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**Case Report**

# Hypothalamic and Pituitary Dysfunction After Extensive Brain Surgery: There Is Thirst for More Knowledge

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## Abstract

Craniopharyngiomas are tumors originating from the infundibular stalk, extending to the parasellar and suprasellar region, thereby conferring multiple risks of this region. In particular, hypothalamic and pituitary damage related to its natural history as well as treatment effects of craniopharyngiomas substantially affect life expectancy and quality of life. Here, we describe an adult patient presenting with polyuria, memory, and visual field impairment secondary to concurrent craniopharyngioma and intraventricular glioma. He was treated with surgical resection with postoperative course notable for hypothalamic-pituitary dysfunction, including central hypothyroidism, central adrenal insufficiency, arginine vasopressin deficiency (AVP-D, formerly diabetes insipidus) with loss of sense of thirst, and hypothalamic hypothermia. The adipsia, combined with memory dysfunction, challenged the management of constant fluctuations in his sodium (129-168 mEq/L), with ultimate treatment through vasopressin repletion, fixed fluid intake, strict urine output monitoring, and close counseling of the patient and his caregiver. This case exemplifies the complexity of the endocrine care of patients with craniopharyngiomas and highlights the need for stepwise algorithms in the treatment of hypothalamic deficiencies such as adipsia.

**Key Words:** brain tumor, adipsia, arginine-vasopressin deficiency (diabetes insipidus), pituitary

**Abbreviations:** ADI, adipsic diabetes insipiduse; AAVP-D, arginine vasopressin deficiency; AVP-D, arginine vasopressin deficiency; DDAVP, desmopressin; DI, diabetes insipidus; POC, point-of-care.

## Introduction

Craniopharyngiomas are rare tumors of the sellar, parasellar, and suprasellar region of the brain. They have bimodal age distribution both in childhood and adults who are more than 50 years old and do not have sex predilection (1, 2). Despite the pathologically benign nature of these tumors, insidious local invasion as well as the side effects of treatments frequently compromise critical adjacent structures including the pituitary, infundibulum, optic apparatus, and hypothalamus and can lead to visual compromise, hypothalamic and pituitary damage, diabetes insipidus (DI), and cognitive impairment (1, 2).

The aim of this manuscript is to report a unique case of synchronous intraventricular low-grade glioma and adamantinomatous suprasellar craniopharyngioma. We highlight the complexities in managing the sequelae of the treatments, including the treatment of hypothalamic injury and adipsic arginine vasopressin deficiency (AAVP-D or ADI) in the setting of cognitive impairment.

## Case Presentation

A previously healthy 72-year-old man presented to the emergency room with complaints of progressive headaches, confusion, forgetfulness, and disorientation. His symptoms started while on vacation with his wife and he could not remember where he was. In addition, for the 6 weeks before his presentation, he had been disoriented to time and date, requiring frequent redirection and at times, he would forget his children and grandchildren's identities. He also reported several months of polyuria but without polydipsia. He denied changes in weight, temperature tolerance, or vision, although his wife characterized his appetite as being poor with low fluid intake for many years. His brother had a history of a pituitary tumor not well characterized. On physical examination in the emergency room, the patient was alert and oriented, with limited attention span, repeatedly asking the same question, and found to have a bitemporal superior visual field deficit. The rest of the neurological examination was unremarkable, and he did not have signs of dehydration.

## Diagnostic Assessment

Baseline laboratory tests showed normal blood counts, electrolytes, and renal function, but elevated prolactin to 21.1 μg/L (normal range, 4-15.2 μg/L). Other pituitary hormones were within normal limits, and testosterone was not measured at this time due to acute illness and difficult interpretation in this setting. Given the severity of his cognitive symptoms, he underwent head computed tomography followed by magnetic resonance imaging (Fig. 1), demonstrating coexistence of a solid, largely nonenhancing intraventricular mass extending

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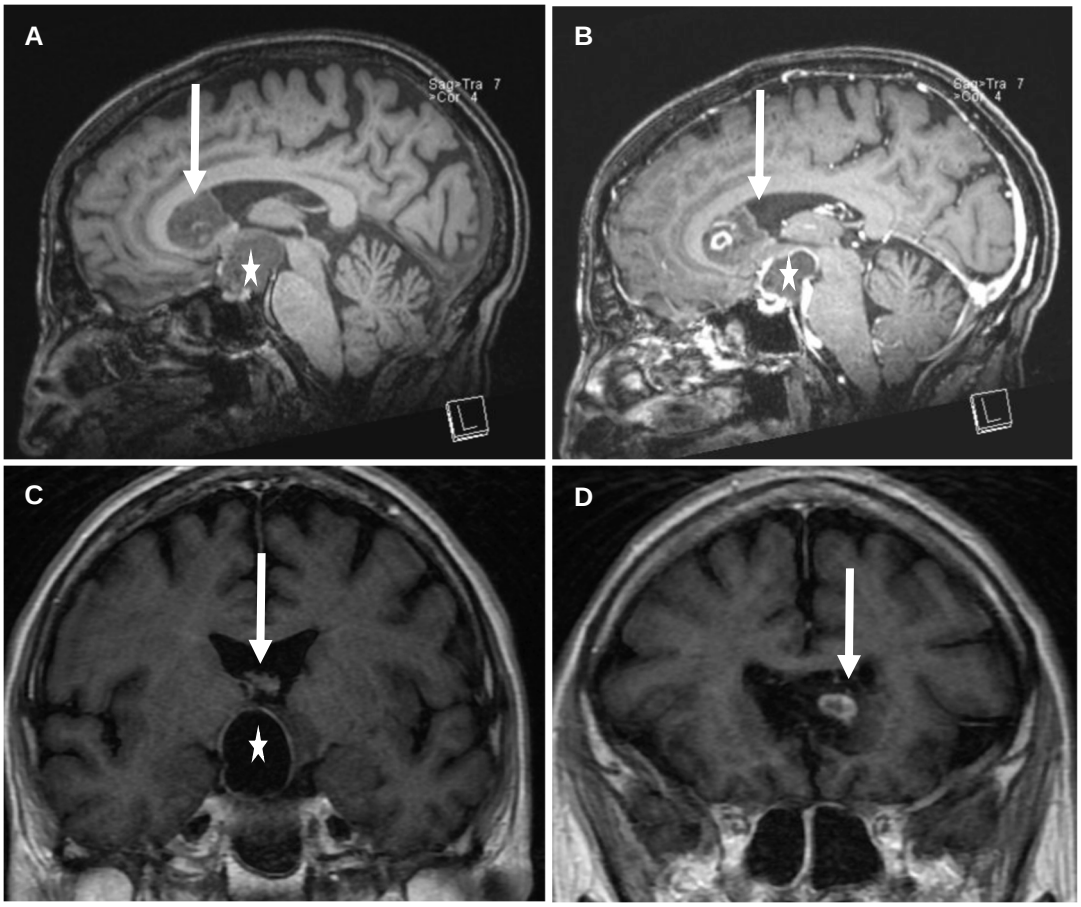


**Figure 1.** Pre-operative brain imaging demonstrating two synchronous brain tumors. (A) Pre-contrast brain MRI, sagittal view; (B) Post-contrast brain MRI, sagittal view; (C) Post-contrast brain MRI, coronal view. The arrows point to the third ventricle glioma and the stars indicate the craniopharyngioma. In both images, cortical brain atrophy is evident.

across the bilateral frontal horns with potential tracking down the forniceal columns and a second distinct cystic rim-enhancing suprasellar lesion.

## Treatment

The patient underwent a bifrontal craniotomy for interhemispheric transcallosal approach for resection of the intraventricular tumor and a transcallosal transforaminal approach with third ventriculostomy for concurrent resection of the suprasellar retrochiasmatic mass. The infundibulum was seen during surgery and appeared normal. The surgeon cut the base of the tumor at the infundibulum, where the margin between the tumor and the normal stalk seemed to transition. No immediate intraoperative complications were noted. Pathology demonstrated the intraventricular tumor to be an *IDH1/2*–wild-type low-grade glioma (with *FGFR3-TACC3* rearrangement, *PIK3CA* point mutation, and *MGMT* promoter partial methylation) and the suprasellar retrochiasmatic mass to be an adamantinomatous craniopharyngioma. His postoperative course was remarkable for a triphasic response with a peak sodium of 164 mEq/L and nadir sodium of 128 mEq/L. During this period, the patient denied being thirsty even when sodium levels were greater than 150 mEq/L, making it clear that his thirst mechanism was not intact. In the hospital, he was treated with desmopressin (DDAVP) (intravenous initially, then oral) and a daily goal of 2 L fluid intake. He developed central hypothyroidism and central adrenal insufficiency post surgery. He was discharged on oral DDAVP 0.1 mg nightly, levothyroxine, and hydrocortisone as well as a fixed daily fluid intake of 2 L per day given the persistence of adipsia.

## Outcome and Follow-up

The patient developed hypernatremia up to 161 mEq/L 5 days after discharge, and DDAVP dose was titrated to 0.1 mg twice a day. He continued to have absent sense of thirst despite remarkable hypernatremia. This complex situation required multiple contacts with the outpatient health care provider team for DDAVP and fluid intake adjustment and frequent laboratory checks to monitor serum sodium levels and urine osmolality. Importantly, his sense of thirst remained absent even during outpatient episodes of hypernatremia. Despite close monitoring, 2 weeks after discharge, the patient presented to the hospital after a witnessed fall accompanied by 1 minute of tonic-clonic activity. On readmission, his sodium was 129 mEq/L and his wife reported considerable difficulty managing his fluid intake because of the patient's refusal to drink. His sodium was 131 mEq/L. This second

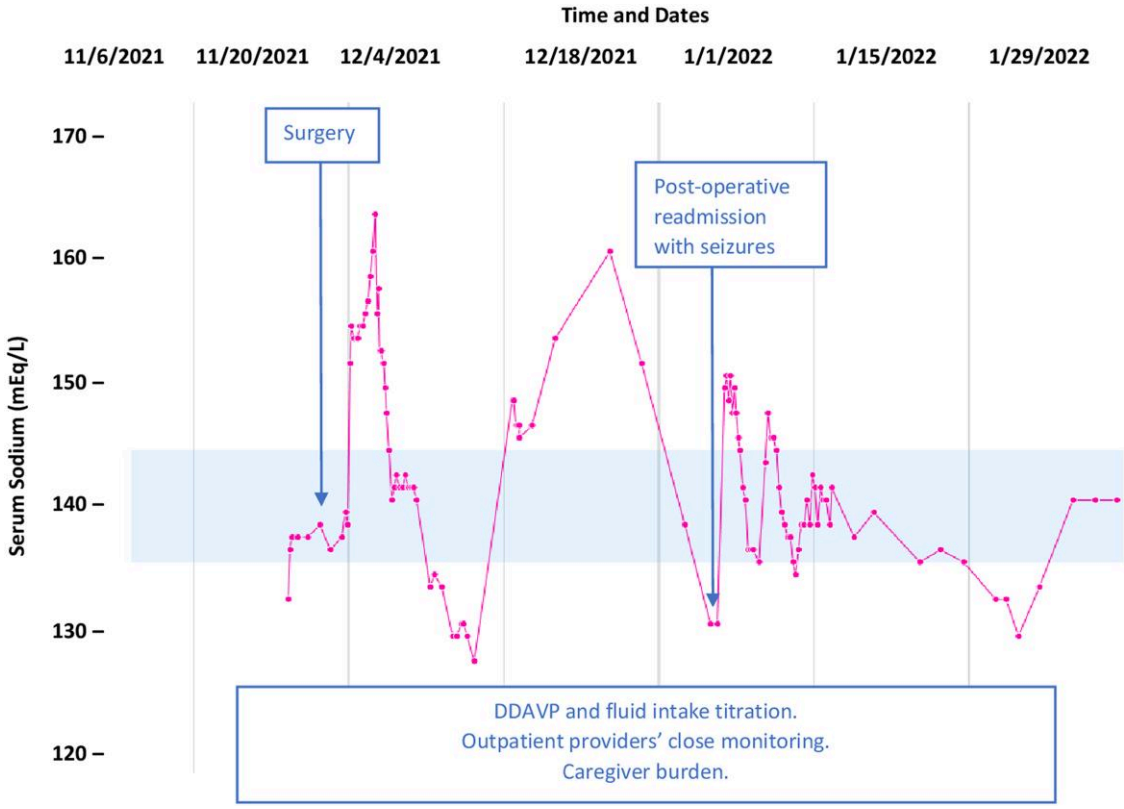


**Figure 2.** Serum sodium trend during the clinical course. Sodium levels in mEq/L (Y axis) over time (X axis) from November 2021 to January 2022. Major events characterizing the patient's clinical course are highlighted by boxes and arrows (surgery, desmopressin [DDAVP] titration, postoperative readmission).

hospitalization was characterized by difficulty adjusting his DDAVP dose and by the patient's refusal to drink a given amount of fluid, requiring intravenous fluid administration as needed. This episode made even clearer the severity of the caregiver burden that can be associated with this clinical setting. He was discharged on DDAVP 0.1 mg twice a day and goal daily fluid intake of 1.5 L. The patient had neuroendocrine follow-up appointments every 3 months and weekly electrolyte checks to ensure eunatremia. His clinical course was also notable for hypothalamic hypothermia (body temperature as low as 32.6 °C despite normal free thyroxine) requiring external rewarming. He was diagnosed with major neurocognitive disorder given the magnitude of his deficits in memory, language, and aspects of executive functioning, which have affected his ability to manage instrumental activities (working, driving, medications) without his wife's assistance. With intense monitoring by his outpatient health care team, fixed daily fluid intake and weight, and his wife's diligent care (which included reminding the patient of drinking), his sodium levels remained normal for months on a DDAVP dose of 0.05 mg orally twice a day and a fluid intake of 1 L a day (Fig. 2). No evidence of tumor progression was seen at 10 months.

## Discussion

Adipsic AVP-D (ADI) is a rare, serious condition deriving from injury to arginine vasopressin neurons and the hypothalamic thirst center (3). Adipsia complicates the management of AVP-D (ADI) that often emerges after surgery in the sellar/suprasellar region. Individuals who cannot compensate for urine losses with water intake because of absent thirst need to be prescribed a fixed amount of daily fluid intake to try to overcome these sodium imbalances. In this manuscript, we propose an algorithm to improve and standardize the care of patients with adipsic AVP-D (ADI) (Fig. 3). Concurrent cognitive impairment challenges adherence to the fluid regimen even more, with subsequent risk of severe serum sodium perturbances, hospitalizations, and potential mortality.

Craniopharyngiomas are among the brain tumors most often associated with AAVP-D (ADI), accounting for 13% to 30% of AAVP-D (ADI) cases (4). Other complications of hypothalamic injury can coexist with AAVP-D (ADI), further confounding morbidity. Among others, patients with AAVP-D (ADI) have a higher incidence of hypothalamic obesity, central sleep apnea, deep vein thrombosis, and severe sodium fluctuations leading to frequent hospital admissions (4).

In this case, the synchronous occurrence of a biventricular glioma with tracking down the forniceal column to the lateral aspect of the hypothalamus along with the suprasellar craniopharyngioma posed unique risks to the patient and the consequences of surgery. To our knowledge, a concurrent diagnosis of glioma and craniopharyngioma has not been previously reported, highlighting the unique scenario of this patient's case.

Consensus on AAVP-D (ADI) management has not been reached. Mainstays of AAVP-D (ADI) management include a fixed daily DDAVP dose to set a urine concentration point, establishing a precise fluid intake amount, daily weights (fluctuation of ±1.5 kg indicates respectively water retention or excessive losses, thus fluid intake adjustments can temporarily

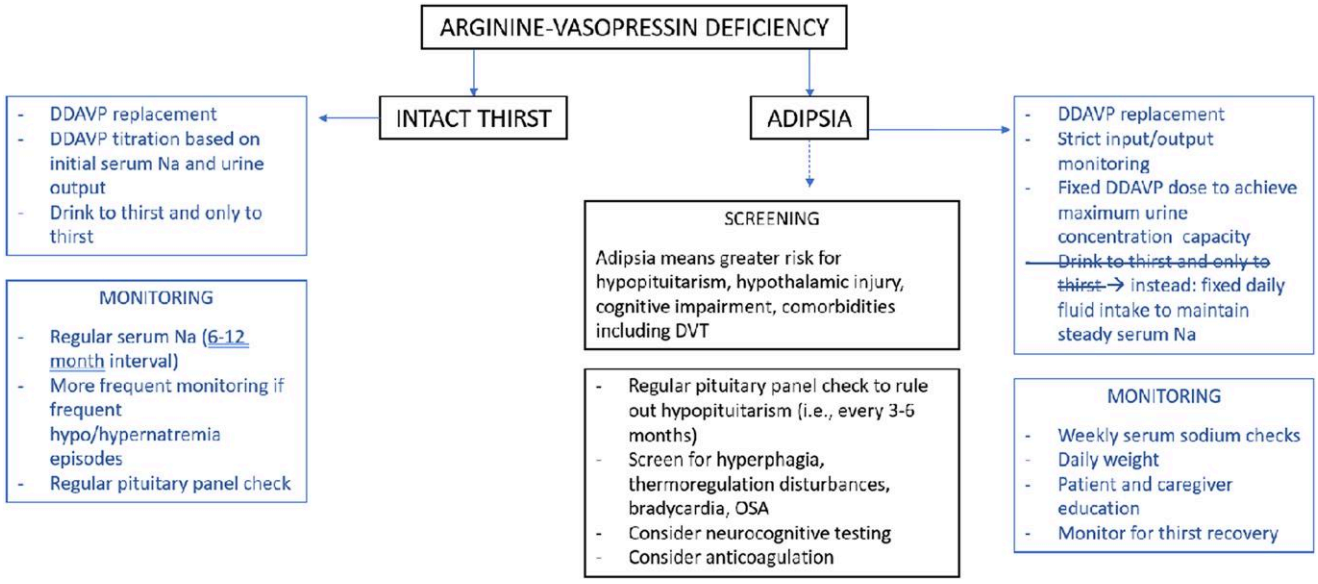


**Figure 3.** Proposed algorithm for management of adipsic arginine-vasopressin deficiency (AAVP-D). Proposed algorithm for management of AAVP-D, highlighting the differences between the mainstays of management for classic AVP-D (left) and AAVP-D (right).

be made based on weight changes), alcohol avoidance, deep vein thrombosis prophylaxis (affecting up to 30.8% of patients) with a personalized approach to anticoagulation that should follow clinical judgment and carefully balance risks and benefits in each patient, sleep study for sleep apnea screening, and calorie counting (5). This multilevel management often concurs with panhypopituitarism, worsening cognition, and behavioral changes resulting in an extremely complex clinical scenario. It has also been suggested that patients with central AVP-D (ADI) could experience a lower quality of life due to oxytocin deficiency (6). This not only affects the patients but their caregivers.

Improved outpatient care of AAVP-D (ADI) is needed to reduce the hospitalization rate and ameliorate quality of life of the patients. Small studies in the pediatric population have explored the use of point-of-care (POC) devices to titrate fluid intake daily and found that hospital admissions, sodium perturbations, and caregiver burden were reduced with the use of devices that measure POC sodium (7, 8). Currently, there are no US Food and Drug Administration–approved POC devices for sodium monitoring and their cost remains elevated. However, improved recognition, increased expertise, and hospital network support can contribute to improving quality of life and mortality for AAVP-D (ADI). At our institution, we are developing specific home hospital pathways for patients presenting to the emergency department with hyponatremia and hypernatremia and with an underlying diagnosis of AAVP-D (ADI). Further studies are needed to determine the efficacy of these pathways on admission rate, morbidity, and mortality.

Lastly, it has been reported that adipsia can recover (9), thus, long-term, regular sodium level monitoring and thirst assessment should be maintained by health care providers to continuously titrate the treatment.

## Learning Points

- AAVP-D (ADI) is a rare but potentially life-threatening condition that can be associated with suprasellar masses, characterized by severe sodium fluctuations, caregiver burden, and substantial comorbidities.
- Tumors of the suprasellar region pose risk for AAVP-D (ADI), pituitary function deficiency, impaired cognition, and behavior disorders.
- Close and regular monitoring of AAVP-D (ADI) is necessary to decrease mortality.

## Contributors

All authors made individual contributions to authorship. F.G., A.P.A., and W.L.B. were involved in the diagnosis and management of this patient. F.G., G.A.S., and A.P.A. conceived the manuscript idea. F.G. wrote the original draft and completed the manuscript submission. All authors contributed to the review and approval of the final manuscript draft.

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## Disclosures

All authors declare no conflict of interest.

## Informed Patient Consent for Publication

Signed informed consent obtained directly from the patient's relatives or guardians.

## Data Availability Statement

Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study.

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