Hypophysitis

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Abstract Hypophysitis is an uncommon inflammatory condition that may affect the pituitary gland and stalk. Patients often present with varying degrees of hypopituitarism. The diagnosis is often made presumptively based on clinical history and biochemical data but may also be supported by magnetic resonance imaging. Therapy is generally supportive in nature but may require surgery for pathological diagnosis and treatment of mass effect.

Keywords Hypophysitis · Pituitary · Hypopituitarism · Transsphenoidal surgery

Demographic and clinical findings

Hypophysitis is an uncommon condition and represents a fairly broad spectrum of inflammatory lesions that can affect the pituitary gland and the pituitary stalk [2, 4, 6, 12]. The clinical presentation ordinarily includes headache, nausea and vomiting, hypopituitarism, and diabetes insipidus which usually is episodic, and these symptoms can respond variably to symptomatic therapy.

Hypophysitis is often associated with pregnancy, but can be associated with other forms of autoimmune disease [1, 5, 13]. In many cases hypophysitis may not obviously be associated with other disorders [7, 10]. Often the clinical course involves relapses and this is particularly true of the active inflammatory aspects of lymphocytic hypophysitis, which may respond temporarily to corticosteroid-based therapy [11].

The condition may affect both sexes and may occur in adults of any age.

There are two basic varieties of hypophysitis [4, 6]. The first of these is lymphocytic hypophysitis, which is usually associated with pregnancy and autoimmune phenomena. The second is granulomatous hypophysitis, which may be associated with sarcoid or other granulomatous processes.

There is a significant differential diagnosis with regard to different forms of hypophysitis, and one must consider the possibility of sarcoid, tuberculosis, histiocytosis, fungal infection, abscess-bacterial or fungal, germinoma and other infiltrative neoplasms in the region, and the Tolosa-Hunt Syndrome. In some cases the imaging characteristics of hypophysitis are identical to those of hyperplasia of the pituitary (e.g. TSH hyperplasia secondary to hypothyroidism).

Diagnosis

Biochemical diagnosis

In most patients, hypophysitis presents with hypopituitarism, and therefore a thorough analysis of the pituitary hormone function and its response to stress is essential in the initial characterization of the disease. Diabetes insipidus, when present, should be documented by appropriate measurement of serum and urine osmolality and electrolytes.

With regard to the nuances of differential diagnosis, one must also consider measuring markers of other types of hypophysitis, which include ACE levels, the hematological profile including the differential count, the CBC, CRP and ESR.

Appropriate laboratory tests and cultures for infectious disease, particularly tuberculosis and fungus, need to be considered as well.
Pituitary imaging

The characteristic imaging features of hypophysitis include a homogeneous enlargement of the pituitary with a peak in the diaphragm giving it a pear-shaped appearance on the coronal images [9]. A typical feature is enlargement of the pituitary stalk with extension of the thickened stalk up toward the hypothalamus. In granulomatous hypophysitis in particular, there may be extension of the disease into the cavernous sinuses which can be detected on MRI studies. MRI with contrast and dedicated pituitary sequences is the best way of diagnosing the anatomic extent of the disease.

Secondary effects of disease

In hypophysitis, involvement of the pituitary stalk and hypothalamus often causes diabetes insipidus, which may be a presenting complaint. Involvement of the stalk may also produce secondary hypopituitarism which can also occur as a result of inflammatory destruction of the normal anterior pituitary gland itself. The process is normally destructive to both the pituitary gland the pituitary stalk, leading to the death of ADH secreting cells in the hypothalamus. For these reasons, patients rarely recover from the diabetes insipidus that is associated with hypophysitis, and often do not recover from the hypopituitarism.

A recognized feature of granulomatous hypophysitis is extension into the cavernous sinus that can produce vascular insufficiency and even occlusion of the cavernous segment of the internal carotid artery. This, of course, can lead to ischemia and stroke.

Treatment

Medical therapy

The diagnosis of hypophysitis can often be made presumptively because of the clinical setting, particularly in association with pregnancy or in the presence of autoimmune disease. If there is a clinical and imaging picture sufficient for the diagnosis of hypophysitis, then a preliminary period of medical management is desirable and is usually done with high dose corticosteroid medication [3]. Pituitary replacement for other pituitary hormones can also be instituted and diabetes insipidus should be treated effectively with dDAVP. Medical therapy in refractory cases may also include the judicious use of Methotrexate, which has been helpful in some difficult cases.

Surgical therapy

Many patients with mass effect and visual loss in association with the hypopituitarism and diabetes insipidus will present with significant and intractable headache [8]. Some of these are candidates for initial surgical therapy with the goal of removing as much of the sellar mass as possible. A definitive diagnosis can also be made on the basis of tissue obtained at surgery. Other indications for surgical management are lack of response to medical therapy or clinical and MRI relapse occurring after cessation of medical therapy. The outcome of surgical treatment is usually satisfactory, however, there have been some cases of relapse even after surgery, and these represent difficult management problems.

Radiotherapy/radiosurgery

Radiotherapy has been utilized in a limited number of patients with refractory hypophysitis. We have had satisfactory experience with these cases using Gamma Knife radiosurgery, and a low dose of radiation is often effective.

Treatment algorithms

It is difficult to generalize with regard to treatment algorithms for hypophysitis. The treatment sequence really depends upon the results of the diagnostic studies as well as upon the tissue diagnosis. Many patients who present with the classical picture of lymphocytic hypophysitis can successfully be treated with medication. If they do not respond to medical therapy, or if they develop a relapse in their clinical course, or if they have mass effect with visual loss, then surgery can be successful management. In other patients who present in an atypical fashion, some can also be treated medically, but often will require surgical management. In patients who represent failures of medical and surgical management, low dose radiosurgery or the use of Methotrexate can be considered.

Criteria for disease control

Control of disease in this category of pituitary pathology would include relief of symptoms, primarily headache and visual loss and the manifestations of inflammatory disease which include vascular compromise, and constrictive involvement of vessels and nerves in the cavernous sinus. As mentioned, hypopituitarism must be characterized and corrected, along with diabetes insipidus.

Follow-up

These patients, treated for one or another form of hypophysitis, require periodic imaging, which should be done at least once a year for the first three or four years and then periodically thereafter depending upon the course of the disease.
Obviously the clinical course must be carefully followed. Some patients require permanent pituitary replacement therapy, which should be carefully monitored using pituitary hormonal analysis every six months. Patients must also be monitored for recurrence or evolution of the disease process.

References