BMJ Case Reports

Reminder of important clinical lesson

An unusual suspect causing behavioural problems and pituitary failure in a child

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Summary

A 9-year-old boy presented with feeding and behavioural problems and was diagnosed with Autistic Spectrum Disorder and Attention Deficit Hyperactivity Disorder. By age 11 he was becoming increasingly disinhibited and was refusing almost all oral food intake. Believing the cause to be psychogenic, he was placed in an inpatient eating disorder facility. After 3 days of continuous vomiting and minimal intake, he was admitted back to hospital for further investigations. A hypovolaemic hypernatraemia prompted an MRI brain scan, revealing several tumour masses with suprasellar and pituitary involvement. Histological investigation revealed primary, non-malignant germ-cell tumours. The tumours were treated with craniopharyngeal radiotherapy and permanent pituitary hormone replacement.

BACKGROUND

Intracranial neoplasms are an unusual cause of isolated behavioural problems in children and often result in delayed diagnosis. However, it is not uncommon to see personality changes and psychological disturbance resulting from these tumours.[1] Germ-cell tumours of the central nervous system account for 0.1–2.4% of all intracranial tumours in European and North American children[2] and are more common in males.[3] They arise from abnormal cellular migration and deposition of gamete producing cells in utero and can arise in several bodily systems, usually the midline structures of the brain (pineal and suprasellar regions), the spine (sacrococcygeal region) and gonads.[4] The presenting features of intracranial germinomas are diverse and depend on their location.[2 5]

Neoplastic causes of paediatric hypopituitarism include craniopharyngiomas, pituitary germinomas and optic gliomas. The radiotherapy and/or surgery following diagnosis often results in hypopituitarism even if the primary tumour does not.[6] Non-neoplastic causes include trauma[7] and lymphocytic hypophysitis.[8] Children with hypopituitarism often present with symptoms and signs of pituitary hormone deficiency (hypoglycaemia, growth failure, hypernatraemia, etc). This is a rare case of panhypopituitarism as a presentation of intracranial germinoma.

CASE PRESENTATION

We describe the case of a young boy who presented with feeding and behavioural problems aged 9 years old. His mother's pregnancy was uneventful and he was born at full-term.

He is the eldest of four children and has a history of developmental delay. He was slow to reach developmental milestones in early childhood (walking at 22 months, talking at 3.5 years), has mild bilateral sensorineural hearing loss, hypermetropia and coordination problems. He was significantly behind his school peers academically, had communication problems and was occasionally aggressive.

He was noted to have hypertelorism and a shawl scrotum and was investigated for congenital syndromes, including Aarskog's syndrome.[9] Cytogenetic testing did not elicit any chromosomal abnormality. Subsequently, he was referred to the Child and Adolescent Mental Heath Services (CAHMS) where he was diagnosed with Autistic Spectrum Disorder (ASD) and Attention Deficit Hyperactivity Disorder (ADHD) with an IQ of 73.

By age 11, his behaviour was deteriorating and he was becoming increasingly disinhibited and obstructive. At this point, his social circumstances necessitated a move to a different area and NHS trust from where he had been previously treated. His notes were transferred to the new trust and his previous diagnoses were accepted.

During the proceeding months he began to develop his first physical indicators of organic disease: polydipsia and polyuria. He was investigated for diabetes mellitus but tests were normal.

Two months later he was admitted to the local district general paediatric department for vomiting, anorexia and weight loss. He claimed, "all food was smelly" and "couldn't bear the thought of eating" and when food was offered he would wretch or vomit. On admission he weighed 29 kg (9th centile) and measured 138.4 cm tall (between 9th–25th centile) having lost 4 kg over the previous 4 months. He had a sinus bradycardia of 50 bpm and bloods were unremarkable, including thyroid function tests. Dieticians recommended high calorie diet alongside multivitamins via a nasogastric (NG) tube.

Nothing suggested an organic cause for his symptoms so he was referred to a specialist inpatient eating disorder clinic to manage his food aversion and re-establish oral feeding. After 3 days in the clinic he was admitted to hospital for NG feeding due to continuous vomiting and failure to establish any significant oral intake. Blood tests detected a hypovolaemic hypernatraemia (Na^+168 mmol/l), resistant to fluid replacement. He was transferred to Great Ormond Street Hospital to test for pituitary hormone

Table 1 Blood investigations after admission to Great Ormond Street Hospital indicating pituitary dysfunction

Test	Result	Normal range[10]
Thyroid function tests		
TSH	2.64	0.5–4.7 mU/l
Free T4	5.5	10.3–35.0 pmol/l
Total T3	3.51	0.92–2.78 nmol/l
Gonadal hormone levels		
LH	<0.2	2.0–12.0 IU/l
FSH	<0.2	1.0–12.0 IU/l
Prolactin	265	0–15 mU/l
Testosterone	<0.69	9.36–37.10 nmol/l
Random cortisol		
	54	138–414 nmol/l
Synacthen test		
0 min:	75 nmol/l	
30 min:	274 nmol/l Poor cortisol stress response	

TSH, thyroid stimulating hormone.

abnormalities and was diagnosed with panhypopituitarism (table 1).

A cranial MRI scan revealed three tumour masses: the largest in the left globus pallidus, another causing thickening of the infundibulum and several other smaller enhancing lesions in the pineal region (figures 1 and 2). There was no obvious spinal cord involvement. Alpha-fetoprotein and human chorionic gonadotropin (hCG) in the serum and cerebrospinal fluid were normal. A stereotactic biopsy of the lesion confirmed the diagnosis of a germinomatous germ-cell tumour. He was treated using craniopharyngeal radiotherapy delivered under general anaesthetic.

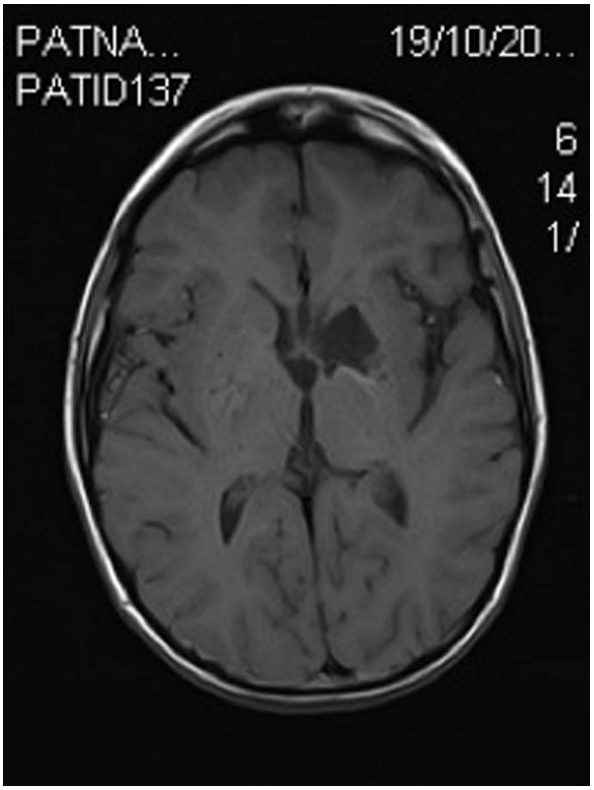

Figure 1 MRI showing a hypodense lesion in the region of the left globus pallidus.

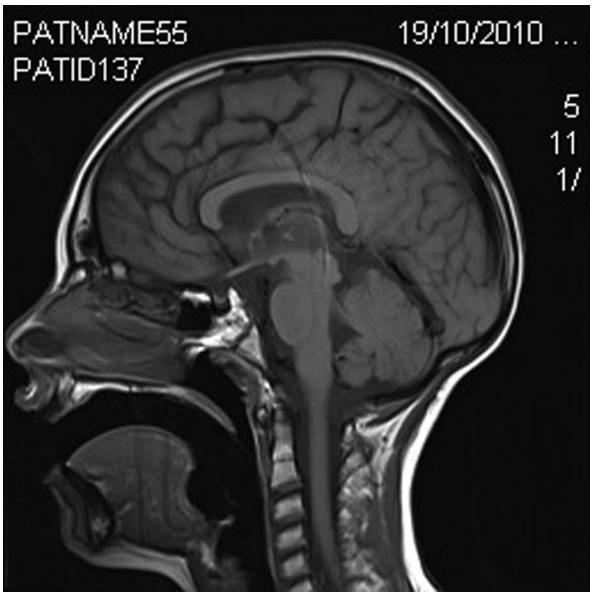

Figure 2 Sagittal MRI illustrating the hypothalamic and pituitary regions.

INVESTIGATIONS

See table 1.

OUTCOME AND FOLLOW-UP

Now 15-year old, his panhypopituitarism is treated with long-term hormone replacement of desmopressin, hydrocortisone and levothyroxine. Due to his aggressive and occasionally violent behaviour full gonadal hormone replacement was restricted. He lives at home with his mother, where he attends a special needs school. His oral intake is minimal and he receives the majority of his food and dietary supplementation via a percutaneous endoscopic gastrostomy tube. He was recently diagnosed with frontal-lobe disorder and oppositional defiant disorder.

DISCUSSION

This case demonstrates the difficulty in effective diagnosis of certain intracranial tumours in children. Psychiatric disease is a rare presentation of intracranial tumours, with macrocephaly, nausea and vomiting, irritability and lethargy being the most common.[11] Diagnosis was complicated in this case, as the patient had difficult social circumstances and may have been predisposed to psychiatric disease. His complex social situation, apparent eating disorder and behavioural problems masked his organic symptoms of panhypopituitarism.

ASD is characterised by impairments in social interaction, communication and imagination.[12] It has been shown to affect up to 1% of the child population in the UK[13] and can be difficult to diagnose due to the breadth of symptoms it can produce. The National Institute for Health and Clinical Excellence (NICE) have produced guidance to help recognise behaviours one might see in a child of primary school age presenting with ASD.[14] Of those listed, the child in question displayed the following: aggressive/disruptive interaction with others, reduced awareness of socially expected behaviours and excessive reaction to taste, smell or appearance of foods. The

BMJ Case Reports 2012; doi:10.1136/bcr-2012-006870

identification of these traits and the high prevalence of ASD may have lead to the initial psychiatric diagnosis and the subsequent delay in diagnosing the underlying organic cause.

When the patient was later investigated for an organic cause of his behavioural problems, his thyroid function test suggested normal pituitary function. When he developed polydipsia and polyuria, diabetes mellitus was investigated but diabetes insipidus was not. He was diagnosed with psychogenic polydipsia due to normal blood sugar levels and his history of psychiatric disease. Although this may have been an overlooked opportunity for earlier diagnosis, his diabetes insipidus may have been masked by concurrent cortisol deficiency and unidentifiable even if tested for.[15]

The patients' transfer between trusts may have meant that his care was continued in the context of an inorganic psychiatric cause, where in fact organic causes had not been thoroughly ruled out. This case highlights the potential problems when children move between healthcare trusts, when the working diagnosis of the previous team may be accepted with minimal enquiry by the new team.

Rigorous clinical assessment of children presenting with progressive behavioural disorders is required to ensure that an organic cause has not been missed; current guidelines issued to general practitioners and trainees emphasise the importance of unexplained deterioration in school performance or developmental milestones, and unexplained behavioural and/or mood changes as a marker for possible central nervous system malignancy. Although organic causes were investigated early on in this case, it is important to maintain suspicion of physiological causes or contributors to extreme behavioural disturbance in children.

Learning points

- The patients' transfer between trusts may have meant that his care was continued in the context of an inorganic psychiatric cause, where in fact organic causes had not been thoroughly ruled out. This case highlights the potential problems when children move between healthcare trusts, when the working diagnosis of the previous team may be accepted with minimal enquiry by the new team.
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Competing interests None.

Patient consent Obtained.

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