Central diabetes insipidus etiology

Central diabetes insipidus has several causes, including a brain tumor, a brain injury, brain surgery, tuberculosis, and some forms of other diseases [1)].

Central DI may be seen in the following situations:

1. following transsphenoidal surgery or craniopharyngioma surgery: (usually transient, therefore avoid long-acting agents until it can be determined if long-term replacement is required).

Injury to the posterior pituitary or stalk usually causes one of three patterns of DI:

a) transient DI: supra-normal urine output (UO) and polydipsia which typically normalizes ≈ 12–36 hrs post-op

b) “prolonged” DI: UO stays supra-normal either for a prolonged period (may be months - about two–thirds of these patients will return to near-normal at one year post-op due to release of ADH directly from the hypothalamus) or permanently

c) “triphasic response”: least common

● phase 1: injury to the pituitary reduces ADH levels for 4–5 days → DI (polyuria/polydipsia producing hypernatremia)

● phase 2: cell death liberates ADH for the next 4–5 days → transient normalization or even SIADH-like water retention producing normonatremia or hyponatremia

(✖ NB: there is a danger of inadvertently continuing vasopressin therapy beyond the initial phase 1 DI into this phase which can produce iatrogenic SIADH)

● phase 3: reduced or absent ADH secretion → DI (transient DI as in “a” above, or “prolonged” DI as in “b” above) producing hypernatremia

2. central herniation: shearing of pituitary stalk may occur

3. brain death: hypothalamic production of ADH ceases

4. with certain tumors:

a) PitNET/adenomas: DI is rare even with very large macroadenomas. DI may occur with pituitary apoplexy

b) craniopharyngioma: DI usually only occurs postoperatively since damage to the pituitary or lower stalk does not prevent the production and release of ADH by hypothalamic nuclei

c) suprasellar germ cell tumors

d) rarely with a colloid cyst

e) hypothalamic tumors: Langerhans cell histiocytosis

5. mass lesions pressing on hypothalamus: e.g., AComA aneurysm

6. following head injury: primarily with basal (clival) skull fractures

7. with encephalitis or meningitis

8. drug induced:

a) ethanol and phenytoin can inhibit ADH release

b) exogenous steroids may seem to “bring out” DI because they may correct adrenal insufficiency (see below) and they inhibit ADH release

9. granulomatous diseases

a) Wegener’s granulomatosis: a vasculitis

b) neurosarcoidosis involving the hypothalamus

10. inflammatory: autoimmune hypophysitis or lymphocytic infundibuloneurohypophysitis (distinct conditions)

Primary central diabetes insipidus

Genetic abnormalities of the vasopressin gene on chromosome 20 are responsible for autosomal dominant forms of primary central diabetes insipidus, but many cases are idiopathic.

Secondary central diabetes insipidus

Central diabetes insipidus may also be secondary (acquired), caused by various lesions, including hypophysectomy, cranial injuries (particularly basal skull fractures), suprasellar tumor and intrasellar tumors (primary or metastatic), Langerhans cell histiocytosis, lymphocytic hypophysitis, granulomas (sarcoidosis or tuberculosis), vascular lesions (aneurysm, thrombosis), and infections (encephalitis, meningitis).

Autoimmune

Sheehan’s syndrome (rarely causes DI).

The most frequent cause of central diabetes insipidus (CDI) are central nervous system tumors (CNS) including craniopharyngioma and germ cell tumors, which could damage the Arginine vasopressin (AVP) neuron system. CDI is also caused by inflammatory diseases such as lymphocytic infundibulo neurohypophysitis (LINH) and IgG4-related disease.

Tumor: craniopharyngioma, metastases, lymphoma...

CDI often manifests after pituitary surgery. In this case, polyuria appears in the first 2 days after surgery and sometimes resolves spontaneously, although it could persist permanently if AVP neurons are damaged substantially.

Diabetes insipidus (DI) is a well-recognized transient or permanent complication following transsphenoidal surgery for pituitary neuroendocrine tumors or other sellar/parasellar lesions. However, data regarding the prevalence of pre-operative DI in sellar/parasellar lesions other than pituitary neuroendocrine tumors are scarce.

Angelousi et al. systematically reviewed the existing data for defining the prevalence of DI before any treatment in adult patients with sellar/parasellar lesions, excluding pituitary neuroendocrine tumors and metastatic lesions. In total, 646 patients with sellar/parasellar lesions presenting with DI at diagnosis were identified. The most common pathologies of sellar/parasellar lesions presenting with DI at diagnosis were lymphocytic hypophysitis (26.5%), craniopharyngiomas (23.4%), Langerhans cell histiocytosis (18.9%) and Rathke's cleft cyst (12.7%), accounting for the vast majority (more than 80%) of these lesions. Overall, DI at diagnosis was found in 23.4% of all patients with sellar/parasellar lesions, albeit with a wide range from 10.6% to 76.7%, depending on the nature of the pathology. The highest prevalence of DI was found in less commonly encountered lesions namely germ cell tumors (76.7%), abscesses (55.4%) and neurosarcoidosis (54.5%), each accounting for less than 3% of all sellar/parasellar lesions. Most DI cases (68.8%) were associated with anterior pituitary hormonal deficiencies, in contrast to pituitary neuroendocrine tumors that rarely present with DI. The enlargement and enhancement of the pituitary stalk were the most common findings on magnetic resonance imaging besides the loss of the high signal of the posterior pituitary on T1-weighted images. Resolution of DI spontaneously or following systemic and surgical management occurred in 22.4% of cases. Post-operative DI, not evident before surgery, was found in 27.8% of non-adenomatous sellar/parasellar lesions and was transient in 11.6% of them. Besides distinctive imaging features and symptoms, early recognition of DI in such lesions is important because it directs the diagnosis towards a non-adenomatous sellar/parasellar tumor and the early initiation of appropriate treatment [2].

1)
Thibonnier M, Barrow DL, Selman W. Antidiuretic Hormone: Regulation, Disorders, and Clinical Evaluation. In: Neuroendocrinology. Baltimore: Williams and Wilkins; 1992:19–30
2)
Angelousi A, Mytareli C, Xekouki P, Kassi E, Barkas K, Grossman A, Kaltsas G. Diabetes insipidus secondary to sellar/parasellar lesions. J Neuroendocrinol. 2021 Mar;33(3):e12954. doi: 10.1111/jne.12954. PMID: 33769630.