HYPOTHALAMIC GERMINOMA MASQUERADING AS SUPERIOR MESENTERIC ARTERY (SMA) SYNDROME

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ABSTRACT

Objective: To report a case of superior mesenteric artery (SMA) syndrome secondary to hypothalamic germinoma.

Methods: We describe the clinical presentation, diagnostic work-up, management, and clinical course of a patient admitted with SMA syndrome who was subsequently found to have a hypothalamic germinoma.

Results: An adolescent boy was admitted to the surgical ward with progressive weight loss over a 2 year period and postprandial vomiting. He was diagnosed with SMA syndrome based on evidence of proximal duodenal dilatation, extrinsic compression of the distal duodenum, and a narrowed aortomesenteric angle (16°). Investigations performed to exclude thyrotoxicosis unexpectedly revealed secondary hypothyroidism and further evaluation demonstrated evidence of pan-hypopituitarism. Psychiatric evaluation excluded anorexia nervosa and bulimia. Magnetic resonance imaging (MRI) of the brain revealed a heterogeneously enhancing hypothalamic lesion, but a normal pituitary gland. Hormone replacement with hydrocortisone, desmopressin, testosterone, and thyroxine resulted in weight gain and resolution of gastrointestinal symptoms. A transventricular endoscopic biopsy subsequently confirmed a hypothalamic germinoma and he was referred to an oncologist.

Conclusion: SMA syndrome secondary to severe weight loss is an uncommon cause of upper gastrointestinal obstruction. While there have been reports of poorly controlled diabetes mellitus and thyrotoxicosis manifesting as SMA syndrome, there are no published reports to date of SMA syndrome secondary to hypothalamic/pituitary disease. Management of SMA syndrome is conservative, as symptoms of intestinal obstruction resolve with weight gain following treatment of the underlying cause. Awareness of this uncommon presentation of endocrine cachexia/hypothalamic disease will prevent unnecessary laparotomies and a misdiagnosis of an eating disorder.

Abbreviations:
ADH = antidiuretic hormone; CT = computed tomography; D3 = 3rd part of the duodenum; SMA = superior mesenteric artery

INTRODUCTION

Superior mesenteric artery (SMA) syndrome is a rare cause of upper gastrointestinal obstruction with prevalence in the general population of 0.03 to 0.3% (1). As a result of man’s upright posture, the SMA, instead of branching off perpendicular to the abdominal aorta, forms an acute downward angle of 25 to 60° (2,3). The 3rd part of the duodenum (D3) makes its passage through the angle between the SMA and aorta, but is cushioned by mesenteric fat from direct contact with these vessels (2). Significant weight loss, regardless of etiology, results in diminished mesenteric fat mass and reduction of the acute aortomesenteric angle, which results in duodenal obstruction secondary to D3 compression by the SMA (2,3). Eating disorders, such as anorexia nervosa, cardiac cachexia, HIV-infection,
malabsorption, cancer, burns, and neurological disorders that result in marked weight loss and subsequent loss of mesenteric/retroperitoneal fat have been linked with SMA syndrome (2,3). SMA syndrome has also been attributed to spinal surgery requiring body casting and external compression of the duodenum by vascular abnormalities of the aorta/mesenteric artery (2). The diagnosis of SMA syndrome is made by imaging studies that confirm a reduced aortomesenteric angle in the setting of upper intestinal obstruction (1,2,3). While there have been reports of poorly controlled diabetes mellitus and thyrotoxicosis resulting in weight loss as being associated with SMA syndrome (2,3), there are currently few published reports of hypothalamic/pituitary lesions presenting with SMA syndrome. We present the case of a young man admitted to the surgery department with postprandial vomiting and severe weight loss who was diagnosed with SMA syndrome and subsequently found to have a hypothalamic germinoma.

CASE REPORT

A 19-year-old boy was admitted to the surgery department with a history of progressive weight loss (20 kg over 2 years), asthenia, early satiety, and postprandial vomiting. His weight on admission was 28 kg [body mass index (BMI): 10.04 kg/m²]. Esophagogastroduodenoscopy revealed narrowing of the distal duodenum secondary to extrinsic compression, with resulting dilatation of the stomach as well as the 2nd and 3rd parts of the duodenum. Computed tomography (CT) confirmed a dilated D3 with a narrowed aortomesenteric angle of 16° (Fig. 1A). He was initiated on parenteral nutrition followed by feeding through a nasojejunostomy tube, which resulted in minimal weight gain (1.5 kg over 2.5 weeks). A thyroid function test was performed to exclude thyrotoxicosis as a cause of cachexia, but unexpectedly revealed evidence of secondary hypothyroidism (Table 1). On further questioning, the

Fig. 1. Contrast-enhanced computed tomography (CT) scan of abdomen from a sagittal view. A. Narrowed aortomesenteric angle of 16° in the patient. B. Normal aortomesenteric angle of 32° in a subject without superior mesenteric artery (SMA) syndrome. C,D. T1-weighted post-gadolinium image of the brain showing a heterogeneously enhanced hypothalamic lesion (arrow) measuring 1.7 x 1.4 x 1.6 cm in size with a normal-sized pituitary gland. C. sagittal view; D. coronal view.
patient denied symptoms of hypothyroidism, headache, or visual field defects. He was depressed and embarrassed by his severe weight loss and emaciated frame. He admitted to polyuria/nocturia, but denied excessive thirst. Examination revealed a tall, emaciated, hypopigmented young man with a masculinized voice. His height was 168 cm (mid-parental height: 169.5 cm), but body proportions were not eunuchoid. Although facial/axillary hair was absent, he had scanty pubic hair and an adult phallus, albeit with evidence of testicular atrophy (testicular volume: 10 mL; Tanner stage IV). Visual fields were normal. Further investigations confirmed growth hormone (GH) deficiency, secondary hypocortisolism, hypogonadotrophic hypogonadism, hyperprolactinemia, and cranial diabetes insipidus (Table 1). Magnetic resonance imaging (MRI) revealed a heterogeneously-enhancing hypothalamic lesion measuring 1.7 × 1.4 × 1.6 cm in size (Fig. 1C and D) and a normal sized pituitary gland. Peripheral blood analysis revealed no evidence of immature blast cells, and the erythrocyte sedimentation rate (ESR) was 3 mm/h. Tumor markers, including beta-human chorionic gonadotropin (β-hCG), alpha-fetal protein (α-FP), carcinoembryonic antigen (CEA), and carbohydrate antigen 19-9 (CA-19-9) as well as an autoimmune screen were within normal limits. CT of the neck, thorax, abdomen, and pelvis revealed no extracranial focus of disease or lymphadenopathy that could be biopsied. Psychiatric evaluation excluded anorexia nervosa. The patient was initiated on replacement oral hydrocortisone and desmopressin, followed by thyroxine, intramuscular testosterone, and mirtazapine. While on cortisol, thyroid hormone, and antidiuretic hormone (ADH) replacement, his weight increased from 29.5 to 36.2 kg within 10 days. The nasojejunostomy tube was removed as the symptoms of SMA syndrome resolved. A transventricular endoscopic biopsy of the hypothalamus subsequently confirmed a diagnosis of hypothalamic germinoma with ventricular dissemination and he was referred to an oncologist for further management (Fig. 2A and B).

**DISCUSSION**

SMA syndrome (Wilkie’s syndrome) is an uncommon and often unrecognized complication of severe weight loss (1). We report an unusual surgical presentation of a rare endocrine disorder (hypothalamic lesion) presenting with emaciation and upper intestinal obstruction. Our patient was diagnosed with SMA syndrome based on CT confirmation of a narrowed aortomesenteric angle (16°) and evidence of proximal duodenal dilatation and extrinsic compression of D3 based on an esophagogastroduodenoscopy. This is the first known report in the English literature of a hypothalamic lesion causing weight loss and consequent SMA syndrome. Other endocrine disorders linked with SMA syndrome include thyrotoxicosis (2) and poorly controlled diabetes mellitus, which results in emaciation (3).

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### Table 1

<table>
<thead>
<tr>
<th>Factors</th>
<th>Patient values</th>
<th>Reference range</th>
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<tbody>
<tr>
<td>Free T&lt;sub&gt;4&lt;/sub&gt;</td>
<td>0.66 ng/dL</td>
<td>0.89-1.80</td>
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<tr>
<td>Free T&lt;sub&gt;3&lt;/sub&gt;</td>
<td>1.2 pg/mL</td>
<td>2.3-4.2</td>
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<td>TSH</td>
<td>1.28 µU/mL</td>
<td>0.4-5.5</td>
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<td>IGF-1 (16-24 y age-specific range)</td>
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<td>182-780</td>
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<td>LH</td>
<td>&lt;0.1 mIU/mL</td>
<td>1.3-13</td>
</tr>
<tr>
<td>FSH</td>
<td>&lt;0.3 mIU/mL</td>
<td>0.9-15</td>
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<tr>
<td>Serum testosterone</td>
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<td>ACTH</td>
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<tr>
<td>8 AM cortisol</td>
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<td>Serum sodium</td>
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<td>Serum osmolarity</td>
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<td>Urine osmolarity</td>
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<tr>
<td>Serum prolactin</td>
<td>95 ng/mL</td>
<td>2-15 ng/mL</td>
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Abbreviations: ACTH = adrenocorticotrophic hormone; Free T<sub>4</sub> = thyroxine; Free T<sub>3</sub> = triiodothyronine; FSH = follicle-stimulating hormone; IGF-1 = insulin-like growth factor-1; LH = luteinizing hormone; TSH = thyroid-stimulating hormone.
SMA syndrome patients classically present with a history of severe weight loss as well as abdominal discomfort, postprandial fullness, and nausea/vomiting exacerbated by meals (3). These symptoms are typically relieved by assuming a left lateral decubitus, prone, or knee-chest position, which widens the aortomesenteric angle (1,2,3). On examination, patients are cachectic with distended tympanic abdomen, positive succussion splash, and abnormal bowel sounds (2). Severe dehydration, acute prerenal failure, and electrolyte imbalance may ensue (1). Barium studies reveal dilatation of the stomach as well as 1st and 2nd parts of the duodenum, and oblique compression of mucosal folds, antiperistaltic flow of contrast proximal to the obstruction, delayed transit of 4-6 hours through the gastroduodenal region, and relief of obstruction in a prone, knee-chest, or left lateral decubitus position (1,4,5). Plain X-rays and CT scans may display the classical double-bubble sign with dilatation of the stomach/duodenal bulb and air fluid levels. Endoscopic studies do not usually reveal abnormalities; our case is unique in that endoscopy provided evidence of proximal duodenal dilatation and extrinsic compression of D3 (2). The diagnosis is confirmed by measuring the aortomesenteric angle by ultrasound, contrasted CT, CT angiography, or MR angiography, which have the additional advantage of excluding neoplastic growth and aneurysms (1,2,3).

Initial management is conservative and in most cases this approach is sufficient. Simple acute measures, such as placing the patient in the left lateral decubitus, knee-chest, or prone positions may relieve the obstruction (1,2,3). All attempts should be made to rehydrate the patient and correct fluid and electrolyte abnormalities (1). Reestablishment of nutrition and a positive nitrogen balance, either enterally (through a nasojejunostomy tube that bypasses the obstruction) or parenterally, may also be used to reverse weight loss and restore retroperitoneal fat mass, which will increase the aortomesenteric angle (1,2). Treating the underlying cause of cachexia when possible, such as by improving glycemia in poorly controlled diabetes mellitus and administering antithyroid drugs for thyrotoxicosis, can also lead to symptom resolution (1,3). Duodenoejunostomy (open/laparoscopic) or duodenal circular drainage are employed only if conservative measures fail (1). Awareness of this condition and timely recognition amongst clinicians will prevent needless surgery and lead to more rapid resolution of the condition, thereby preventing malnutrition, electrolyte imbalance, prostration, and even death. The etiology of weight loss in this case was multifactorial: disruption of appetite control secondary to the hypothalamic tumor coupled with cortisol/ADH insufficiency. In our patient, commencement of cortisol/desmopressin hormonal replacement therapy led to a weight gain of 6.7 kg over 10 days and thus to resolution of the SMA syndrome. On the other hand, attempts to reverse weight loss with parenteral and nasojejunostomy feeds alone prior to hormonal replacement therapy resulted in minimal weight gain (1.5 kg over 2.5 weeks). However, despite the hormonal replacement therapy, the patient remained significantly underweight (BMI improving from 10.8 to 12.8 kg/m²) as the underlying primary cause of anorexia (i.e., hypothalamic germinoma remained unresolved).

The hypothalamus is the body’s master regulator and is responsible for blood pressure, fluid/electrolyte, body weight, and temperature homeostasis (6). Hypothalamic disorders can result in either polyphagia/obesity or anorexia/cachexia (secondary to disturbances of appetite), disrupted circadian sleep rhythms, behavioral disorders, temperature dysregulation, and autonomic dysregulation (7,8).

Lesions of the hypothalamus are uncommon compared to pituitary gland lesions. Similar to pituitary tumors, hypothalamic mass lesions may present with symptoms
secondary to the local mass effect (hydrocephalus, visual field defects, or headache) or hormonal deficiencies secondary to impaired secretion of hypothalamic releasing-hormones, such as growth-hormone-releasing hormone (GHRH), gonadotropin-releasing hormone (GnRH), corticotropin-releasing hormone (CRH), and thyrotropin-releasing hormone (TRH), which regulate anterior pituitary function. Hypothalamic lesions may also present with hyperprolactinemia, as dopamine secreted by the hypothalamus is the main regulator of prolactin secretion. Our patient’s mildly elevated serum prolactin levels in the presence of multiple anterior pituitary hormonal deficiencies was most likely due to loss of dopaminergic inhibition of prolactin secretion secondary to destructive tumor effects (9). In contrast, panhypopituitarism secondary to pituitary disease that spares the pituitary stalk (the conduit for dopamine) and the hypothalamus may be associated with prolactin deficiency (10). Hypothalamic dysfunction also has an impact on posterior pituitary function. As ADH is synthesized in the paraventricular nucleus of the hypothalamus and stored and released by the neurohypophysis, patients with hypothalamic lesions have a higher prevalence of cranial diabetes insipidus compared to pituitary lesions (6). Indeed, the presence of diabetes insipidus is an absolute predictor of neoplastic involvement of the hypothalamus in patients with intracranial germinomas (11). Since the hypothalamus also regulates thirst, these patients manifest with adipsic hyponatremia, being unable to self-compensate with increased water intake (7). Pediatric manifestations of hypothalamic disease include dienecephalic syndrome and precocious puberty (6).

Weight loss was a major presenting feature of this case. We postulate that our patient’s emaciation was in part due to cortisol and ADH insufficiency, compounded by anorexia secondary to disruption of satiety centers within the hypothalamus. This was borne out by the fact that our patient failed to gain significant weight with nasojejunos-tomy/parenteral feeds alone and only improved considerably after initiation of cortisol/desmopressin treatment. Hypothalamic dysfunction variably modulates body weight through pituitary insufficiency. Hypothyroidism predisposes patients to weight gain, while cortisol insufficiency results in weight loss. Growth hormone deficiency is associated with increased visceral adiposity and waist-hip ratio as well as reduced lean body mass (12). Decompensated diabetes insipidus on the other hand results in hypovolemia/dehydration and consequently weight loss. The net effect on body weight is therefore variable depending on which hormonal deficiencies predominate.

Our patient presented with emaciation that was only partially corrected by anterior- and posterior-pituitary axis hormone replacement. One of the main differential diagnoses for weight loss during adolescence (the predominant age group in which suprasellar germinomas manifest) is anorexia nervosa, which is also characterized by hormonal profiles that mimic secondary hypothyroidism and hypogonadotrophic hypogonadism (13). Our patient, however, did not report body dysmorphism, and in contrast was ashamed of his emaciated features, expressing a strong desire to gain weight. Psychiatric evaluation excluded anorexia nervosa, but he was diagnosed with reactive depression requiring treatment with mirtazapine, a mild anti-depressant that stimulates appetite. The fact that our patient presented with panhypopituitarism in the absence of mass effect symptoms (visual field abnormalities or headache) resulted in a delayed diagnosis. Peak cortisol at 60 min with cosyntropin stimulation was 9.8 µg/dL, which is an inadequate response that attests to chronic ACTH insufficiency and resulting adrenal atrophy. In addition, we believe that the onset of germinoma was postpubertal, as he had adult (albeit atrophied) genitalia and exceeded estimated midparental height. A prepubertal onset of disease resulting in growth retardation and delayed puberty may have led to earlier endocrine consultation and the resulting diagnosis.

Management of hypothalamic lesions is dependent on the underlying etiology. Differential diagnoses include cystic lesions (Rathke’s cleft cyst or craniopharyngioma), primary tumors (germinoma or glioma), infiltrative inflammatory/granulomatous diseases (Langerhans histiocytosis, tuberculosis, or sarcoidosis), metastatic lesions, and infiltrative hematologic malignancies (lymphoma or leukemia) (6,8). Our patient had a pure germinoma of the hypothalamus that had spread to the ventricles by the time it was finally diagnosed after 2 years of unexplained weight loss. Intracranial germ cell tumors (IGCTs) constitute 0.4 to 3.4% of primary CNS tumors in Western series and commonly arise in the pineal and suprasellar region (14). Pineal gland germinomas are frequently floridly symptomatic and present with hydrocephalus, Parinaud’s syndrome, and other neurological manifestations (14). Suprasellar germinomas, on the other hand, typically present more subtly with hormonal manifestations, such as cranial diabetes insipidus in the vast majority of cases or delayed sexual development and/or growth retardation (14). Most patients with intracranial germinomas are diagnosed between the ages of 10 and 21 years and approximately 1/3 of patients with suprasellar tumors are asymptomatic for at least 6 months (14). A confirmatory biopsy is required for diagnosis and subsequent planning of therapy. Pure germinomas are very radiosensitive and have 5-year progression-free survival rates and cure rates of >90% with treatment (14,15). Nongerminomatous GCTs (embryonal carcinoma, yolk sac tumor, choriocarcinoma, teratoma, or mixed GCT), however, have less favorable outcomes (14).

CONCLUSION

To conclude, this is the first report of SMA syndrome complicating severe weight loss secondary to a
Hypothalamic tumour and SMA syndrome. Our case of an adolescent presenting with a wasting syndrome illustrates the fact that endocrine cachexia may present with subacute upper intestinal obstruction, and also underscores that fact that hypothalamic lesions can morphologically and biochemically mimic anorexia nervosa. A high index of clinical suspicion is required to diagnose both SMA syndrome and hypothalamic disorders. Awareness of the association between these clinical syndromes will avoid unnecessary surgical procedures and psychiatric misdiagnoses.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

REFERENCES