Sarcoidosis of the Hypothalamus and Pituitary

Key words: neurosarcoidosis, hypothalamus, pituitary, diabetes insipidus

Sarcoidosis is a granulomatous disease of unknown origin affecting multiple systems. Involvement of the central nervous system is a well-known manifestation of the disease occurring in approximately 5% of the cases (1). However, subclinical neurosarcoidosis and neuromuscular involvement is higher in pathological studies. The occurrence of neurosarcoidosis of the hypothalamus and pituitary is a rare complication. In the series reported by Chapelon et al, endocrine involvement was observed in a small number of patients within 35 patients with neurosarcoidosis (1). Central diabetes insipidus occurs in 25% of patients with neurosarcoidosis (2). In most of the cases, the disease occurs in the hypothalamus alone or in both the hypothalamus and pituitary, but rarely in the pituitary alone (3).

In this issue, Tabuena and colleagues report four cases of neurosarcoidosis affecting the hypothalamus and pituitary followed-up for more than 8 years (4).

All of them complained of polyuria and polydipsia due to central diabetes insipidus. Hypogonadism and hyperprolactinemia and in some cases panhypopituitarism were noted at endocrine evaluation. Most of them had pulmonary involvement and eye involvement. Most of the cases of neurosarcoidosis are associated with intrathoracic lesions (about 70%) (1). However, it must be emphasized that isolated neurosarcoidosis must be appropriately diagnosed in the early course of the disease because delay in appropriate treatment may result in a poor prognosis.

As the mortality associated with neurosarcoidosis is high, it is very important to diagnose it in early course of the disease. Differential diagnosis of central diabetes insipidus by sarcoidosis is a difficult problem. There are several diseases with similar clinical manifestations. These include infectious disease such as tuberculosis and syphilis, autoimmune hypophysitis, histiocytosis X, lymphoma, and germinoma.

In patients suspected of neurosarcoidosis, MRI imaging of the brain with Gd enhancement, cerebrospinal fluid examination including angiotensin-converting enzyme (ACE) and tumor markers, CSF cytology, and evaluation of other system involvement including the lung, eye, heart, and gastrointestinal systems are necessary. With neurosarcoidosis, brain MRI is most sensitive imaging procedure for detecting cerebral sarcoidosis and its response to steroid therapy (5). In some patients, the diagnosis is made only by biopsy of the granulomatous lesion. Evaluation of the endocrine systems and neurological systems should be done in patients with hypothalamic or pituitary involvement and be repeated in the follow-up period. Moderately elevated or high body temperature, polyuria, polydipsia, symptoms of hypogonadism such as decreased libido and amenorrhea, and hiccups are suggestive of hypothalamic involvement. General malaise, vague gastrointestinal symptoms such as nausea and decreased appetite are suggestive of adrenal insufficiency. Decreased pigmentation of the physiologically pigmented area in both sexes, loss of axillary hair and pubic hair in women are suggestive of central adrenal insufficiency. In these patients, increased eosinophil count, low serum sodium concentration, and low blood sugar are sometimes noted in laboratory tests. If the symptoms, signs, and laboratory data suspect hypothalamic involvement, hypothalamic-pituitary function should be evaluated thoroughly.

Although unpredictable, the long term prognosis of neurosarcoidosis is favorable if the management is timely and appropriate. In most cases corticosteroid remains the mainstream of treatment. In advanced disease with extensive intraparenchymal involvement and neurological deficit, the results of the treatment are poor (6). Various adjuvant immunosuppressants have been employed including cyclophosphamide, cyclosporine, azathioprine, methotrexate, chlorambucil and radiation therapy in cases with poor response to corticosteroid therapy or to minimize side effects of high dose corticosteroid therapy (6). Pulse cyclophosphamide therapy seems to have significant effects in adjuvant treatment of neurosarcoidosis (7).

The clinical course of sarcoidosis is variable. Some are monophasic, some are relapsing and remitting, and others are progressive. Potentially fatal organ involvement such as neurosarcoidosis and cardiac sarcoidosis cannot be predicted by the involvement of other organs. These indicate that patients with sarcoidosis should be evaluated and followed-up via a multidisciplinary approach with the assistance of doctors of various specialities including neurology, endocrinology, cardiology, respiratory disease, gastrointestinal disease, and ophthalmology.

Koji Takano, MD, PhD
University of Tokyo Faculty of Medicine,
Division of Nephrology and Endocrinology, Tokyo 113-8655
References