Partial Improvement of Anterior Pituitary Deficiency Following Steroid Treatment in a Patient with Neurosarcoidosis Accompanied by Central Diabetes Insipidus

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Abstract

A 58-year-old woman was admitted due to visual field abnormalities, thirst, polydipsia, polyuria and fever. T1-weighted magnetic resonance imaging revealed an absence of the usual bright signal in the posterior lobe of the pituitary gland, and an enlarged pituitary gland with a thickened stalk was enhanced by the gadolinium contrast medium. Computed tomography revealed tumor lesions in the left maxillary sinus and right retroperitoneum and axillary and subclavian lymph node swelling. An endocrinological provocation test demonstrated that her pituitary endocrine function was disturbed, although her ACTH and TSH secretion was normal. The patient was histologically diagnosed with neurosarcoidosis accompanied by hypopituitarism and central diabetes insipidus upon an examination of a subclavian lymph node specimen. Six months of prednisolone treatment resulted in the disappearance of any morphological abnormalities in the pituitary gland and stalk as well as a partial improvement in her LH, FSH and GH secretions. Pituitary endocrine functions can be rescued if steroid treatment is performed under conditions that maintain several hormonal axes.

Key words: neurosarcoidosis, diabetes insipidus, hypopituitarism, steroid

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Introduction

Sarcoidosis is a systemic inflammatory granulomatous disease with an undetermined etiology that affects the central nervous system in 5-15% of cases (1); the disease is termed neurosarcoidosis in these cases. Diabetes insipidus is one clinical manifestation of neurosarcoidosis in patients with involved pituitary lesions (2), and this presentation of the disease is generally not cured by steroid treatment (3). In contrast, whether glucocorticoid administration improves the endocrine dysfunction of the anterior pituitary gland in neurosarcoidosis is unclear. We herein report a case of neurosarcoidosis accompanied by central diabetes insipidus and anterior pituitary deficiency that was partially improved by steroid treatment.

Case Report

A 51-year-old Japanese woman was admitted to our hospital with low-grade fever, polyuria, and a bilateral external visual field defect. Four months prior to admission, she experienced extreme thirst and suffered from polyuria. A mild fever persisted for longer than one month, and she noted a narrowed visual field around the same time. Her body temperature was 37.1°C, and her daily urine volume was 4-6 L. An ophthalmoscopic examination did not find uveitis, although her external visual field had been lost bilaterally. A blood examination revealed that her C-reactive protein (CRP) level and erythrocyte sedimentation rate (ESR) were 1.73 mg/dL and 110 mm, respectively. A computed tomography (CT) scan demonstrated left axillary and subclavian lymph node swelling (10 mm and 15 mm, respectively;
Figure 1. A computed tomography (CT) scan of the chest and abdomen and magnetic resonance imaging (MRI) of the pituitary on admission. The CT scan revealed left axillary and subclavian lymph node swelling (10 mm and 15 mm, respectively) (A, B), left maxillary sinus tumor (C) and right ureteral dilatation (D). MRI revealed an enlarged pituitary gland (20×14×17 mm) and a thickened pituitary stalk that was accompanied by marked gadolinium enhancement (E).

Figure 2. Histology of the left subclavian lymph node biopsy (Hematoxylin and Eosin staining). Granulomatous lesions were widely interspersed throughout the lymph node specimen (A) (low-power magnification). An epitheloid cell granuloma with Langerhans-like giant cells (arrow) composed with lymphocytes, plasma cells and fibrocytes (B) (high-power magnification).

Fig. 1A, 1B) and a rounded homogenous tumor in the left maxillary sinus (Fig. 1C). This scan also found evidence for right hydronephrosis (Fig. 1D), which was the result of extrinsic pressure on the lower urinary duct from a right retroperitoneal tumor. T1-weighted magnetic resonance imaging revealed the absence of the usual bright signal at the posterior lobe of the pituitary gland and an enlarged pituitary gland (20×14×17 mm) with a thickened stalk (Fig. 1E).
angiotensin-converting enzyme, lysozyme and 1,25-dihydroxyvitamin D3 were not elevated.

Next, we investigated the endocrine insufficiency of the patient. The anti-diuretic hormone level was relatively low, and there was an elevated osmotic level (0.9 pg/mL and 294 mosm/kg, respectively). The basal levels of LH, FSH and E2 were low, regardless of the postmenopausal state of the patient (<0.1 mIU/mL, 2.4 mIU/mL and 15 pg/mL, respectively). The decreased IGF-1 concentration (74 ng/mL) suggested a latent GH deficiency. Each endocrine provocation test for GnRH, CRH, TRH and GHRP-2 found that these pituitary endocrine functions were disturbed, although ACTH and TSH secretion were normal (Fig. 3A; basal and peak levels, respectively: ACTH, 45 pg/mL and 756 pg/mL; cortisol, 7 μg/mL and 17 μg/mL; TSH, 4.45 μU/mL and 39.5 μU/mL; PRL, 92.5 ng/mL and 101.7 ng/mL). A diagnosis of neurosarcoidosis accompanied by hypopituitarism and central diabetes insipidus was made on the basis of these endocrine results. Immunoglobulin (Ig) G4-related systemic disease was thought to be unlikely due to the absence of increased IgG4 levels or eosinophilic infiltration in the biopsy specimens of the subclavian lymph nodes.

This patient was treated with prednisolone (50 mg/day) for neurosarcoidosis. Nasal administration of DDAVP (7.5 μg/day) was required to improve the polyuria because the prednisolone aggravated the latent diabetes insipidus. The MRI and CT scans revealed that six months of steroid treatment had shrunk the enlarged pituitary gland, the thickened pituitary stalk (Fig. 4), the left axillary and subclavian lymph nodes. Biopsy specimens of the subclavian lymph nodes.

The MRI and CT scans revealed that six months of steroid treatment had shrunk the enlarged pituitary gland, the thickened pituitary stalk (Fig. 4), the left axillary and subclavian lymph nodes. Biopsy specimens of the subclavian lymph nodes.
shown). In addition, the basal IGF-1 levels were increased (144 ng/mL) and PRL levels were decreased to within the upper limit of the normal range (21.1 ng/mL). An endocrine provocation test following the steroid treatment revealed that the peak levels of LH and FSH after GnRH, GH and GHRP-2 loading were increased compared to the pre-treatment levels (26.5 mIU/mL, 28.5 mIU/mL and 10.6 ng/mL, respectively; Fig. 2B). In contrast, the posterior lobe did not appear in the T1-weighted MRI, and the diabetes insipidus was not healed.

Discussion

The present patient had diabetes insipidus accompanied by a thickened pituitary stalk and multiple tumors, including a right retroperitoneal lesion. The clinical findings of multiple tumor lesions and lymph node swellings were against the diagnosis of adenohypophysitis or infundibulo-neurohypophysitis. The possibility of IgG4-related disease was excluded (4), because elevated serum IgG4 levels or IgG4-positive plasma cells in the lymph node specimens from this patient were not observed.

Sarcoidosis is a systemic inflammatory granulomatous disease that affects the central nervous system (CNS) in 5-15% of cases (1). These cases are called neurosarcoidosis, which are not always accompanied with bilateral hilar lymphadenopathy or uveitis (5). A definitive diagnosis of neurosarcoidosis requires the confirmation of histological involvement in a CNS lesion. In this case, a histological diagnosis of neurosarcoidosis would have been nearly impossible, because it was very difficult to safely collect specimens from suprasellar lesions. Some previous cases also were diagnosed as neurosarcoidosis by clinical manifestations such as diabetes insipidus or image findings of central nervous lesion without confirmation by histologic studies (6). Thus, according to the criteria for “probable neurosarcoidosis” (7), a diagnosis was made for the presence of systemic sarcoidosis, which was confirmed by multiple tumor lesions and the histological findings from the left subclavian lymph node specimens.

The present patient demonstrated the endocrine dysfunction of LH, FSH, and GH secretion in addition to diabetes insipidus. Diabetes insipidus is a well-known comorbid endocrine disorder that is a result of hypothalamic involvement during sarcoidosis (2, 8); it occurs in 17-25% of patients with neurosarcoidosis (9). In contrast, the incidence of endocrine dysfunction in the anterior pituitary is rare disorder compared to that in the posterior pituitary (2). The base of the brain is a common location for infiltration of neurosarcoidosis (10). The distance from the base of the brain to the sella turcica is greater than that to the hypothalamus or the pituitary stalk, thus the sarcoidosis lesion may not yet completely invade the anterior pituitary region in the early stage of neurosarcoidosis. Therefore, the secretion disorders of the anterior pituitary hormone may occur less frequent and be more salvageable by steroid therapy than those of the posterior pituitary hormone. Considering the MRI findings of the remarkable enhancement of pituitary stalk in the present case, it appears reasonable that the upper region of the pituitary stalk was the prime sarcoidosis lesion, which then infiltrated into the pituitary gland. This diagnosis was compatible with the changes of PRL levels accompanied with the shape of pituitary stalk before and after steroid treatment, because thickened -upper lesion of the pituitary stalk could stem a delivery of PRL inhibitory factors from hypothalamus to the pituitary gland and thereby result in secondary hyperprolactinemia.

A notable finding of the present case report was that impaired anterior pituitary hormone secretion was partially restored after steroid treatment. There have been few case reports that diabetes insipidus could be cured in this situation, except for one spontaneous remission case (11). It has been considered that anterior pituitary function is difficult to restore, because hypopituitarism is not improved although the thickened pituitary stalk and enlarged pituitary gland return to their normal shapes after steroid treatment (3, 12). However, a few case reports have shown that steroid therapy is able to partially improve anterior pituitary hormone secretion, which was confirmed by an endocrine provocation test (12-14). In all of these cases, endocrine axes were partially present prior to steroid therapy. In this case, the provocation test revealed the potential for ACTH and TSH secretion. This finding suggested that anterior pituitary function may not have been completely abolished by sarcoidosis invasion, and steroid therapy may partly rescue the function of GH and LH/FSH secretion under these conditions.

In conclusion, we have presented a case of partially improved anterior pituitary deficiency that was treated with steroids in a patient with neurosarcoidosis accompanied by central diabetes insipidus. In general, the endocrine functions of patients with neurosarcoidosis rarely recover after therapy even though the morphological abnormalities of the pituitary gland and stalk have disappeared. However, the present case suggests that the pituitary endocrine system can be rescued if steroid treatment is given to patients whose hormonal axes were partially preserved.

The authors state that they have no Conflict of Interest (COI).

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