CASE REPORT

Pituitary macroadenoma: a rare cause of thyrotoxic hypokalaemic periodic paralysis

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SUMMARY

Thyrotoxic hypokalaemic periodic palsy (THPP) is a well-recognised but under-diagnosed complication of hyperthyroidism and is commonly seen in Asian males. Patients usually present fully conscious with acute onset of severe motor weakness. Baseline investigation reveals severe hypokalaemia due to Na^+/K^+ ATPase overactivity causing a massive influx of intracellular potassium ions. The most common cause of THPP identified in the medical literature is Graves' disease. We report an interesting and unusual case of THPP due to previously undiagnosed hyperthyroidism secondary to a pituitary macroadenoma. The patient was consequently found to have a tumour secreting gonadotropin and thyrotropin.

BACKGROUND

This case has the rare underlying pathology of secondary hyperthyroidism causing the more common hypokalaemic periodic palsy. Thyrotoxic periodic palsy (THPP) secondary to hyperthyroidism due to a thyrotropin (TSH) secreting pituitary adenoma is very uncommon and only two other cases have been previously described. Mixed TSH and gonadotropin secreting adenomas are extremely rare, with only seven cases reported in the medical literature to date. The described pituitary adenoma had an atypical initial clinical presentation of hypokalaemic periodic palsy, which led to its diagnosis.

CASE PRESENTATION

A 40-year-old previously healthy man presented to the emergency department of our hospital with a 2-day history of weakness in all four limbs. The weakness was acute in onset and fluctuating in intensity, but with no obvious aggravating or alleviating factors or diurnal variation. At times the patient was so weak that he could not raise his limbs, sit up by himself or roll over in bed. Over the past 3 months he had experienced profound weakness on multiple occasions that had persisted for 2 days and gradually disappeared after medication. The patient also complained of a 2-month history of holocranial headache which was insidious, gradually progressive and constant with no diurnal variation. There was no history of convulsions, diplopia, visual loss, facial palsy, nasal regurgitation, dysphagia, pin-prick or tingling sensation or numbness, bladder or bowel involvement, or band-like sensations. There was no history of fever, pain in the abdomen or joints, dyskinesia, diarrhoea, vaccination or animal bite. There is no history of similar disease in the family. The patient was non-diabetic and normotensive, with no past history of any major illness or surgery,

or long-term drug use. The patient denied any history of addictions.

On examination the patient was conscious with vital signs stable except for a heart rate of 117/min regular. There was no pallor or lymphadenopathy. Neck veins and neck glands were unremarkable. Higher mental functions were within normal limits. There was no dysphonia, dysarthria or nasal twang in the speech. There were no signs of cranial nerve deficits except that bedside confrontation perimetry showed bitemporal visual field defects. There was no nystagmus, meningeal irritation or spinal deformity. Examination of the motor system revealed muscles of the proper bulk (suggesting adequate nutrition) with no wasting or fasciculation. Power was 1/5 at the shoulder and elbow joints and 3/5 in the wrists and fingers. In the lower limbs, power was also 1/5 in the hip and knee joints and 4/5 in the ankles and toes. Superficial reflexes were preserved with both plantar flexor, but deep tendon reflexes were sluggish. The sensory system was normal.

INVESTIGATIONS

A complete haemogram and a liver function test were normal: fasting blood sugar 84 mg%, blood urea 26 mg%, serum Na^+ 140 meq/l, K^+ 2.8 meq/l, Cl^- 106 meq/l, Ca^{2+} 10.3 mmol/l, Mg^{2+} 1.9 mmol/l, total cholesterol 158 mg/dl, serum triglyceride 227 mg/dl, and HIV (1 and 2) negative. An ECG revealed paroxysmal supraventricular tachycardia and a chest x-ray was normal. Routine and microscopic urine examination was also unremarkable.

Thyroid profiles revealed TSH 56.8 $\mu\text{IU/ml}$ (normal 0.35–5.5), fT_4 4.87 ng/dl (normal 0.8–1.76), fT_3 19.9 pg/dl (normal 2.0–4.4) and anti-TPO 19 U/ml (normal <50). 2D echocardiography revealed grade 1 diastolic dysfunction with normal ejection fraction and other parameters. Ultrasonography of the thyroid was normal. Fundus examination was within normal limits but perimetry revealed a visual field defect in the bilateral temporal fields. During investigation of the persistent headache, an abnormal perimetry MRI of the brain revealed a fairly large growth in the sella turcica suggestive of pituitary macroadenoma (figures 1 and 2). Other pituitary hormonal assays showed the following results: serum prolactin 7.22 ng/ml (normal 2–18), follicle-stimulating hormone (FSH) 10.9 $\mu\text{IU/ml}$ (normal 1.5–12.4) and luteinising hormone (LH) 27.9 $\mu\text{IU/ml}$ (normal 1.8–12.0). Serum free testosterone levels were 396 pg/ml (normal 50–210). Ultrasound of both testes and the prostate revealed no abnormality.

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Figure 1 Contrast MRI of the brain: coronal section showing a pituitary macroadenoma.

TREATMENT

A diagnosis of thyrotoxic hypokalaemic periodic palsy (THPP) was made in a case of secondary hyperthyroidism due to a hyperfunctioning pituitary macroadenoma. The patient was given potassium supplements to improve the weakness and started on antithyroid medication (carbimazole) supplemented with propranolol and finasteride (5 α reductase inhibitor) for prophylaxis of the hyperandrogenic state. The patient quickly became euthyroid with serum fT₄ within the reference range. The patient subsequently refused transphenoidal resection of the pituitary macroadenoma.

OUTCOME AND FOLLOW-UP

A subcutaneous injection of depot octreotide (a somatostatin analogue) 20 mg every 4 weeks was initiated as the patient refused surgery.

DISCUSSION

THPP is a rare manifestation of hyperthyroidism characterised by episodic proximal muscle weakness which increases and decreases.¹ It most frequently affects Asian males with hyperthyroidism in the second and third decades of their lives. The incidence of TPP in Chinese and Japanese thyrotoxic patients is reported to be 1.8% and 1.9%, respectively, but only 0.1–0.2% in North Americans.² The genetic basis of TPP has been studied: an association with the HLA-DRw8 gene in Japanese

Figure 2 MRI of the brain: sagittal section showing multiple nodular outgrowths of a pituitary macroadenoma with central necrosis.

patients and the A2BW22 and AW19B17 genes in Chinese patients has suggested the possibility that these haplotypes may serve as genetic markers.³ Some other human leukocyte antigen subtypes (B5, BW46) and genetic mutations (KCNE3) have also been associated with TPP.⁴ The high incidence of this disorder in the Asian population suggests that although the basic defect may be genetically determined, it manifests itself only when challenged by thyrotoxicosis. A male predominance has been widely described, with an overall male to female ratio ranging from 17:1 to 70:1.⁵

The Na⁺/K⁺ ATPase ion channel helps to maintain the ionic equilibrium and electrical stability of the resting membrane potential of muscle fibres by translocating the Na⁺ and K⁺ ions between the extra and intracellular compartment thus producing electro-mechanical contraction coupling to generate muscle power.⁶ The basic underlying mechanism of THPP has been elucidated due to this increased activity of ion channels as a result of thyrotoxicosis synergised by hyperinsulinaemia after a carbohydrate rich meal, hyperadrenalism under stressful conditions, or hyperandrogenism due to increased circulating testosterone or during menstruation.^{7, 8}

This is a very rare case of THPP in the uncommon setting of secondary hyperthyroidism due to a TSH secreting adenoma^{9, 10} together with a hyperfunctioning pituitary gonadotrophic tumour secreting FSH and LH. The resulting stimulation of the gonads produces increased testosterone and inhibin. While LH and testosterone cycle in a positive feedback loop, FSH is controlled by the negative feedback cycle of inhibin.¹¹ This additional gonadotropin effect may have dramatically impacted the clinical and biochemical status of our patient by causing a hyperandrogenic state, which led to early disease manifestation with a short history.

The incidence of pituitary macroadenoma due to a thyrotropin secreting pituitary adenoma is estimated at about 2.8/million population.¹² However, a mixed TSH and gonadotropin secreting adenoma is very rare, with only seven cases reported in medical literature to date.¹³ We identified only two other similar cases documented with TPP secondary to hyperthyroidism caused by a TSH secreting pituitary adenoma.

Learning points

- ▶ Thyrotoxic hypokalaemic periodic palsy (THPP) is a fairly common cause of episodic generalised periodic paralysis.
- ▶ THPP can rarely be secondary to a TSH secreting pituitary adenoma, which should be considered in the differential diagnosis.
- ▶ Pituitary macroadenoma can have atypical features such as an initial presentation of thyrotoxic hypokalaemic periodic paralysis.
- ▶ A hyperandrogenic state may indicate THPP.
- ▶ Evaluation and treatment of the underlying pathology (pituitary macroadenoma in this case) is key, rather than just supportive treatment for hypokalaemia.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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