Endocrinology, Diabetes & Metabolism CASE REPORTS

A Puchalski and H Elias | Hypopituitarism from metastatic pineal mass

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Panhypopituitarism in a patient with a hypothalamic and pineal germ cell tumor

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Summary

Central diabetes insipidus (DI) is characterized by decreased release of antidiuretic hormone, resulting in a variable degree of polyuria. The etiologies are variable, with the vast majority of cases either being idiopathic or resulting from primary or secondary tumors. Such tumors include craniopharyngioma, Langerhans cell histiocytosis, or a variety of inflammatory, vascular, or granulomatous diseases. It is exceptionally rare for pituitary adenomas to present with DI. We describe a young patient who first presented with symptoms consistent with DI. He was tested for DI and found to have panhypopituitarism due to a metastatic pineal germ cell tumor causing thickening of his pituitary stalk.

Learning points:

- New onset central diabetes insipidus requires dedicated pituitary MRI for determination of etiology.
- Germ cell tumors in the pineal and suprasellar regions most commonly cause central diabetes insipidus.
- Determining the etiology of new-onset central diabetes insipidus can radically affect treatment.

Background

Adult endocrinologists do not often see pineal masses, such as germ cell tumors. These tumors are seen in the pediatric population. However, such tumors can cause pituitary and other endocrine dysfunction, most commonly new-onset central diabetes insipidus (DI). Therefore, it is important for adult endocrinologists to consider these diagnoses when evaluating young adult patients with new-onset central DI.

Case presentation

A 20-year-old Caucasian male was referred to Endocrinology by his primary care physician for the evaluation of polyuria and polydipsia. These symptoms started approximately 6 months prior to that visit. He went from drinking one cup of water in the morning to drinking 3 L of water per day. He reported urinating every 30–60 min and waking up three to four times at night to urinate. Sometimes, the patient was actually incontinent at night. He stated that he urinates large volumes and that his urine appeared clear.

He endorsed cold intolerance and fatigue. He attributed his fatigue due to waking up at night so frequently to urinating. He denied changes in vision, issues with balance, or changes in weight. He has had frequent headaches. Given the above symptoms, the patient was evaluated for diabetes mellitus and for thyroid disease. His serum glucose and thyroid-stimulating hormone were normal.

In his mid-teen years, he had several syncopal episodes. He was evaluated and told that it was due to vasovagal syncope and he was told to drink more water and eat more salt. With the increased fluid intake and salt intake, the episodes disappeared. Because of an episode of loss of consciousness, head CT scan was performed, which showed no acute pathology.

He had no significant past medical history; his appendix was removed due to acute appendicitis 1 month

after presenting to the endocrinology clinic. He was not taking any medication nor had been on any chronic medication in the past. He was a non-smoker, non-drinker, and denied use of any illicit drugs or over-the-counter supplements.

Vital signs in the clinic were unremarkable. Physical exam revealed that the patient had a soft, non-virilized voice and little to no facial hair growth. A genital exam was not done at this time.

Investigation

Initial labs revealed normal electrolytes, mildly elevated liver function tests, and low urine osmolality (Table 1).

The patient underwent a water deprivation test. Urine volume was measured every 2 h and it ranged from 625 to 650 cm^3. His serum osmolality steadily increased to 296; he was then given desmopressin 2 µg subcutaneously. His urine volume dropped significantly after 2 h, ranging from 50 to 315 cm^3. Urine osmolality was collected 1 and 2 h after desmopressin injection, rangedfrom 182 to 838 mosm/kg. This confirmed the diagnosis of central DI, and he was started on desmopressin nasal spray every night. Due to this diagnosis, there was a concern for a sellar or suprasellar mass and thus pituitary hormonal testing was recommended, which revealed panhypopituitarism and mildly elevated prolactin from stalk effect (Table 2). He was initially started on oral hydrocortisone and levothyroxine was later added on to prevent potential adrenal crisis.

Table 1 Labs on initial evaluation.

Reference range and units	9/5/2020	9/9/2020
Sodium 135–146 mmol/L	139	142
BUN 7 –24 mg/dL	15	17
Creatinine, blood 0.6–1.3 mg/dL	1.2	1.0
Glucose, blood 70–118 mg/dL	77	83
Calcium 8.5–10.5 mg/dL	9.7	9.5
Estimated GFR (CKD-EPI) ≥60 mL/min/BSA	87	108
Osmolality 275–310 mosm/kg	287	
Osmolality, Ur 300–1000 mosm/kg	145 (L)	105 (L)
TSH 0.30–4.50 uIU/mL		1.38
Initial urine sodium <172 mmol/L		23
Creatinine, random urine ≥15 mg/dL		18.0

Table 2 Hormonal testing demonstrating panhypopituitarism. Prolactin was mildly elevated due to stalk effect.

Reference range and units	10/22/2020 100 PM	10/24/2020 840 AM
Testosterone >280 ng/dL	87 (L)	84 (L)
Sex hormone-binding globulin 13–90 nmol/L	72	62
Albumin, blood 3.4–5.2 g/dL	4.3	3.8
IgF-1 83–456 ng/mL		64 (L)
IGF-1 Z score calculation, male −2.0 to 2.0 SD		−2.9 (L)
Cortisol, plasma 4.0–17.0 µg/dL	1.7 (L)	0.7 (L)
Free thyroxine 0.6–1.5 ng/dL	0.6	0.5 (L)
Prolactin 4–15 ng/mL	51 (H)	54 (H)
FSH 1.7–8.6 mIU/mL	0.1 (L)	
LH 1.7–8.6 mIU/mL	<0.1 (L)	
TSH 0.30–4.50 uIU/mL		0.98
ACTH 6–50 pg/mL		7

L - low, H - high

Because of the concern for sellar or suprasellar mass an MRI of the brain with the pituitary protocol was performed, which revealed a 2.3 × 1.7 × 1.7 cm pineal region mass impinging on the superior colliculus and superior aspect of the midbrain and superiorly displacing the internal cerebral veins. There was also abnormal enhancement and thickening of the pituitary infundibulum with an extension of enhancement to the hypothalamus and floor of the third ventricle (Fig. 1). Due to the concern for germinoma, radiology recommended imaging of his spine which did not show metastases. Testicular ultrasound was normal as well.

Treatment

The patient was referred to the neurosurgery team. Given the high suspicion for germ cell tumor, a lumbar puncture to obtain cerebrospinal (CSF) markers was recommended. Per the neurosurgery team, the CSF markers would allow diagnosis without surgical intervention, which could expedite treatment with radiation. A stereotactic biopsy for tissue would have been done if lumbar puncture would not be successful. The lumbar puncture was performed in neuroradiology which showed elevated beta-hCG at

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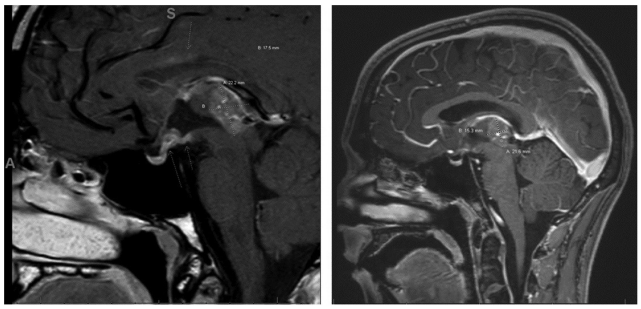

Figure 1
Large heterogeneously enhancing mass in the pineal region measuring a maximum diameter of 2.2 cm with mass effect on the superior colliculus and posterior midbrain. Enhancement and thickening of the infundibulum with extension of enhancement to the floor of the third ventricle and hypothalamus.

11 IU/L (0–3 IU/L) but normal alpha-fetoprotein levels. Cytology was negative for malignancy. The patient's case was discussed at the tumor-board meeting at our institution. It was determined that due to the infrequent nature of these tumors in the adult population, which our center treats, he should be treated with radiotherapy and neoadjuvant chemotherapy at a children's hospital that has more treatment experience with this type of tumor.

The patient was transferred to the local children's hospital for further care. At the tumor board, it was determined that biopsy was not necessary and that chemotherapy should be initiated given high suspicion of germinoma based on imaging studies and spinal fluid studies. The patient had a port-a-cath placed and underwent a testicular biopsy for fertility preservation. The patient received four rounds of etoposide and carboplatinum chemotherapy. He was then seen by radiation oncology and received proton beam craniospinal irradiation treatment for three weeks with a total of six fractions.

Outcome and follow-up

The patient underwent imaging after completing chemotherapy. This demonstrated shrinkage of the lesion without evidence of recurrent disease.

The patient is currently on levothyroxine 75 µg every day, desmopressin (DDAVP 50 µg in the morning and 100 µg in the evening, and hydrocortisone 10 mg in the morning and 5 mg in the afternoon. Treatment for hypogonadotropic hypogonadism will potentially be started but this is awaiting clearance from the oncology team. Growth hormone therapy is contraindicated at this time due to his underlying malignancy.

Discussion

Pineal gland tumors are rare and account for less than 1% of all intracranial tumors (1, 2). Germ cell tumors (GCTs) account for almost half of tumors found in the pineal region, with the majority being pure germinomas (1). They are most commonly found in the pineal gland (50–65%), suprasellar region (25–35%), and basal ganglia/thalamus (5–10%) (1). The median age of diagnosis is 10–12 years, with a male predominance (1). Bifocal lesions may also occur, which means that the tumor is present in both the pineal and suprasellar regions. This phenomenon is seen in 5–10% of patients and is more common in males (1). Spinal evaluation is a key factor as 10–15% of cases may have leptomeningeal spread (1, 2, 3).

The clinical presentation of a pineal germinoma includes findings of increased intracranial pressure such as headache, nausea, vomiting, papilledema, lethargy, and somnolence. Parinaud syndrome can be found in patients with pineal GCTs and is characterized by paralysis of upward gaze in addition to the loss of accommodation, convergence, and pupillary light reflex (1).

Endocrine abnormalities often appear prior to clinical or radiologic findings (2). DI is often an early clinical manifestation of a suprasellar germ cell tumor; endocrinopathies in patients with only pineal tumors are less common. Jorsal *et al*. pooled a table of 97 patients from 16 different studies that were diagnosed with intracranial germ cell tumors. Multiple endocrine abnormalities were seen, with DI being the most common (78/95 patients). Hypocortisolism was found in 44 of 76 patients. Thyroid abnormalities were seen in 28 of 83 patients, and gonadotropins and sex hormone levels were abnormal in 40 patients. Serum prolactin was elevated in 33 of 41 patients. Low GH levels were seen in 51 of 78 cases (3). Buchfelder *et al*. examined eight patients with suprasellar germinomas and found that all had hypogonadism and hypocortisolism (4). Additionally, seven of the eight patients had DI (4).

Germinomas are particularly sensitive to radiation therapy, and long-term survival rates between 79 and 90% have been routinely achieved (1). The addition of neoadjuvant chemotherapy can lead to reduced radiation doses.

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Surgery and radiotherapy can damage pituitary cells, reflecting the clinical observation that pre-existing hypopituitarism worsens after treatment. Radiotherapy can occasionally induce slowly progressive deterioration of residual pituitary function (3). Kumanogogh *et al*. looked at seven patients with intracranial germ cell tumors; six received conventional radiotherapy and one received only chemotherapy. All patients went into remission. DI was not improved and hypopituitarism continued in all radiotherapy patients (5). The patient who received only chemotherapy had complete hormonal remission (5).

None of the different endocrine abnormalities are pathognomonic for germ cell tumors. Such tumors should be considered in the differential diagnosis of young adult patients who present with new-onset central DI or hypopituitarism.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Patient consent
Patient has given written informed consent for using his case for write up.

Author contribution statement
Both the authors contributed to the care of the patient and in writing this manuscript.

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