463e Special Issues in Inpatient Neurologic Consultation

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Inpatient neurologic consultations usually involve questions regarding specific disease processes or prognostication after various cerebral injuries. Common reasons for neurologic consultation include stroke (Chap. 446), seizures (Chap. 445), altered mental status (Chap. 34), headache (Chap. 21), and management of coma and other neurocritical care conditions (Chaps. 328 and 330). This chapter focuses on additional common reasons for consultation that are not addressed elsewhere in the text.

CONSULTATIONS REGARDING CENTRAL NERVOUS SYSTEM DYSFUNCTION

HYPERPERFUSION STATES LEADING TO POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME

A group of neurologic disorders shares the common feature of hyperperfusion, probably related to endothelial dysfunction, playing a key role in pathogenesis. These seemingly diverse syndromes include hypertensive encephalopathy, eclampsia, postcarotid endarterectomy syndrome, and toxicity from calcineurin-inhibitor and other medications. Modern imaging techniques and experimental models suggest that vasogenic edema is typically the primary process leading to neurologic dysfunction; therefore, prompt recognition and management of this condition should allow for clinical recovery as long as superimposed hemorrhage or infarction has not occurred.

The brain's autoregulatory capability successfully maintains a fairly stable cerebral blood flow in adults despite alterations in systemic mean arterial pressure (MAP) ranging from 50 to 150 mmHg (Chap. 330). In patients with chronic hypertension, this cerebral autoregulation curve is shifted, resulting in autoregulation working over a much higher range of pressures (e.g., 70–175 mmHg). In these hypertensive patients, cerebral blood flow is kept steady at higher MAP, but a rapid lowering of pressure can lead to ischemia on the lower end of the autoregulatory curve, even at values typically thought of as normotensive. This autoregulatory phenomenon is achieved through both myogenic and neurogenic influences causing small arterioles to contract and dilate. When the systemic blood pressure exceeds the limits of this mechanism, breakthrough of autoregulation occurs, resulting in hyperperfusion via increased cerebral blood flow, capillary leakage into the interstitium, and resulting edema. The predilection of all of the hyperperfusion disorders to affect the posterior rather than anterior portions of the brain may be due to a lower threshold for autoregulatory breakthrough in the posterior circulation or a vasculopathy that is more common in these blood vessels.

Although elevated or relatively elevated blood pressure is common in many of these disorders, some hyperperfusion states such as calcineurin-inhibitor toxicity occur with no apparent pressure rise. In these cases, vasogenic edema is likely due primarily to dysfunction of the capillary endothelium itself, leading to breakdown of the blood-brain barrier. It is useful to separate disorders of hyperperfusion into those caused primarily by increased pressure and those due mostly to endothelial dysfunction from a toxic or autoimmune etiology (Table 463e-1). In reality, both of these pathophysiologic processes likely play some role in each of these disorders.

The clinical presentation of all of the hyperperfusion syndromes is similar with prominent headaches, seizures, or focal neurologic deficits. Headaches have no specific characteristics, range from mild to severe, and may be accompanied by alterations in consciousness ranging from confusion to coma. Seizures may be present, and these can be of multiple types depending on the severity and location of the edema. Nonconvulsive seizures have been described in hyperperfusion states; therefore, a low threshold for obtaining an electroencephalogram (EEG) in these patients should be maintained. The typical focal deficit in hyperperfusion states is cortical visual loss, given the tendency of the process to involve the occipital lobes. However, any focal deficit can occur depending on the area affected, as evidenced by patients who, after carotid endarterectomy, exhibit neurologic dysfunction referable to the ipsilateral newly reperfused hemisphere. In conditions where increased cerebral blood flow plays a role, examination of the inpatient vital signs record will usually reveal a systemic blood pressure that is increased above the patient's baseline. It appears as if the rapidity of rise, rather than the absolute value of pressure, is the most important risk factor.

TABLE 463e-1 SOME COMMON ETIOLOGIES OF HYPERPERFUSION SYNDROME

Disorders in which increased capillary pressure dominates the pathophysiology
Hypertensive encephalopathy, including secondary causes such as renovascular hypertension, pheochromocytoma, cocaine use, etc.
Postcarotid endarterectomy syndrome
Preeclampsia/eclampsia
High-altitude cerebral edema
Disorders in which endothelial dysfunction dominates the pathophysiology
Calcineurin-inhibitor toxicity
Chemotherapeutic agent toxicity (e.g., cytarabine, azathioprine, 5-fluorouracil, cisplatin, methotrexate, tumor necrosis factor α antagonists)
Glucocorticoids
Erythropoietin
HELLP syndrome (*h*emolysis, *e*levated *l*iver enzyme levels, *l*ow *p*latelet count)
Thrombotic thrombocytopenic purpura (TTP)
Hemolytic-uremic syndrome (HUS)
Systemic lupus erythematosus (SLE)
Granulomatosis with polyangiitis (Wegener's)

The diagnosis in all of these conditions is clinical. The symptoms of these disorders are common and nonspecific, so a long differential diagnosis should be entertained, including consideration of other causes of confusion, focal neurologic deficits, headache, and seizures. Magnetic resonance imaging (MRI) has improved the ability of clinicians to diagnose hyperperfusion syndromes, although cases have been reported with normal imaging. Patients classically exhibit the high T2 signal of edema primarily in the posterior occipital lobes, not respecting any single vascular territory (Fig. 463e-1). Diffusion-weighted images are typically normal, emphasizing the vasogenic rather than cytotoxic nature of this edema. Imaging with computed tomography (CT) is less sensitive but may show a pattern of patchy hypodensity in the involved territory. Previously this classic radiographic appearance had been termed *reversible posterior leukoencephalopathy* (RPLE). However, this term has fallen out of favor because none of its elements are completely accurate. The radiographic and clinical changes are not always reversible; the territory involved is not uniquely posterior; and gray matter may be affected as well, rather than purely white matter as the term "leukoencephalopathy" intimates. The now more commonly used radiologic term *posterior reversible encephalopathy syndrome* (PRES) suffers from many of these same limitations. Vessel imaging may demonstrate narrowing of the cerebral vasculature, especially in the posterior circulation; whether this noninflammatory vasculopathy is a primary cause of the edema or occurs as a secondary phenomenon remains unclear. Other ancillary studies such as cerebrospinal fluid (CSF) analysis often yield nonspecific results. It should be noted that many of the substances that have been implicated, such as cyclosporine, can cause this syndrome even at low doses or after years of treatment. Therefore, normal serum levels of these medications do not exclude them as inciting agents.

In cases of hyperperfusion syndromes, treatment should commence urgently once the diagnosis is considered. Hypertension plays a key role commonly, and judicious lowering of the blood pressure with IV agents such as labetalol or nicardipine is advised along with continuous cardiac and blood pressure monitoring, often through an arterial line. It is reasonable to lower MAP by ~20% initially, as further