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CENTRAL DIABETES INSIPIDUS CAUSED BY A PITUITARY ADENOMA, MASQUERADING AS BENIGN PROSTATE HYPERPLASIA IN A NATIVE HAWAIIAN

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ABSTRACT
Objective an aggressively infiltrative pituitary lesion might suggest an inflammatory or granulomatous condition such as lymphocytic hypophysitis or neurosarcoidosis; however, here we demonstrate that though rare, it is possible for pituitary adenoma invasion to sufficiently interrupt secretion of AVP and cause diabetes insipidus. We report on a native Hawaiian patient who presented critically after months of polyuria and nocturia that had been attributed to benign prostatic hyperplasia and treated with finasteride. He had become accustomed to ignoring his thirst drive due to social pressures in his workplace where he was teased for drinking copious amounts of water and taking frequent bathroom breaks. As a result, he eventually presented in hypovolemic shock with tachycardia and hypernatremia. After stabilization, the patient was found to have an infiltrative sellar mass that did not respond to corticosteroids. Transsphenoidal excision yielded tissue consistent with infarcted non-functioning pituitary adenoma. His pituitary function did not recover, but after receiving coaching to properly respond to his thirst, the patient has remained stable on intranasal desmopressin. An intact thirst drive and access to water are essential backup mechanisms to combat the life-threatening hypernatremia caused by diabetes insipidus. This case illustrates the importance of social history for clarifying etiology as well as managing an unusual manifestation of pituitary macroadenoma.

INTRODUCTION

Pituitary adenomas can be classified on the basis of whether they are hormonally hyperfunctioning or clinically silent. When silent, a macroadenoma can grow large enough to cause compressive effects on local structures, from which the patient may experience headache, visual disturbances, cranial nerve deficits, or changes in hormone expression arising from compression of the pituitary stalk or disruption of normal tissue [1]. Of the non-functioning tumors, the most common are silent gonadotroph adenomas, followed by null cell adenomas, and silent corticotroph adenomas [2]. Very rarely do these tumors grow to proportions that disrupt antidiuretic hormone resulting in diabetes insipidus. In one retrospective review of 108 patients with a non-functioning adenoma, only one had diabetes insipidus as a presenting feature [3].

We describe a case that highlights a difficult diagnosis arising from a perfect storm of unusual presenting signs, misinterpretation of long standing polyuria, and a patient who learned to ignore his thirst drive due to sociocultural pressures.

CASE REPORT

A 67 year-old native Hawaiian male presented to his local emergency department for a severe headache associated with nausea and was found to be hypotensive.

For the past year, he had complaints of nocturia and urinary frequency. He worked construction with other men near his age and was teased frequently for excessive water consumption and bathroom breaks. They told him that they all had similar symptoms and that it was from an enlarged prostate, causing him to gradually learn to ignore his thirst. He went to his primary care doctor and was given finasteride for presumed benign prostatic hyperplasia. His only known medical conditions at the time were obesity with a BMI of 42 and essential hypertension not treated with any medications. Family history was noncontributory. When he arrived at the emergency department, he was tachycardic, hypotensive, and hypernatremic. He was noted to have large volume diuresis. He required a large amount of fluid resuscitation with temporary vasopressor therapy to achieve hemodynamic stability. A CT head without contrast showed a suprasellar mass. A diagnosis of diabetes insipidus was presumed. He was given a dose of desmopressin and was subsequently transported from his local medical center to Oahu for neurosurgical and endocrine evaluation. After the patient was stabilized, he received a MRI brain which revealed a concentric sellar mass with T2 hypointensity and superior displacement of optic chiasm. Lymphocytic hypophysitis became the working diagnosis, having given appropriate consideration to craniopharyngioma, neurosarcoidosis, tuberculous hypophysitis, and pituitary abscess; suspicion for non-functioning pituitary adenoma was low.

Laboratory evaluation, shown in Table 1, revealed a prolactin of 4.0 ng/mL, free T4 0.88 ng/dL, thyrotropin 0.415 mIU/mL, free testosterone <0.2 pg/mL, total testosterone <1 ng/dL, alpha-subunit <0.3 ng/mL, follicle stimulating hormone 2.3 mIU/mL, luteinizing hormone <1.0 mIU/mL, somatotropin 0.4 ng/mL, cortisol 10.5 mcg/dL, and vasopressin 1.1 pg/mL. Serum osmolality was 287 mOsm/kg with a urine osmolality of 253 mOsm/kg (after dose of DDAVP at outside hospital). White blood cell count was 10,400 per cubic millimeter, hemoglobin 15.3 g/dL, hematocrit 44.3%, and mean corpuscular volume 88.6 femtoliters, and platelets 158,000 per cubic millimeter. Repeat MRI [Fig. 1] showed a 2.0 x 1.3 x 2.5 centimeter lobulated, peripherally enhancing mass in the sella and sphenoid body with extension into the sphenoid sinus. Heterogeneous T1/T2 contents with hypodensity were consistent with internal hemorrhagic or proteinaceous content.

The patient was started on stress dose corticosteroids and desmopressin, which was titrated to serum sodium and urine output. He subsequently underwent transsphenoidal excision following his initial stabilization and was discharged on oral and nasal desmopressin. Following excision, pathologic examination demonstrated small fragments of necrotic and fibrous tissue showing non-specific staining with synaptophysin and prolactin with effaced reticulin [Fig. 2 and 3], consistent with an infarcted non-functioning pituitary adenoma. The patient was stable and recovered uneventfully. Desmopressin was attempted to be weaned however patient continued to have symptomatic polyuria and hypernatremia. The rest of his pituitary function has yet to recover more than one year post surgery. He continues to be followed by endocrinology for management of his panhypopituitarism.

Table 1. Laboratory Values

Test (units)	Value	Reference Range
Prolactin (ng/mL)	4	(3 – 23)
Free T4 (ng/dL)	0.88	(0.8 – 1.6)
Thyroid Stimulating Hormone (mIU/mL)	0.415	(0.35 – 5)
Free testosterone (pg/mL)	< 0.2	
Total testosterone (ng/dL)	< 1	(250 – 1100)
Alpha-subunit (ng/mL)	< 0.3	<0.6
Follicle stimulating hormone (mIU/mL)	2.3	(0.95 – 11.95)
Luteinizing hormone (mIU/mL)	< 1.0	(0.57 – 12.07)
Insulin Growth Factor-1 (ng/mL)	51	(41-279)
Cortisol (mcg/dL)	10.5	(3.7 – 19.4)
Vasopressin (pg/mL)	1.1	(0 – 4.7)
Serum osmolality (mOsm/kg)	287	(280 – 295)
Urine osmolality (mOsm/kg); drawn after first dose of desmopressin	253	(500 – 800)
White blood cell count (per mm^3)	10.4	(3.9 – 10.6)
Hemoglobin (g/dL)	15.3	(13.3 – 17.7)
Hematocrit (%)	44.3	(40 – 53.1)
Mean corpuscular volume (femtoliters)	88.6	(80 – 100)
Platelets (per mm^3)	158,000	(150 – 440)

Figure 1. Sagittal T1 image on MRI demonstrates the heterogenous mass extending through the floor of the sella into the sphenoid sinus.

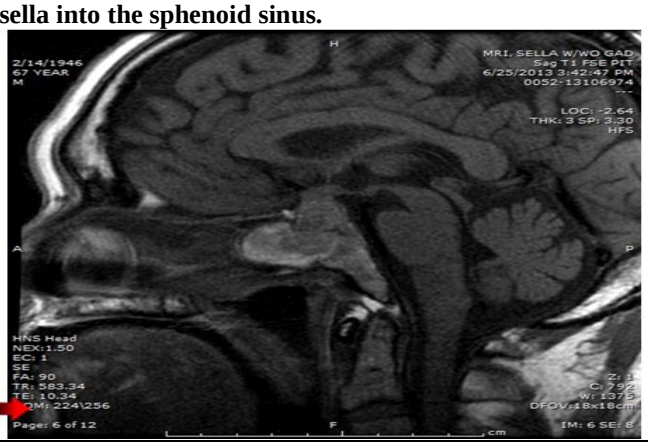


Figure 2. H&E stain showing necrotic tissue and ghost cells consistent with an infarcted pituitary adenoma.

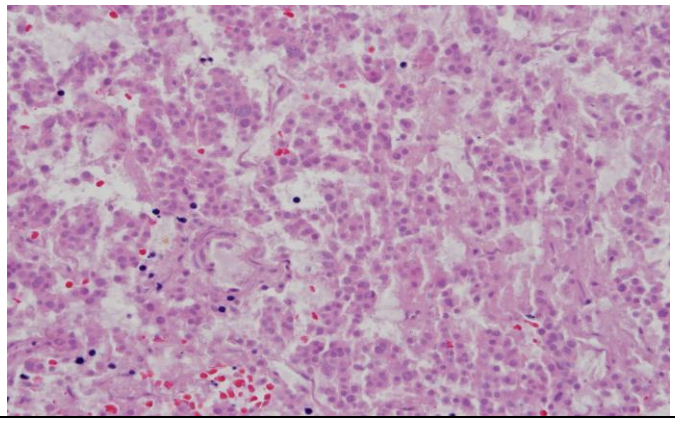
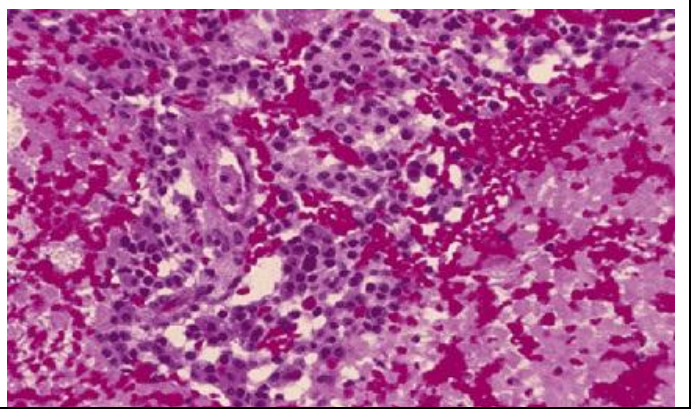


Figure 3. Reticulin staining demonstrating a completely disrupted reticulin network.

Figure 4. H&E stain suggesting non-secreting adenoma.



DISCUSSION

AVP is secreted by the posterior pituitary when hypothalamic osmoreceptors sense subtle fluctuations in plasma osmolality [4]. AVP subsequently stimulates insertion of aquaporin channels into the renal tubule cells to facilitate resorption of water and concentration of urine. Failure of the pituitary to release AVP or of renal cells to respond creates a situation in which thirst becomes the indispensable mechanism for maintaining fluid homeostasis, often resulting in polyuria and polydipsia [5]. In fact, effective renal conservation of water is not essential for successful osmoregulation of body fluids, provided that the thirst mechanism is operating properly and that access to water is unrestricted [6].

Our patient worked in an environment in which the social norm was to ignore thirst and avoid drinking water in order to maximize productivity. Coworkers of the same age convinced him that he must have an enlarged prostate and as a result, the patient developed a great ability to resist the instinct to drink water which contributed to avoidance of appropriate medical care and the development of hypovolemic shock. In the absence of trauma or transsphenoidal surgery, acquired central DI after the age of 50 should suggest metastasis or craniopharyngioma involving the hypothalamus; it is extremely rare for a pituitary adenoma to become large enough to cause disruption in the posterior pituitary gland [7,8].

Aggressively infiltrative sellar lesions with atypical presenting symptoms to include DI should raise a red flag for inflammatory or granulomatous lesions [8], which is why lymphocytic hypophysitis became a working diagnosis for our patient. His failure to respond to corticosteroids prompted excision and the final histologic diagnosis of adenoma.

Our patient was placed on desmopressin sprayed intranasally twice daily with an oral dose every night before going to sleep. In addition, he required coaching prior to discharge on how to properly respond to his thirst in order to achieve stable serum sodium levels.

Patients with true hypodipsia often require a fluid prescription based on a sliding scale accounting for daily changes in weight and/or plasma sodium [9]. However, by responding appropriately to basic coaching and the medications as prescribed, our patient demonstrated that his osmoreceptors were still intact and that the combination of social pressures at work with his macroadenoma-induced diabetes insipidus were at the root of his hypernatremia and hypovolemia.

CONCLUSION

It is very rare for pituitary adenoma invasion to sufficiently interrupt AVP secretion to cause diabetes insipidus. An appropriate thirst drive and access to water are essential backup mechanisms to combat the life-threatening hypernatremia caused by diabetes insipidus. A good social history can provide the missing link to clarifying the etiology of a patient's disease process.

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CONFLICT OF INTEREST: Nil

STATEMENT OF HUMAN AND ANIMAL RIGHTS

All procedures performed in human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Army, Department of Defense, nor the US Government.

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