Preparation for Anaesthesia - Pituitary Abnormalities

Anterior Pituitary Hypersecretion

The anterior pituitary gland consists of five identifiable types of secretory cells (and the hormones they secrete): somatotrophs (growth hormone [GH]), corticotrophs (ACTH), lactotrophs (prolactin), gonadotrophs (luteinizing hormone [LH] and follicle-stimulating hormone), and thyrotrophs (TSH). The secretion of these pituitary hormones is regulated largely by a negative feedback loop by hypothalamic regulatory hormones and by signals that originate from the target site of pituitary action. Six hypothalamic hormones have been characterized: dopamine, the prolactin-inhibiting hormone; somatostatin, the GH release-inhibiting hormone; GH-releasing hormone; corticotropin-releasing hormone; gonadotropin-releasing hormone (or LH-releasing hormone); and thyrotropin-releasing hormone. Most pituitary tumors (>60 percent) are hypersecretory and are classified according to the excess production of a specific anterior pituitary hormone.

The three most common disorders of pituitary hypersecretion are those related to excesses of prolactin (amenorrhea, galactorrhea, and infertility), ACTH (Cushing syndrome), or GH (acromegaly). In addition to knowing the pathophysiologic processes of the disease involved, the anesthesiologist must determine whether the patient recently underwent air pneumoencephalography. If so, nitrous oxide should not be used; this practice lessens the risk of intracranial hypertension from gas collection. CT or MRI scanning of the sella has largely replaced neuroencephalography, but the latter is still performed.

Acromegaly is a syndrome that presents with characteristic facies, weakness, enlargement of the hands (often to the point of rendering the usual oximeter probes difficult to use) and feet, thickening of the tongue (often to the point of making endotracheal intubation difficult), and enlargement of the nose and mandible with spreading of the teeth (often to the point of requiring larger than normal laryngoscopic blades). [204], [20] The patient may even appear myxedematous. Other findings include abnormal glucose tolerance and osteoporosis. The most specific test for acromegaly is measurement of GH before and after glucose administration. The typical acromegalic has very elevated fasting levels of GH (usually >10 g/mL), and the levels do not change appreciably after oral administration of glucose. In the normal state, glucose markedly suppresses the GH level. A few patients with active acromegaly have normal levels of fasting GH, and GH levels are not suppressed by glucose. In addition, an elevated plasma insulin-like growth factor-I (IGF-I), also known as somatomedin-C, is pathognomonic of growth hormone excess. The drugL-dopa, which normally causes an elevation of GH in normal subjects, in the acromegalic either has no effect or lowers GH levels. More than 99 percent of cases of acromegaly are attributable to pituitary adenoma. Thus, the primary treatment of acromegaly is trans-sphenoidal surgery. If the pituitary tumor is not totally removed, patients are often offered external pituitary irradiation. In the case of suprasellar extension, conventional transfrontal hypophysectomy is often employed. The dopaminergic agonist bromocriptine can lower GH levels, but long-term follow-up with this drug is not favorable. Octreotide, a long-acting analogue of somatostatin, is an effective palliation in 50 percent of patients.

The effects of excessive GH stem from both direct actions of the hormone on tissue and stimulation of the production of somatomedins. Excessive GH often results in retention of sodium and potassium, inhibition of the peripheral action of insulin (which can result in diabetes mellitus), and premature atherosclerosis (often associated with cardiomegaly). Exertional dyspnea may be related to either heart failure or respiratory insufficiency due to kyphoscoliosis. Cardiac arrhythmias are common. The incidence of these problems in elderly men now being treated with or receiving GH (recombinant) for the possible improvement of functional status is not known. Preoperative evaluation of the patient who

has acromegaly or who is receiving GH might begin by determining whether significant cardiac, hypertensive, pulmonary, or diabetic problems exist. If so, preoperative evaluation should proceed along the lines described in sections discussing those topics. In addition, difficulty with endotracheal intubation should be anticipated in the acromegalic patient; lateral neck films or CT scans of the neck and direct or indirect visualization can identify the patient who has subglottic stenosis or an enlarged tongue, mandibles, epiglottis, or vocal cords. [205, 206] If placement of an arterial line is necessary, a brachial or femoral site may be preferable to a radial site. [207]

Prolactin has been one of the most interesting markers to identify patients with pituitary tumors. Elevated prolactin levels are often but not invariably associated with galactorrhea. Females commonly present with amenorrhea, and males present with impotence. Optimal therapy for prolactin-secreting tumors is now believed to be the dopamine agonist bromocriptine. This drug, which is extremely effective in controlling the prolactin level and restoring gonadotropin function, is used when fertility is desired. When normal menses, contraception, and skeletal integrity are desired, birth control pills are the treatment. [208]

The side effects of bromocriptine include orthostatic hypotension, gastroparesis (possible increased risk of aspiration), constipation, and nasal congestion (possible need for oral intubation). [208] With large prolactin-secreting tumors (macroadenomas), loss of other pituitary function is common, and evaluation of thyroid and adrenocortical status is indicated. Preoperative preparation of patients with Cushing syndrome is discussed in the section on ACTH excess.

Anterior Pituitary Hypofunction

Anterior pituitary hypofunction results in deficiency of one or more of the following hormones: GH, TSH, ACTH, prolactin, or gonadotropin. Preoperative preparation of those patients who are chronically deficient in ACTH and TSH was discussed previously. No special preoperative preparation is required for the patient deficient in prolactin or gonadotropin; deficiency in GH can result in atrophy of cardiac muscle, a condition that may necessitate preoperative cardiac evaluation. However, anesthetic problems have not been documented in patients with isolated GH deficiency. Acute deficiencies are another matter. Acute pituitary deficiency is often caused by bleeding into a pituitary tumor. In surgical specimens of resected adenomas, as many as 25 percent show evidence of hemorrhage. Patients with this condition often present with acute headache, visual loss, nausea or vomiting, ocular palsies, disturbances of consciousness, fever, vertigo, or hemiparesis. In such patients, rapid transsphenoidal decompression should be accompanied by consideration of replacement therapy, including glucocorticoids and treatment for increased intracranial pressure.

The obstetrical anesthesiologist is often aware of these pituitary failure problems: Sheehan's syndrome is the clinical manifestation of pituitary infarction associated with hypotension after or during obstetric hemorrhage. Conditions that strongly suggest this diagnosis are failure to start postpartum lactation, increasing fatigue, cold intolerance, and especially hypotension unresponsive to volume replacement and pressors.

Posterior Pituitary Hormone Excess and Deficiency

The secretion of vasopressin, or antidiuretic hormone (ADH), is increased by increased serum osmolality or the presence of hypotension. Inappropriate secretion of vasopressin, without relation to serum osmolality, results in hyponatremia and fluid retention. This inappropriate secretion can result from a variety of CNS lesions; from drugs such as nicotine, narcotics, chlorpropamide, clofibrate, vincristine, vinblastine, and cyclophosphamide; and from pulmonary infections, hypothyroidism, adrenal insufficiency, and ectopic production from tumors. Preoperative management of the surgical patient with inappropriate secretion of vasopressin includes appropriate treatment of the causative

disorders and restriction of water. Occasionally, drugs that inhibit the renal response to ADH (e.g., lithium or demeclocycline) should be administered preoperatively to restore normal intravascular volume and electrolyte status.

Most of the clinical features associated with the syndrome of inappropriate ADH (SIADH) secretion are related to hyponatremia and the resulting brain edema; these features include weight gain, weakness, lethargy, mental confusion, obtundation, and disordered reflexes and may progress, finally, to convulsions and coma. This form of edema rarely leads to hypertension.

SIADH should be suspected in any patient with hyponatremia who excretes urine that is hypertonic relative to plasma. The following laboratory findings further support the diagnosis:

1. Urinary sodium >20 mEq/L
2. Low serum levels of BUN, creatinine, uric acid, and albumin
3. Serum sodium <130 mEq/L
4. Plasma osmolality <270 mOsm/L
5. Urine hypertonic relative to plasma

Noting the response to water loading is a useful way of evaluating the patient with hyponatremia. Patients with SIADH are unable to excrete dilute urine even after water loading. Assay of ADH in blood can confirm the diagnosis. Too vigorous treatment of chronic hyponatremia can result in disabling demyelination. [209, 210] The increase in serum sodium should not be greater than 1 mEq/L/h. [209, 210] (See the discussion of hyponatremia in the later section, *Electrolyte Disorders.*)

Patients with mild to moderate symptoms of water intoxication can be treated with restriction of fluid intake to about 500 to 1,000 mL/d. Patients with severe water intoxication and CNS symptoms may need vigorous treatment, with intravenous administration of 200 to 300 mL of 5 percent saline solution over several hours, followed by fluid restriction.

Treatment should be directed at the underlying problem. If SIADH is drug induced, the drug should be withdrawn. Inflammation should be treated with appropriate measures, and neoplasms should be managed with surgical resection, irradiation, or chemotherapy, whichever is indicated.

No drugs are available that can suppress release of ADH from the neurohypophysis or from a tumor. Dilantin and narcotic antagonists such as naloxone and butorphanol have some inhibiting effect on physiologic ADH release but are clinically ineffective in patients with SIADH. Drugs blocking the effect of ADH on renal tubules include lithium, which is rarely used because its toxicity often outweighs its benefits, and demethylchlortetracycline in doses of 900 to 1,200 mg/d. The latter drug interferes with the ability of the renal tubules to concentrate urine, causing excretion of isotonic or hypotonic urine and thereby lessening hyponatremia. Demethylchlortetracycline can be used for ambulatory patients with SIADH when it is difficult to restrict fluids.

When a patient with SIADH comes to the operating room for any surgical procedure, fluids are managed by measuring the central volume status by central venous pressure, pulmonary artery lines, or cross-sectional left ventricular area at end-diastole on transesophageal echocardiography, and by frequent assays of urine osmolarity, plasma osmolarity, and serum sodium, including during the period immediately after surgery.

Despite the common impression that SIADH is frequently seen in elderly patients in the postoperative period, studies have shown that the patient's age and the type of anesthetic used have no bearing on the postoperative development of SIADH. It is not unusual to see many patients in the neurosurgical intensive care unit suffering from this syndrome. The

diagnosis is usually one of exclusion. Patients with SIADH usually require only fluid restriction; very rarely is hypertonic saline needed.

Lack of ADH, which results in diabetes insipidus, is caused by pituitary disease, brain tumors, infiltrative diseases such as sarcoidosis, head trauma (trauma after neurosurgery), or lack of renal response to ADH. The last can occur with such diverse causes as hypokalemia, hypercalcemia, sickle cell anemia, obstructive uropathy, or renal insufficiency. Preoperative treatment of diabetes insipidus consists of restoring normal intravascular volume by replacing urinary losses, by using nasal desmopressin, and by giving daily fluid requirements intravenously.

Perioperative management of patients with diabetes insipidus is based on the extent of the ADH deficiency. Management of a patient with complete diabetes insipidus and a total lack of ADH usually does not present any major problem as long as side effects of the drug are avoided and the presence of the condition is known before surgery. Just before surgery, the patient is given the usual dose of desmopressin acetate intranasally or an intravenous bolus of 100 mU of aqueous vasopressin, followed by constant infusion of 100 to 200 mU/h. [211] The dose is usually adjusted to permit daily breakthrough polyuria that avoids the iatrogenic syndrome of SIADH. We have found it useful to continue that dosing regimen perioperatively in all ambulatory patients who can take fluid orally in the postoperative period. All the intravenous fluids given intraoperatively should be isotonic, to reduce the risk of water depletion and hypernatremia. Plasma osmolality should be measured every hour, both intraoperatively and immediately after surgery. If plasma osmolality rises well above 290 mOsm/L, hypotonic fluids can be administered; the rate of the intraoperative vasopressin infusion can be increased to more than 200 mU/h.

For patients who have a partial deficiency of ADH, it is not necessary to use aqueous vasopressin perioperatively unless plasma osmolality rises above 290 mOsm/L. Nonosmotic stimuli, for example, volume depletion, and stress of surgery usually cause the release of large quantities of ADH perioperatively. Consequently, these patients require only frequent monitoring of plasma osmolality during this period.

Because of side effects, the dose of vasopressin should be limited to that necessary for control of diuresis. [212] The oxytoxic and coronary artery-constricting properties of vasopressin make this limit especially applicable to patients who are pregnant or who have coronary artery disease. [210]

Another problem for anesthesiologists is the care of patients who come to the operating room with a vasopressin drip for treatment of bleeding from esophageal varices. This treatment is less common since the advent of laser therapy for varices. However, when vasopressin is given, the vasoconstrictive effect of vasopressin on the splanchnic vasculature is used to decrease bleeding. Such patients are often volume depleted and may have concomitant coronary artery disease. Because vasopressin has been shown to decrease oxygen availability markedly, primarily because of a decreased stroke volume and heart rate, monitoring of tissue oxygen delivery may be useful. In 1982, Nikolic and Singh [213] described a patient with a history of angina pectoris who received a combination of cimetidine and vasopressin for esophageal varices. Bradyarrhythmias and AV block occurred, necessitating placement of a pacemaker. On two occasions, discontinuation of either of these drugs alleviated the symptoms. This effect indicates that the combination of cimetidine and vasopressin could be deleterious to the heart because of the combined negative inotropic and arrhythmogenic effects of the two drugs.