

Background

Hypothalamic obesity is a syndrome of hyperphagia and weight gain arising from impaired hypothalamic regulation of body weight and energy expenditure. This syndrome is most commonly associated with pituitary tumors but can also be caused by hypothalamic dysfunction from surgery, trauma, infiltrative disorders, congenital malformations and genetic mutations. Our case examines a particular cause of hypothalamic obesity and the associated syndromic psychological and behavioral changes that can often accompany hyperphagia with weight gain.

Case

The patient is a 38-year-old female who was diagnosed with a hemorrhagic left basal ganglia cavernoma three years ago after initially presenting with seizures. Resistance of the seizures to medication and the location of the cavernoma led to treatment after several months with stereotactic radiosurgery. Changes post-surgery included significant weight gain (BMI increased from 22 to 40), cognitive decline with recurrent hemorrhages, post-radiation edema, hypothyroidism, and hydrocephalus managed with a VP shunt. The patient was admitted for progressive increase in fatigue and weakness for 1 week noticed by her caregiver.

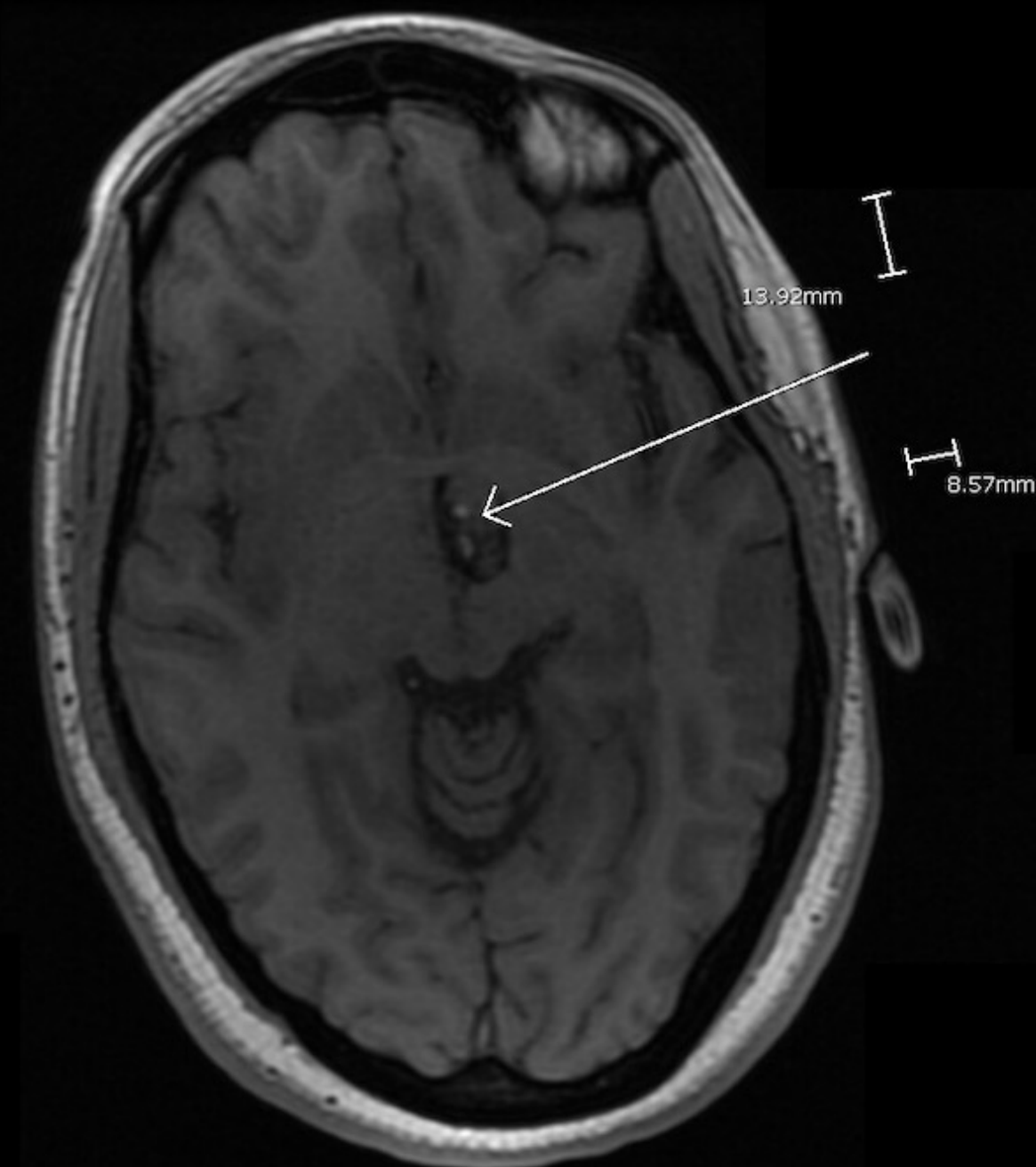
Pertinent features on history were poor motivation, fatigue, weakness and increased appetite. Family reported she requires significant encouragement to perform ADLs, needs strict monitoring to limit food intake, and expresses hopelessness about her condition.

On exam, she was a morbidly obese woman, with poor attention, memory and recall. She was oriented to place and person only.

Work up yielded a negative EEG for seizures. MRI showed a stable hemorrhagic mass in the left inferior thalamus with decreased surrounding vasogenic edema and stable mild obstructive hydrocephalus. TSH was elevated with low T4.

Discussion

Hypothalamic obesity was first defined as hyperphagia and weight gain in the setting of suprasellar tumors and their surgical excision. This syndrome occurs with many causes of hypothalamic impairment and can manifest clinically as psychosocial disorders, hyperphagia, sleep disturbance, decreased energy expenditure, hyperinsulinemia and hypopituitarism (Van Iersel L 2019). Behavioral, social, emotional and neurocognitive dysfunction may include impulsivity, aggression, anger, inattention, depression and anxiety, and symptoms may be aroused when food access is restricted. Hormonal regulation of appetite, satiety, sleep, wakefulness, autonomic tone, metabolic rate, and pituitary function by hypothalamic nuclei can all be disrupted. The choice of surgical versus radiological intervention against bleeding cerebral cavernomas must balance accessibility and efficacy against the risk of hypothalamic-pituitary axis disruption (Shih YH 2005).



MRI: left inferior thalamus cavernoma two months after stereotactic radiosurgery

Symptoms and treatment of hypothalamic obesity

Psychosocial disorders

- Specialized support clinic
- Dextroamphetamine

Hyperphagia

- Diet, physical activity
- Impulse control management
- GLP-1 agonists
- Methylphenidate
- Bariatric surgery

Sleep Disturbance

- Behavioral interventions
- Melatonin
- Stimulants
- OSA assessment

Decreased Energy Expenditure

- Lifestyle interventions
- Physical exercise
- Dextroamphetamine

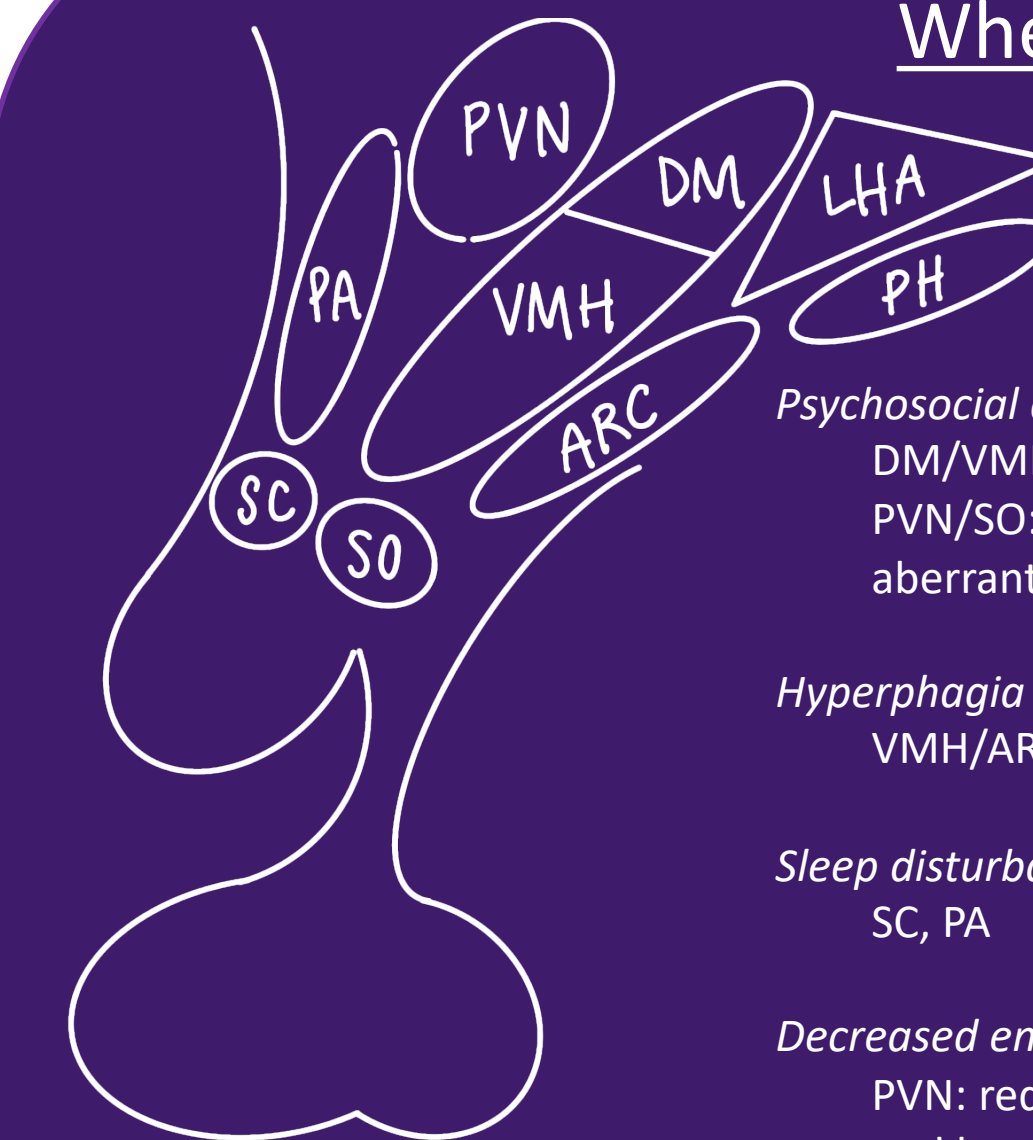
Hyperinsulinemia

- Lifestyle interventions
- Weight loss
- GLP-1 agonists

Hypopituitarism

- Exogenous hormone administration
- GH therapy (for children)
- Levothyroxine (target mid-high range)
- Low hydrocortisone doses

Where is the lesion?



Psychosocial disorders

DM/VMH: aggression, impulse control, rage
PVN/SO: reduced oxytocin causing aberrant social behavior

Hyperphagia

VMH/ARC: inability to integrate satiety signals

Sleep disturbance

SC, PA

Decreased energy

PVN: reduced temperature and heart rate

PVN: paraventricular nucleus
PA: preoptic area
VMH: ventromedial hypothalamus
DM: dorsomedial hypothalamic nucleus
SC: suprachiasmatic nucleus
SO: supraoptic nucleus
ARC: arcuate nucleus

Hyperinsulinemia

PVN/SC: disruption of sympathetic and parasympathetic tone, increased vagal activity, increased insulin

Hypopituitarism

PVN

1. Shih YH: Management of supratentorial cavernous malformations: craniotomy versus gamma knife radiosurgery. *Clinical neurology and neurosurgery* 2005; 107(2):108-12.

2. Van Iersel L: Pathophysiology and individualized treatment of hypothalamic obesity following craniopharyngioma and other suprasellar tumors: a systematic review. *Endocrine reviews* 2019; 40(1):193-235.