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Graduate Medical Education

Lymphocytic Hypophysitis

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Introduction

Lymphocytic hypophysitis, a rare pathology of the pituitary gland with incidence of 1 in 9 million, presents with features of hypopituitarism due to inflammation of the pituitary gland.[1,2] It is an autoimmune condition affecting women and men with a ratio of 8 to 1.[1.6] It consists of infiltration of the pituitary gland by T and B lymphocytes.[2] Endocrine symptoms include central diabetes insipidus, anterior pituitary hormone deficiencies, and hyperprolactinemia, or hyperprolactinemia.[4]

Etiology

Hypophysitis can be categorized based on etiology as primary or secondary and lymphocytic hypophysitis is the most common form of primary hypophysitis.[5] Lymphocytic hypophysitis can affect either the anterior pituitary gland, the posterior pituitary gland or both.[2] While primary hypophysitis describes pituitary gland inflammation itself, secondary hypophysitis describes pituitary gland inflammation due to diseases such as sarcoidosis, hemochromatosis, granulomatosis with polyangitis, tuberculosis, syphilis, and pituitary gland inflammation due to immune checkpoint inhibitors such as cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) and programmed death 1 (PD-1) medications.[5]

Histopathology

While histology provides a definitive diagnosis, it requires biopsy or resection of the sellar tissue, which poses a high risk and therefore is not a very practical approach.[4] The histological evaluation shows the infiltration of the adenohypophysis with T and B lymphocytes, plasma cells, and macrophages. If the pituitary tissue is destroyed due to the extensive degree of lymphocytic infiltration, it is replaced by fibrous tissue, and hypopituitarism occurs.[2]

Symptoms

Lymphocytic hypophysitis can cause central diabetes insipidus, adrenal insufficiency and hypothyroidism.[5,6] Other conditions include hypogonadotropic hypogonadism and growth hormone deficiency.[2] Enlargement of the pituitary gland can also compress the optic apparatus/chiasm and cause a decrease in vision and color perception.[4,7] Often times, headache is the first symptom and is usually followed by visual field defects and diplopia when the cavernous sinus, cranial nerves three, four and six are affected.[6]

Evaluation

Lymphocytic hypophysitis continues to be a diagnosis of exclusion and tissue biopsy is needed for a definitive diagnosis.[3] However, clinical, laboratory data, and imaging can all help with the diagnosis.[7] Patients must undergo all pituitary hormone evaluation. At times, antipituitary and antihypothalamus antibodies have also been found. Assessment for other autoimmune diseases should be performed.[2]

Gadolinium-enhanced MRI of the pituitary is important to distinguish lymphocytic hypophysitis from a pituitary adenoma. With a pituitary adenoma, MRI shows asymmetrical pituitary enlargement, with the pituitary stalk being deviated. In lymphocytic hypophysitis, the pituitary gland and the pituitary stalk is symmetrically enlarged, and there is no stalk deviation. MRI also shows a homogeneously intense pituitary with dura enhancement/dural tail along with arachnoid enhancement in lymphocytic hypophysitis.[4,6]

Management

Pituitary function needs to be assessed and any pituitary hormone deficiencies need to be managed.[2] Corticosteroid therapy with its anti-inflammatory response can also help patients regain pituitary function and decrease the need for lifelong replacement hormone therapy. Trials have been done with 20-500 mg of daily prednisolone for a duration of 4 days to a year.[9] For those that show no improvement with corticosteroids or have relapsed after treatment with corticosteroids, immunosuppressive medications such as methotrexate, azathioprine, and cyclosporine can be used.[8] Dopamine agonists have also been used in those with hyperprolactinemia due to pituitary inflammation.[4]

Surgery is only an option for those who have visual problems or a mass like effect from compression of nearby structures. Many patients are noted to have undergone surgery because a pituitary adenoma is suspected to be the cause of their symptoms. Surgery involves transsphenoidal or transcranial resection of the pituitary lesion and has a recurrence rate of the lesion and symptoms at 11-25%. Fractionated radiotherapy can be used if all other treatments fail.[6]

References

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