CASE REPORT

Unusual cause of profound weight loss in a young woman

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SUMMARY

A 27-year-old woman presented with anorexia, weight loss and psychiatric symptoms for the past 4 years. She did not have history of headache, visual disturbances or symptoms of raised intracranial pressure. She was sarcopenic with body mass index of 10.16 kg/m². Her systemic examination was normal except for temporal hemianopia suggesting a sellar/suprasellar lesion. Hormonal evaluation revealed pan-hypopituitarism with central diabetes insipidus. Subsequent neuroimaging revealed sellar-suprasellar mass lesion with intense contrast enhancement and leptomeningeal metastases. Cerebrospinal fluid analysis showed elevated β human chorionic gonadotropin and the presence of syncytiotrophoblast germ cells. Histopathology from the mass lesion confirmed the diagnosis of germinoma. Immunohistochemistry of the tumour tissue was positive for c-kit and placental alkaline phosphatase. She received a combination of chemotherapy with craniospinal irradiation. Significant weight loss in a young woman may not always be an eating disorder like anorexia nervosa albeit more common than germ cell tumour.

BACKGROUND

Significant weight loss in a young woman with psychiatric symptoms usually point towards common eating disorders like anorexia or bulimia nervosa. Anorexia nervosa and bulimia nervosa affect 1–5% of young women of age 15–35 years, and 19% of normal adolescent girls and young women report bulimic symptoms.¹ However, unintentional weight loss and psychiatric symptoms with preserved body image may need careful evaluation for disorders like malabsorption syndromes, coeliac disease, thyrotoxicosis, occult malignancy with paraneoplastic syndrome, AIDS and rarely intracranial pathology like germ cell tumour (GCT). The clinical presentation of intra cranial GCT includes headache, vomiting, visual disturbances and endocrine dysfunction depending on the location, size of the tumour and the age of the patient.² Rarely they may be associated with precocious puberty (in boys), seizures, psychiatric symptoms and weight loss.^{3,4} However, GCT with a monosymptomatic presentation of weight loss without headache, visual field disturbances or endocrine abnormalities is rare as was seen in the index case.

CASE PRESENTATION

A 27-year-old woman presented with gradual but profound weight loss (20 kg) accompanied with anorexia, fatigue, psychiatric symptoms and secondary amenorrhoea over the past 4 years. Her

psychiatric manifestations varied in presentation including angry outbursts and occasional hallucinations. Her scholastic performance progressively deteriorated and she dropped out from the college. Her parent sought psychiatry consultation and she was prescribed antipsychotic medications. Owing to significant weight loss, she was also treated with anti-tubercular therapy and other indigenous medicines with no respite in weight loss and psychiatric manifestations. Suspecting an organic aetiology for her symptoms, a non-contrast CT (NCCT) scan of the brain was performed, which incidentally revealed a suprasellar mass lesion that led the referral to endocrinology services.

Clinical examination revealed alert and oriented woman with sarcopenia, and was strikingly pale with sallow complexion. Anthropometric examination revealed height 172 cms, weight 30 kg and body mass index (BMI) of 10.16 kg/m². She had bradycardia with supine blood pressure of 100/60 mm Hg and 80/60 mm Hg in standing position. Ophthalmic examination revealed temporal hemianopia in the right eye with 6/36 acuity and finger count at 1 m in the left eye, and had bilateral afferent papillary defect. Mental functions revealed no active psychopathology except for possibility of loss of insight.

INVESTIGATIONS

Investigations revealed haemoglobin 9.8 gm/dL, and normal liver and renal function tests. She had hyponatremia with increased serum osmolality and low urine osmolality (table 1) suggestive of central diabetes insipidus. Hormonal evaluation suggested hypocortisolism, hypothyroidism and hypogonadotropic hypogonadism with hyperprolactinaemia.

Contrast-enhanced MRI (CEMRI) sella revealed a well-defined moderately enhancing solid sellar and supra sellar mass lesion of size 3.1×2.5×2.5 cm, which was isointense to hypointense on T1-weighted, isointense to hyperintense on T2-weighted images showing intense heterogeneous contrast enhancement without any calcification or haemorrhage. Posterior pituitary bright spot was absent (figures 1A–D). CEMRI spine showed diffuse leptomeningeal enhancement (figure 2). She underwent transphenoidal surgery and the tumour was quite vascular therefore, only biopsy could be performed.

Histopathology revealed a tumour arranged predominantly in sheets with marked pleomorphism, round nuclei, coarse chromatin, and prominent eosinophilic nucleoli with a moderate amount of cytoplasm with distinct cell margins. Brisk mitotic activity and atypical mitoses were noted. Septa

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between tumour lobules contained numerous lymphocytes. Immunohistochemistry (IHC) for c-kit and placental alkaline phosphatase showed diffuse membranocyttoplasmic positivity, whereas synaptophysin was negative. Tumour tissue histopathology and IHC was suggestive of germinoma (figures 3A–D).

Retrospectively, tumour markers were obtained in serum and cerebrospinal fluid (CSF; table 1) and CSF analysis was negative

for malignant cells. Finally, a diagnosis of malignant suprasellar germinoma with leptomeningeal metastasis was made.

DIFFERENTIAL DIAGNOSIS

Clinically, eating disorders like anorexia or bulimia nervosa are differential diagnosis in a young female presenting with significant weight loss and psychiatric symptoms.

A differential diagnosis of coeliac disease, hyperthyroidism, AIDS and occult malignancy should be considered. However, a suprasellar mass on neuroimaging in the given context could be a glioma, germinoma, non-functioning pituitary adenoma with supra sellar extension, or meningiomas (associated with calcification in most cases).

TREATMENT

Hormone supplementation with hydrocortisone, levothyroxine, subcutaneous vasopressin in optimal doses and correction of electrolytes was carried out. She underwent lesional biopsy through left endonasal trans-sphenoidal route. Intraoperative examination revealed a soft bluish-red tumour with apparent pituitary infiltration. Frozen section suggested a possibility of germinoma.

After confirmation of the diagnosis of malignant germinoma by neuroimaging and histopathology/immunohistochemistry, she was treated with chemotherapy BEP cyclical regimen (bleomycin-30 units/iv on day1, cisplatin-20 mg/m² D1-D5 and etoposide 100 mg/m² D1-D5 of each cycle).

Table 1 Relevant biochemical and hormonal investigations

Test (serum)	Value	Normal range
Sodium	158	135–145
Serum osmolarity (mOsm/kg)	310	275–290
Urine osmolarity (mOsm/kg)	232	–
Total T4 (µg/dL)	4.64	4.8–12.7
TSH (mIU/L)	2.04	0.27–4.2
Cortisol(8AM) (nmol/L)	130.7	171–536
ACTH (pg/mL)	<1.00	5–60
DHEAS (µg/dL)	5.42	98.8–340
LH (mIU/L)	0.10	2.4–12.6
FSH (mIU/L)	0.38	3.5–12.5
Prolactin (ng/mL)	150.7	4.79–23.3
Estradiol (pg/mL)	14.34	12.5–166
Serum β-hCG (IU/L)	3.32	<5
CSF for β-hCG (IU/L)	55.0	<5

ACTH, adrenocorticotrophic hormone; β-hCG, β-human chorionic gonadotropin; CSF, cerebrospinal fluid; DHEAS, dehydroepiandrosterone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone.

Figure 1 (A,B) MRI sella (T1 weighted) coronal and sagittal sections showing a well-defined isointense to hypointense solid sellar and supra sellar mass lesion of size 3.1×2.5×2.5 cm. (C,D) Contrast-enhanced MRI (CEMRI) sella coronal and sagittal sections showing a well-defined solid sellar and supra sellar mass lesion showing intense heterogeneous contrast enhancement.

Figure 2 CEMRI dorsolumbar and sacral spine showing diffuse leptomeningeal enhancement suggestive of leptomeningeal metastasis. CEMRI, contrast-enhanced MRI.

OUTCOME AND FOLLOW-UP

Visual acuity and right eye hemianopia improved after the fourth cycle of chemotherapy without significant improvement

Figure 3 (A) Photomicrograph (high power) showing tumour cells with marked pleomorphism, round nuclei, coarse chromatin, prominent eosinophilic nucleoli and moderate amount of cytoplasm with distinct cell margin. Mitotic activity is brisk with atypical mitosis. (B) Immunohistochemistry photomicrograph showing diffuse strong membranocyttoplasmic PLAP positivity of the tumour cells. (C) Immunohistochemistry photomicrograph showing diffuse strong membranocyttoplasmic c-kit positivity of the tumour cells. (D) Immunohistochemistry photomicrograph showing synaptophysin negative tumour cells. PLAP, placental alkaline phosphatase.

in psychiatric symptoms. Her appetite and weight significantly improved (BMI 12.54 kg/m²). Follow-up CEMRI brain and spine showed complete resolution of sellar-suprasellar mass with non-visualised posterior lobe, a poorly defined stalk and no leptomeningeal enhancement (Figure 4A, B). Follow-up CSF β human chorionic gonadotropin (β -hCG) was normal after 4 months.

She was subjected to craniospinal irradiation with skull boost (cumulative dose of 45 Gy in 20 fractions) but was subsequently withheld because of significant thermoregulatory dysfunction and pancytopenia that she developed after initial few days of radiation.

DISCUSSION

Significant weight loss is frequently insidious and often serves as a harbinger of serious underlying disease. The association of weight loss with psychiatric symptoms in a young female can be diagnostically enigmatic. Infections, inflammatory, eating disorders and rarely low-grade malignancy are the first to be considered in the differential diagnosis. Prior to the diagnosis of

Figure 4 (A,B) T1-weighted MRI sella sagittal sections (non-contrast and contrast) showing complete disappearance of tumour with normal sella.

germinoma, the index patient was unfortunately treated with antitubercular, antipsychotic and indigenous drugs at multiple centres without proper workup.

Profound anorexia and weight loss in a young female may be because of the more common eating disorders like anorexia or bulimia nervosa. However, the body image was preserved and there was unintentional weight loss in the index case suggesting an organic aetiology for her symptoms. The other differentials considered in the index case were excluded by clinical and laboratory evaluation. Intracranial GCTs usually present with headache, visual field defects and symptoms related to hormonal disturbances like short stature, diabetes insipidus and rarely precocious puberty.

Weight loss may be present in 10–15% of patients with suprasellar mass lesions but rarely the presenting manifestation as was seen in the index patient. The loss of appetite and weight loss in GCTs is multifactorial and could be due to lateral hypothalamic damage (satiety and feeding centre), adrenocorticotrophic hormone deficiency, cytokines secreted by the metastatic germinoma or due to associated psychiatric symptoms. Psychiatric and behavioural abnormalities are partly explained by hypothalamic damage and hyponatremia due to central antidiuretic hormone deficiency. Previously, only one case of germinoma in basal ganglia associated with psychotic symptoms (obsessive and compulsive neurosis) has been reported.⁵

Central nervous system GCTs account for 5% of the intracranial tumours in patients of age <20 years. They are mainly thought to arise from migration failure of embryonic remnants during childhood.² They are broadly divided into germinomas and non-germinomatous GCTs (NGGCTs-teratoma, yolk sac tumour, embryonal carcinoma, choriocarcinoma).³ Central nervous system GCTs may secrete tumour markers like α foeto-protein (α -FP) and β -hCG and their measurement particularly in CSF and sometime in serum and may aid to the diagnosis.

Germinomas are more common in men and seen most commonly in the pineal region. A delay in diagnosis is seen in significant proportion of patients, particularly in malignant suprasellar germinomas and the index case is a befitting example.^{2–4} CEMRI features of isointense to hypointense on T1-weighted and isointense to hyperintense on T2-weighted imaging with intense contrast enhancement can be associated with meningioma, gliomas, intracranial lymphoma, lymphocytic hypophysitis or granular cell tumours.⁶ Hence, a histopathological diagnosis is a must to initiate on appropriate therapy, as was performed in the present case clinching the diagnosis.

Retrospectively, tumour markers estimation was sought in serum and CSF, which were elevated. According to recent consensus guidelines, patients with consistent radiological imaging and elevated α -FP and β -hCG elevation (serum or CSF) above defined thresholds, in fact do not even require surgical biopsy for making a diagnosis of intracranial GCTs and treatment may be initiated.⁷ This pitfall helped us to change our hospital policy for evaluation of suprasellar masses towards an initial tumour marker analysis in serum and CSF before proceeding for biopsy. Chemotherapy combined with craniospinal irradiation has been the standard-of-care for GCT, as these are highly radiosensitive and chemosensitive tumours.⁷ Likewise, she was treated with a combination of chemotherapy plus radiotherapy and improved significantly.

In summary, this case highlights an unusual presentation of a rare suprasellar tumour. Profound anorexia with weight loss and psychiatric symptoms in a young woman may require neuroimaging after excluding the other relatively common causes. The

aetiology of the tumour in the index case taught us to change our approach towards evaluation for the suprasellar mass in favour of the assessment of tumour markers before contemplating biopsy from the mass lesion.

Patient's perspective

I never imagined that I could have such a severe disease like cancer. Thankfully, I was diagnosed in time, though it took four long years.

Learning points

- ▶ Significant weight loss in a young woman demands diligent evaluation after excluding common causes like eating disorders, hyperthyroidism and occult low grade malignancy.
- ▶ Neuroimaging of the brain should be contemplated after exclusion of common aetiologies for weight loss.
- ▶ Suprasellar germinomas are associated with delayed diagnosis in significant proportion of patients.
- ▶ Germinoma should be considered among differentials in a young woman, if contrast-enhanced MRI shows isointense to hypointense suprasellar mass on T1-weighted and isointense to hyperintense on T2-weighted imaging with intense heterogeneous contrast enhancement without calcification.
- ▶ Tumour markers like β human chorionic gonadotropin and α -fetoprotein should be sought in serum and cerebrospinal fluid before the histopathological confirmation, as this may alter the treatment strategies.
- ▶ Chemotherapy along with craniospinal irradiation is an effective strategy to maximise their chance of cure in metastatic intracranial germ cell tumours.

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