoplastic syndrome causing SIADH. [1, 4, 11] The important triad of “NPC”, “complex ophthalmoplegia” and “hyponatraemia” as important warning signs of NPC or any other aggressive sellar mass causing hypopituitarism has never been reported.

Nasopharynx is located very near to cavernous sinus, which lie laterally to the pituitary fossa. The nerves contained in cavernous sinus include the third, fourth, sixth and branches of the fifth cranial nerve. Thus, local spread of NPC may affect these nerves, and then to the pituitary fossa. Cranial nerve involvement, especially cranial nerve VI palsy is one of the known manifestations in the advanced stage of NPC. [12] Compression of cranial nerves, especially cranial nerve VI has been reported as a warning sign which can be missed. [13] Any mass lesion in the vicinity of the sella turcica in combination with hyponatraemia should be assumed hypocortisolism until proven otherwise.

Due to the nature of NPC which spread haematogenously, this tumour usually metastasises to the bone, liver and lungs and seldom to the brain. [14] However, the possibility of direct extension to intracranial structures leading to ophthalmoplegia and hypopituitarism should not be neglected.

The intracranial extension of NPC in this patient had caused a reduction of most of the anterior pituitary hormones, resulting in hypocortisolism. Cortisol deficiency may lead to a reduction in cardiac output causing an increased in vasopressin level through the carotid sinus baroreceptors.

Besides, Cortisol feeds back negatively on corticotropin-releasing hormone (CRH) from the hypothalamus. Thus, hypocortisolaemia may result in an increased secretion of CRH, which is a vasopressin secretagogue. [15] This may lead to a reduction in free water clearance leading to the state of hypoosmolar hyponatraemia. The case illustrates the importance of fully testing for adrenal insufficiency before diagnosis and treatment of hyponatraemia is made. Besides, in this patient, the hyperthyroidism probably had worsened the hyponatraemia, because thyroxine increases hepatic corticosteroid metabolism, and adrenal insufficiency uncovered.

4 CONCLUSION

This case illustrates the important presentations of NPC progression. Hyponatraemia, together with cranial nerve palsy, especially the sixth cranial nerve [13] are both warning signs of NPC extension cranially.

LEARNING POINTS

- In the face of a patient with nasopharyngeal neoplasia, complex ophthalmoplegia and hyponatraemia, a sellar lesion must be ruled out.
- The diagnosis of SIADH is an exclusion diagnosis that must be established only after ruling out adrenal insufficiency or drugs, among others.
- Proper diagnosis of the cause of hyponatraemia is important to provide effective treatment.
- Hyperthyroidism could unmask adrenal insufficiency.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

CONSENT FOR PUBLICATION

Written consent was granted from the patient for publication of this case report and the accompanying images. Institutional Review Board approval is not required at the authors' institutions for the presentation of a single case report.

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