TEACHING CASE REPORT

## Headache and failure to thrive

**The Case:** An 11-year-old boy presented with a 2.5-year history of fatigue, poor appetite and growth failure (weight loss and decreased height velocity) (Fig. 1).

He described episodes of lethargy and loss of appetite that were often associated with headache and vomiting. They typically lasted a couple of days and were followed by a return to his "new baseline" status of generalized fatigue and poor energy intake. He also experienced weekly headaches over the temporal areas bilaterally that usually occurred in the morning, were not associated with vomiting and resolved quickly without treatment. He had no associated vision or balance problems. Despite his symptoms, he was attending school and participating in sporting activities, but with much more difficulty than in the past.

He reported no bowel change, polyuria or polydipsia; joint, muscle or bone pain; or fever or night sweats. He denied any body image distortion or wishes to be thin. He did not have any other symptoms or signs of depression.

He had a history of allergic rhinitis. He had received all of the recommended vaccinations. There was no family history of childhood illness or growth failure. His parents and 2 brothers were well, and there were no obvious social stressors.

On physical examination, he was pale and gaunt. He weighed only 34.5 kg, a drop of 5.5 kg over 2 years. His height was 147 cm, an increase of only 6 cm in the preceding 2.5 years. The results of the remainder of his physical examination, which included a detailed neurologic examination, were normal. Tanner staging was prepubertal.

Laboratory investigations revealed a mild normochromic normocytic anemia, with a hemoglobin level of 117 (normal range 120–160) g/L and a mean corpuscular volume of 84 (80–94) fL. The erythrocyte sedimentation rate was slightly elevated at 24 (1–10) mm/h. His electrolyte levels were normal, as were the results of liver and renal function studies. Albumin, immunoglobulin, and vitamin A and E levels were also normal. The patient's thyroid-stimulating hormone level was 1.5 (0.5–5) mU/L, but both his free thyroxine and total triiodothyronine levels were low, at 8.8 (10–23) pmol/L and 0.9 (1.4–4.1) nmol/L respectively.

An MRI of his head showed a well-defined lesion at the sellar and suprasellar region measuring 3.4 × 2.3 × 2.1 cm, which was causing superior displacement of the optic chiasm (Fig. 2). The lesion was radiologically compatible with a craniopharyngioma.

Further testing revealed a low random cortisol level of 35 nmol/L. The patient's prolactin level was mildly elevated at 0.93 (normal range 0.13–0.87) nmol/L, and his insulin-like growth factor 1 level was low at 14 (20.5–102) nmol/L. His urine was appropriately concentrated. The results of an ophthalmologic assessment were normal.

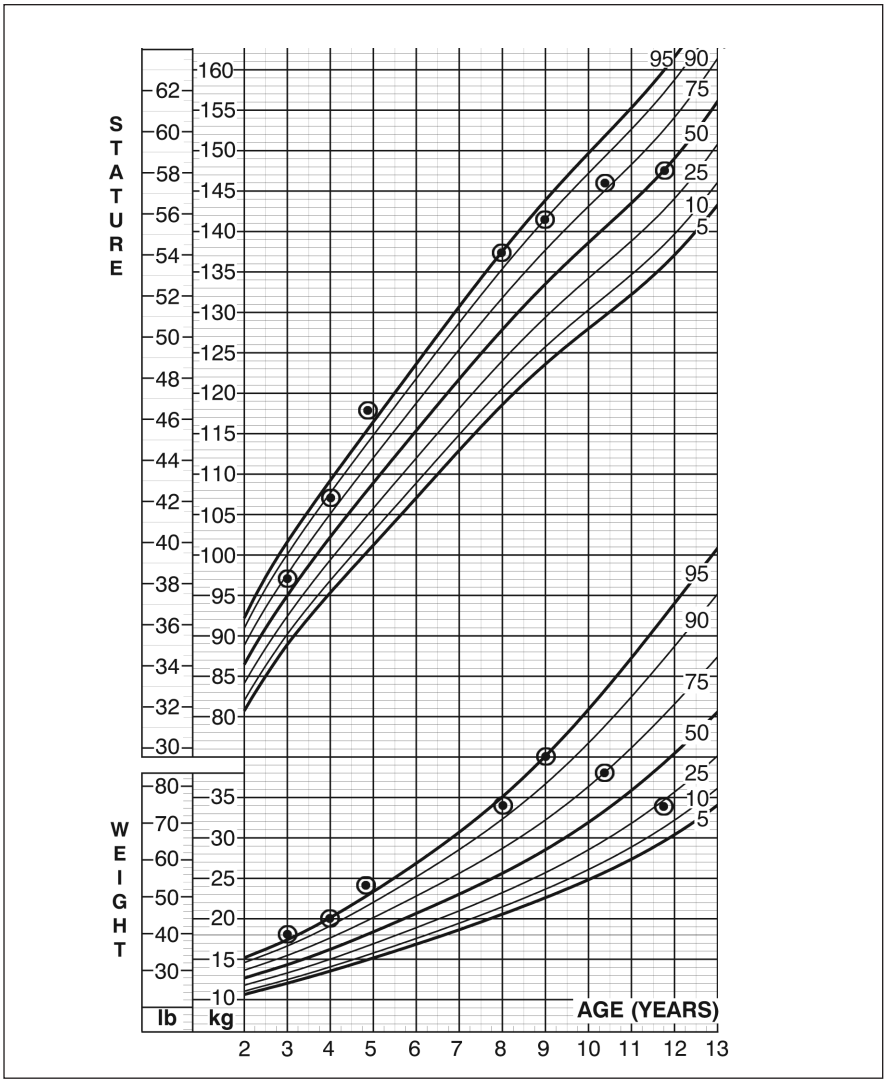


**Fig. 1:** Section of the growth chart showing the onset of the patient's failure to thrive after 9 years of age. The numbers inset on the top right show the stature-for-age percentiles, and the numbers inset on the bottom right show the weight-for-age percentiles.

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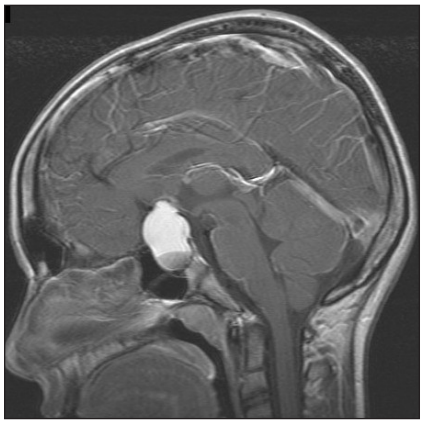

**Fig. 2:** MRI showing lesion at the sellar and suprasellar region.

The patient was started on L-thyroxine and hydrocortisone, which was followed by surgical resection of the craniopharyngioma.

Craniopharyngioma is a histologically benign and slow-growing tumour that predominantly involves the sellar and suprasellar space. The tumour originates from squamous rest cells in the remnant of Rathke's pouch (an embryologic structure). There is a bimodal peak in incidence at 5–14 years of age and again after the age of 50. Craniopharyngioma is the fourth most common pediatric brain tumour (7%–10% of pediatric brain tumours), after astrocytoma (40%), primitive neuroectodermal tumours (20%–25%) and ependymomas (10%).[1]

Children with craniopharyngiomas commonly present with vomiting, headaches and visual disturbances.[2] Up to 50% of patients have short stature at the time of diagnosis.[3] Disturbance of the hypothalamus can also result in hyperphagia, precocious or delayed puberty, and temperature instability. Personality and mood changes can occur when craniopharyngiomas involve the forebrain and frontal lobes.

Because of the close proximity of craniopharyngiomas to the hypothalamus and pituitary gland, up to 80%–90% of children have endocrine abnormalities at the time of diagnosis.[3] Growth hormone deficiency is the most frequent finding in 75% of children, followed by gonadotropin deficiency in 40%. Adrenocorticotropic hormone and thyroid-stimulating hormone deficiency occurs in about 25% of children.[2]

Approximately 20% of patients have mild hyperprolactinemia secondary to compression of the pituitary stalk by the craniopharyngioma,[2] which interferes with the transport of dopamine from the hypothalamus (an inhibitor of prolactin secretion) to normal lactotropes in the anterior pituitary gland.

Central diabetes insipidus occurs in about 9%–17% of children with craniopharyngioma.[2] The tumour causes disruption of the hypothalamic–pituitary axis, which leads to decreased secretion of antidiuretic hormone from the posterior pituitary gland and decreased concentration of the urine.[1]

In addition to these endocrinologic investigations, evaluation should include a neuro-ophthalmolgic evaluation with formal visual field testing and a neuropsychological assessment.

CT and MRI are complementary imaging techniques. A CT scan can indicate the diagnosis of craniopharyngioma by showing characteristic calcifications, as well as cystic and solid components. MRI is superior to CT at determining the relation of the tumour to adjacent structures and aids surgical planning.

The outcome after surgical resection of a craniopharyngioma depends on the size, location and extension of the tumour. Complete tumour resection results in high long-term survival rates but increases the risk of damage to surrounding structures, postoperative endocrine dysfunction and neurobehavioural prob-

**Box 1: Possible causes of growth failure in children**

**Inadequate energy intake**
- Lack of appetite (e.g., medication side effect, malignant disease)
- Poor oral-motor coordination (neurologic disorders) or structural abnormalities (cleft lip and palate)
- Eating disorders (e.g., anorexia nervosa, bulimia)
- Psychosocial or environmental factors

**Malabsorption**
- e.g., cystic fibrosis, celiac disease, Schwachman-Diamond syndrome

**Increased utilization of energy intake**
- Cardiac disease leading to congestive heart failure
- Respiratory disorder (e.g., chronic lung disease, obstructive sleep apnea)
- Renal disorder (e.g., renal tubular acidosis, chronic renal failure)
- Liver disease or failure
- Hyperthyroidism
- Inborn errors of metabolism
- Chronic infection (e.g., HIV, tuberculosis, parasite)
- Chronic inflammatory condition (e.g., inflammatory bowel disease, systemic lupus erythematosus, etc.)
- Malignant disease

**Increased energy loss**
- Chronic diarrhea (e.g., lactose intolerance, cow's milk protein intolerance)
- Chronic vomiting (e.g., gastroesophageal reflux disease)
- Renal (diabetes mellitus)

**Endocrine pathology**
- Hypothyroidism, growth hormone deficiency, disturbance of the hypothalamic-pituitary axis (central nervous system irradiation, tumour)

**Congenital disorders**
- Chromosomal abnormalities (e.g., Down syndrome, Turner syndrome, Russell-Silver syndrome)
- Syndromes (e.g., fetal alcohol syndrome)

Adapted, with permission, from Behrman.[1]

lems. Subtotal tumour resection with radiotherapy is an alternative treatment.

The differential diagnosis of growth failure is broad, and making a diagnosis can be challenging, especially when the presenting symptoms are nonspecific (Box 1). This case illustrates the importance of considering central nervous system pathology in children with growth failure, especially when it is accompanied by symptoms of headache and vomiting.

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PUBLIC HEALTH

# Taking away the sting of malaria

More than 40% of the world's population is at risk of malaria, and more than a million people die of it each year. Malaria kills a child every 30 seconds: 90% of people who die from malaria are children not yet 5 years of age, and most (90%) of these deaths take place in sub-Saharan Africa.[1]

Where malaria is endemic, related illness and death have severe economic as well as human costs. It is estimated that US$12 billion is lost in Africa each year to the costs of care and reduced productivity, and that a high endemic malaria burden lowers the growth of a country's annual GNP (gross national product) by 2%.[1]

Currently, affected countries are beset by limited access to rapid diagnostic tests and to the resources required to support prevention strategies and overcome drug resistance. Turning the malaria problem around requires an ongoing multipronged attack emphasizing both prevention and treatment.

CDC

Malaria is commonly diagnosed and treated according to clinical symptoms rather than laboratory test results; the result of this is that many of the people treated may not in fact be infected. Appropriate diagnosis is limited by a lack of laboratory services, or services of poor quality; and although rapid tests (which are currently effective for *Plasmodium falciparum* infections only) are available, they are not widely accessible because of their cost.[1] The lack of good diagnostic tests increases drug use (and costs), and contributes to more rapid development of drug resistance.[2]

The treatment of malaria has also become increasingly problematic. Common and sequential use of monotherapies and reliance on quinoline and antifolate compounds have contributed to a burgeoning problem of drug resistance.[1,2] In an effort to combat ineffective treatment, the World Health Organization (WHO) has recommended that all countries where resistance to conventional monotherapies such as chloroquine or amodiaquine is common or growing use combination therapies (CTs), preferably ones containing artemisinin derivatives (ACTs). As an indication to switch to ACTs, WHO has also lowered the endemic resistance threshold from 25% to 15% among children younger than 5 years.[2]

WHO's change in recommendation follows evidence that ACTs are well tolerated, produce rapid therapeutic responses, are effective against *P. falciparum* and can cure infections after just 3 days of treatment.[2] They also reduce gametocyte carriage and may therefore reduce malaria transmission. To improve ease of use, a fixed-dose combination (2 drugs combined in one pill) and dissolvable pills for children are being developed.

Despite clear indications for their use, in 2005 ACTs were used in the public sectors of only 9 countries in Africa. This is partly due to increased cost: ACTs cost 10 times that of older therapies.[1] Although the Global Fund for Fighting AIDS, Tuberculosis and Malaria, the largest funder of ACTs in developing countries, has committed US$41 million for ACT purchases, the

**Box 1: Who is working on malaria-related issues?**

- Roll Back Malaria (RBM): www.rbm.who.int
- Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM): www.theglobalfund.org
- Bill and Melinda Gates Foundation: www.gatesfoundation.org
- PATH Malaria Vaccine Initiative (MVI): www.malariavaccine.org
- Medicines for Malaria Venture (MMV): www.mmv.org
- Multilateral Initiative on Malaria (MIM): www.mim.nih.org
- Drugs for Neglected Diseases Initiative (DNDi)
- Malaria R&D Alliance: www.malariaalliance.org

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