CASE REPORT

Masking of Central Diabetes Insipidus and Hypogonadotrophic Hypogonadism by Germ Cell Tumour in Suprasellar - Pineal Region

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Summary

A patient with β hCG-secreting germ cell carcinoma of the pineal and suprasellar regions presented with hydrocephalus, Parinaud's syndrome, hypopituitarism and polyuria. Central diabetes insipidus was strongly suspected although the water deprivation test was not diagnostic. The polyuria however, responded to ADH analogue when the hypothyroidism and hypocortisolism were treated. Pubertal development was evident and serum testosterone was normal despite the low FSH/LH, suggesting hCG stimulation of Leydig cells. This case illustrates that a β hCG-germ cell tumour of the suprasellar region causing hypopituitarism can mask the presence of central diabetes insipidus and hypogonadotrophic hypogonadism.

Key Words: Diabetes insipidus, Water deprivation, Germinoma, Hypopituitarism

Introduction

Pineal region tumours typically present with altered biological rhythm such as timing of puberty, Parinaud's syndrome and hydrocephalus. Suprasellar tumours on the other hand may cause disturbance of the hypothalamic functions, giving rise to anterior and posterior pituitary dysfunctions. We report a patient with an extensive β human chorionic gonadotrophin (hCG)-producing germ cell carcinoma affecting the pineal and suprasellar regions, who presented with hydrocephalus and Parinaud's syndrome. Despite the biochemical evidence of hypopituitarism, his pubertal development was evident as a result of Leydig cell stimulation by excessive β hCG. The patient also had polyuria and polydipsia owing to the concomitant central diabetes insipidus. However, a water deprivation test failed to confirm the diagnosis due to the coexisting hypopituitary state.

Case Report

A 19 year-old man presented to a private hospital with a two month history of headache associated with nausea and vomiting. He also complained of blurred vision, diplopia on both lateral gazes and difficulty looking up. An urgent magnetic resonance imaging (MRI) of the brain revealed a pineal region tumour extending into the suprasellar area with hydrocephalus (Figure 1). A ventriculo-peritoneal shunt was inserted resulting in partial symptom relief. His serum β hCG was elevated at 16783 mIU/mL (< 5 mIU/mL) giving a diagnosis of germ cell tumour. He was referred for further management.

On further questioning, he admitted to having polydipsia and polyuria with urinary frequency of every one to two hours for the past three years. He also complained of lethargy and postural giddiness but

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denied having cold intolerance or constipation. In terms of pubertal development, he had a change in voice at the age of 16 and started shaving at 17.

Physical examination revealed a pale man with a normal male voice. Pulse was 70/minute and supine blood pressure was 120/65 mmHg with no postural drop. Axillary hair and male pattern pubic hair distribution were present. There were no cerebellar signs and reflexes were normal. Eye examination showed convergent nystagmus on attempting vertical gaze, bilateral VIth nerve palsies, equal pupils reactive to accommodation but not to light and bilateral papilloedema; features consistent with Parinaud's syndrome and raised intracranial pressure.

In view of the involvement of the suprasellar region, evaluation of the anterior pituitary hormones and investigation for central diabetes insipidus were performed. His random blood glucose, serum calcium and potassium were normal. Initial urine osmolality was 207 mOsm/kg, serum osmolality was 287 mOsm/kg and serum sodium was 139 mmol/L. Results of the water deprivation test are shown in Table I. The test was abandoned prior to administration of desmopressin in view of persistent hyponatraemia, hypo-osmolality and inappropriately low urine osmolality, which did not increase despite water deprivation and marked polyuria.

His anterior pituitary hormones revealed hypopituitary state with TSH of 2.41 uIU/mL (0.32-5.00 uIU/mL), free thyroxine 6.97 pmol/L (9.10-23.8 pmol/L), ACTH < 10 pg/mL (0-48 pg/mL) and cortisol < 22 nmol/L (68-469 nmol/L). The serum LH was < 0.5 mIU/mL (1.4-7.7 mIU/mL) and FSH < 0.4 mIU/mL (1.5-14.0 mIU/mL) but serum testosterone was normal at 29.9 nmol/L (9.9-52.4 nmol/L) implying stimulation of Leydig cells by the raised β hCG. He was subsequently replaced with oral hydrocortisone followed by thyroxine. Since central diabetes insipidus remained a strong clinical suspicion despite the low serum osmolality, intranasal desmopressin was commenced in anticipation that this condition might worsen after steroid and thyroxine replacement. His urine output and polydipsia improved dramatically and his hyponatraemia and hypoosmolality also normalized with desmopressin and steroid replacement.

During his stay, he developed a mild right-sided weakness and a repeat MRI scan showed perilesional oedema near the the pons, midbrain and thalamus. The patient subsequently underwent surgical resection of the tumour via retrosplenial approach. At operation, the tumour was found to be adherent to the surrounding structure and therefore was not completely excised. Histopathological examination revealed poorly differentiated germ cell tumour, most probably embryonal carcinoma (Figure 2). Postoperatively, he required ventilatory support, developed several nosocomial infections and later succumbed to septicaemia.

Discussion

Primary intracranial germ cell tumours account for 1-2% of all intracranial tumours[1]. In Asia, this type of tumour contributes 78% of the pineal region tumours whereas the figure is much lower in the Western countries[2]. About 5-10% of germ cell tumours are found in both suprasellar and pineal regions. It is unclear whether they represent the actual spread of the tumour or simultaneous tumour development at both sites. Suprasellar germinomas usually present with hypothalamic/pituitary dysfunctions which include central diabetes insipidus, hypopituitarism and delayed sexual development. Germinoma of the pineal region may also delay the onset of puberty. Embryonal tumours however, secrete excessive β hCG which can stimulate Leydig cells to produce testosterone, masking

Table I: Results of the water deprivation test.

Time (Hours)	Weight (kg)	BP (mmHg)	Urine specific gravity	Urine osmolality (mOsm/kg)	Serum osmolality (mOsm/kg)	Urine volume (mL)	Serum Sodium (mOsm/kg)
0800	75.5	116/63	1.015	ND	266	ND	135
1000	75.5	113/60	1.010	207	274	350	132
1200	75.0	117/67	1.010	152	271	400	132
1400	75.1	122/66	1.005	121	267	700	132

ND- not done

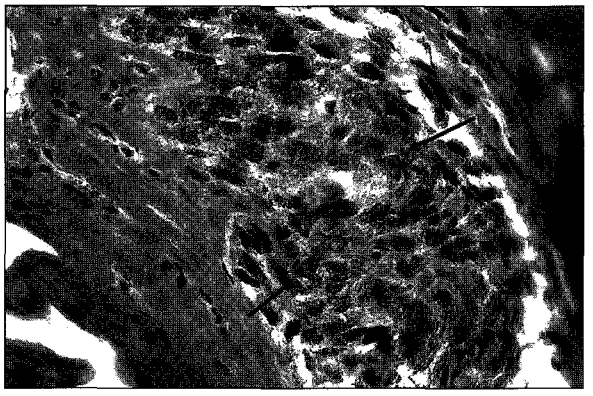

Fig 1: Sagittal T1-weighted, post gadolinium MRI scan of the patient showing a large lobulated heterogenous mass in the pineal region extending anteriorly into the suprasellar region.

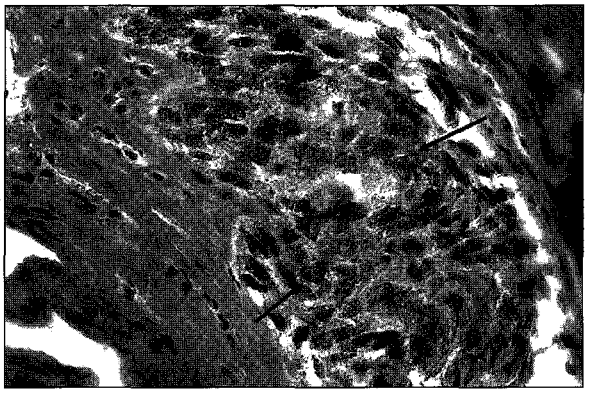

Fig 2: Malignant cells displaying markedly pleomorphic nuclei with coarse chromatin and some of them have prominent nucleoli (arrows). (20x10, Haematoxylin and Eosin)

the hypogonadotrophic hypogonadism as seen in this patient. Increased testicular steroidogenic activity as a result of prolonged exposure to excessive hCG is a well recognized phenomenon, although some degree of desensitization of LH/hCG receptor may occur resulting in variable levels of serum testosterone[3].

The most common presenting feature of pineal region tumours is Parinaud's syndrome characterized by failure of upward gaze, convergent nystagmus on vertical gaze, preserved pupillary response to accommodation but not to light. These signs are attributed to injury of the superior colliculi, which is in the vicinity of the pineal gland. The tumour may also obstruct the aqueduct of Sylvius causing hydrocephalus. Due to the hypothalamic involvement of the tumour, central diabetes insipidus was considered to be the cause of this patient's polyuria and polydipsia. The water deprivation test however, posed a diagnostic conundrum with features of water intoxication as reflected by low serum osmolality and low serum sodium. This could be explained by impaired free water excretion due to hypocortisol and hypothyroid states, therefore masking the presence of diabetes insipidus. A repeat test after hormonal correction would have been ideal but was not performed so as not to delay surgical intervention. The patient was treated with desmopressin which is an ADH analogue, on the premise that central diabetes insipidus was highly likely and hormone replacement would worsen his polyuria. Treatment with desmopressin would have decreased urine output nonetheless and worsened the hypo-osmolar state as well as hyponatreamia if it were not diabetes insipidus. This was proven not to be the case with this patient.

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References

1. Saitoh M, Tamaki N, Kokumai T, *et al.* Clinicobiological behavior of germ cell terms/tumours. Child's Nervous System 1991; 7: 246-50.
2. Pendl G. Management of pineal region tumours. Neurosurgery Quarterly 2002; 12: 279-98.
3. Rieu M, Reznik Y, Vannetzel JM, Mahoudeau J, Berrod JL, Kuhn JM. Testicular steroidogenensis in adult men with human chorionic gonadotrophin-producing tumours. JCEM 1995; 80: 2404-409.