Case Report

Vasopressin Cell Antibodies and Central Diabetes Insipidus in a Patient with Systemic Lupus Erythematosus and Dermatomyositis

HIROSHI KAJIYAMA, CHIHIRO TERAI, ANNAMARIA DE BELLIS, ANTONIO BIZZARRO, ANTONIO BELLASTELLA, SHUJI OHTA, HIROSHI OKAMOTO, MASASHI UESATO, MASAKO HARA, and NAOYUKI KAMATANI

ABSTRACT. We describe a 39-year-old woman who presented central diabetes insipidus (CDI), during active systemic lupus erythematosus (SLE) concomitant with dermatomyositis. CDI is rarely reported in association with SLE and has never been reported with dermatomyositis. After treatment with intravenous cyclophosphamide (IV CYC) with concurrent oral prednisolone, CDI improved and vasopressin replacement therapy was completely withdrawn. Serum autoantibodies to vasopressin cell (AVPcAb), detected at diagnosis before immunosuppressive treatment, disappeared in 2 months. To our knowledge, this is the first case of CDI in SLE overlapping with dermatomyositis. Interestingly, it was characterized by the presence of AVPcAb before the treatment and by their disappearance after IV CYC and steroid therapy with restoration of normal postpituitary function. (J Rheumatol 2004;31:1218–21)

Key Indexing Terms:
CENTRAL DIABETES INSIPIDUS SYSTEMIC LUPUS ERYTHEMATOSUS
VASOPRESSIN CELL ANTIBODIES

Central diabetes insipidus (CDI) is a rare disease caused by impaired synthesis and/or excretion of arginine-vasopressin (AVP), which is produced by supraoptic and paraventricular nuclei in the hypothalamus. The etiology of CDI is varied and includes familial forms, tumors, cerebrovascular diseases, surgery, trauma, inflammatory diseases, and autoimmune processes[1-6]. CDI is rarely reported in association with systemic lupus erythematosus (SLE), and has never been reported with dermatomyositis. We describe a rare case of SLE overlapping with dermatomyositis associated with CDI. The presence of serum vasopressin cell antibodies (AVPcAb) at diagnosis and their disappearance after treatment with intravenous cyclophosphamide (IV CYC) and steroid therapy suggest an autoimmune variant of CDI in this case.

From the Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan; and the Department of Clinical and Experimental Medicine and Surgery, Second University of Naples, Naples, Italy.

H. Kajiyama, MD, PhD, Research Associate; C. Terai, MD, PhD, Associate Professor; S. Ohta, MD, Research Associate; H. Okamoto, MD, PhD, Research Associate; M. Uesato, MD, Research Associate; M. Hara, MD, PhD, Professor; N. Kamatani, MD, PhD, Director and Professor, Institute of Rheumatology, Tokyo Women's Medical University; A. De Bellis, MD; A. Bizzarro, MD, PhD; A. Bellastella, MD, PhD, Chair of Endocrinology, Department of Clinical and Experimental Medicine and Surgery, Second University of Naples.

Address reprint requests to Dr. H. Kajiyama, Institute of Rheumatology, Tokyo Women's Medical University, Kawada-cho 10-22, Shinjuku-ku, Tokyo 162-0054, Japan.

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CASE REPORT

A 39-year-old Japanese woman presented with pain, redness, and swelling in her right wrist in April 1999. Laboratory investigations revealed positive antinuclear antibodies at a titer of 1:80, anti-DNA antibody 24.5 IU/ml (normal ≤ 6 IU/ml), and a biological false positive VDRL. The diagnosis of SLE was based on the appearance of butterfly rash, palmar erythema, and polyarthritis. Prednisolone therapy at 10 mg/day was started in January 2000 and maintained. She was hospitalized in July 2000 because of general fatigue, an oral ulcer, heliotrope erythema of eyelids, and an edematous face. Bronchiolitis obliterans with organizing pneumonia in the right upper lobe and pancreatitis were evident; myositis of the bilateral thighs was seen on magnetic resonance images (MRI) and mild nephritis was also revealed. A diagnosis of SLE concomitant with dermatomyositis was made, and high dose corticosteroid therapy was started (methylprednisolone pulse therapy 500 mg/day for 3 days followed by oral prednisolone at 50 mg/day). Pancreatitis, nephritis, myositis, and bronchiolitis obliterans with organizing pneumonia had improved a month after initiation of treatment, whereas 2 weeks after steroid pulse therapy, she had presented with polyuria (8 to 10 l/day), polydipsia, and hyposthenuria (Figure 1). On the 25th hospital day, CDI was diagnosed following a 5% NaCl loading test, in which a scant secretion of AVP and hypotonic urine were observed (Figure 2). The presence of nocturia without psychogenic polydipsia also supported the diagnosis of CDI. AVP replacement therapy was started at a dosage of 40 U/day. Brain MRI performed before treatment showed inflammatory lesions in the left claustrum, right parahypocampal area, and right putamen; there were no findings of any alteration in the hypothalamic pituitary system (Figure 3). In particular, a hyperintense MRI signal of the posterior pituitary was present, indicating the existence of vesicles including AVP

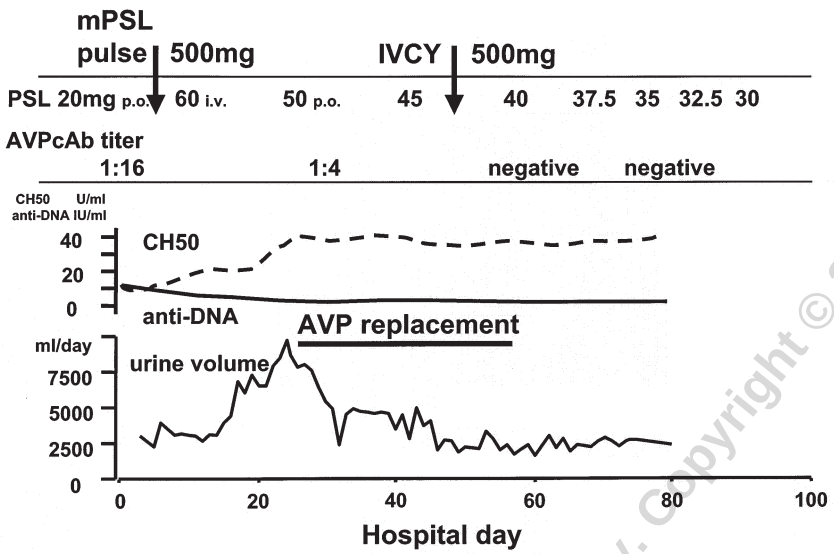

Figure 1. Clinical course. Changes of AVPcAb titer are presented. mPSL: methylprednisolone; IVCY: intravenous cyclophosphamide.

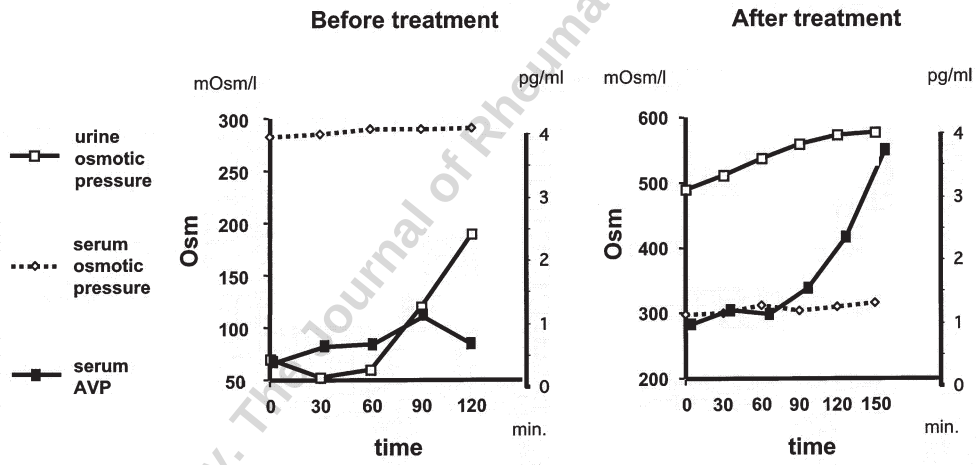

Figure 2. 5% NaCl loading test. Left panel: hyposthenuria and a scant excretion of AVP under the osmotic stimuli. Right panel: both are improved after treatment.

(Figure 3) and excluding the presence of tumors, cerebrovascular diseases, and lymphocytic infundibuloneurohypophysitis[5,6]. Moreover, anterior pituitary function was normal and urinary levels of N-acetyl glucosaminidase and ß$_2$-microglobulin were within normal limits. Laboratory data showed normal glucose tolerance. IV CYC treatment was added for the central nervous system (CNS) involvement, the polyuria improved gradually, and AVP replacement was completely withdrawn within 4 weeks. AVP excretion under osmotic stimuli and hyposthenuria had improved by the 74th hospital day (Figure 2). To date, no recurrence of CDI or any other symptoms of SLE have been observed.

Serum samples collected from this patient before the appearance of CDI and after IV CYC therapy, sera from patients with untreated active and treated inactive SLE without CDI, and sera from normal controls were tested for AVPcAb.

AVPcAb were detected by an immunofluorescence method as described[6-8]. Briefly, unfixed cryostat sections of young normal baboon hypothalamus were incubated with undiluted serum samples, which were preincubated with rat liver acetone powder to exclude nonspecific binding. Fluorescein isothiocyanate-conjugated goat anti-human IgG sera were used to detect antibodies to hypothalamic cells. In positive samples, the specificity of the reaction to vasopressin cells was shown with a 4-layer double fluorochrome immunofluorescence test in which the second sandwich consisted of rabbit anti-AVP serum reacting with rhodamine-labeled goat anti-rabbit immunoglobulins. Levels of AVPcAb were expressed as endpoint dilution titer.

The patient's serum was positive for AVPcAb at a 1:16 titer, which decreased to 1:4 one month after methylprednisolone pulse therapy and disappeared after 2 months (Figure 1). AVPcAb were negative in all 5 controls and in all 6 patients with inactive SLE; however, they were positive at a titer of 1:8 in one out of the 6 patients with active SLE without CDI. Since this patient also showed the presence of anti-SSA antibodies, a possible cross-reaction between AVPcAb and SSA was excluded using a rat liver acetone powder preincubation. Our case with CDI showed no anti-SSA antibodies in the clinical course.

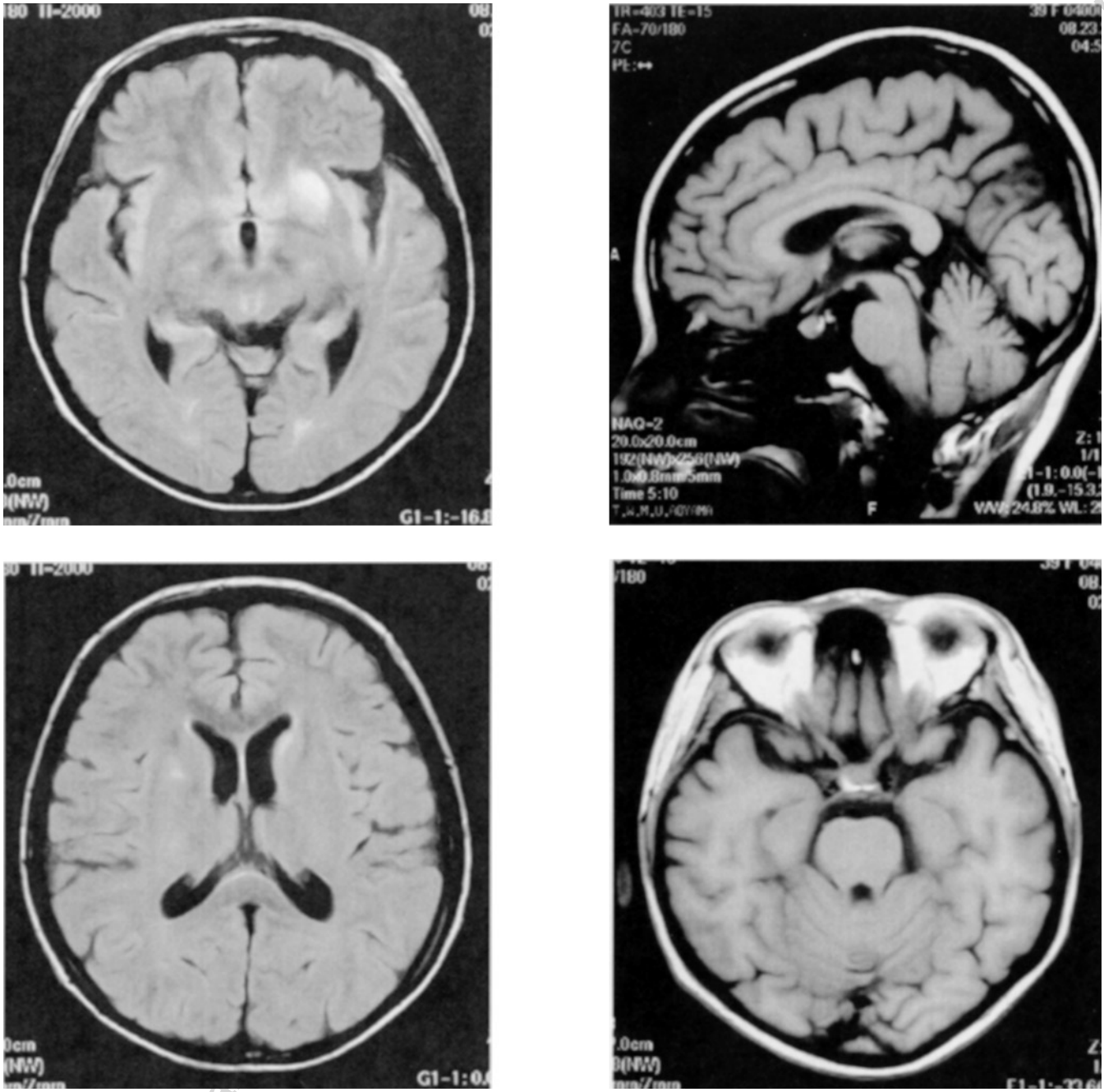

Figure 3. MRI of the brain. Left panel: fluid attenuated inversion recovery imaging of MRI showing CNS lesions of lupus. Right panel: T1 image showing the intact bright signal in the neurohypophysis.

DISCUSSION

AVPcAb have been detected in patients with CDI associated with autoimmune diseases[7] and also in patients with idiopathic CDI without autoimmune diseases[6,7]. Although to date a pathogenic role for AVPcAb in autoimmune CDI has not been recognized, these antibodies can be considered as good markers of an autoimmune process involving the hypothalamus, pituitary stalk, and neurohypophyseal tract[6,7]. Although SLE is a typical autoimmune disease with frequent CNS involvement, CDI is an extremely rare complication in SLE. Indeed, only 3 SLE cases associated with CDI have been reported[9,10].

In this report, we first observed the presence of CDI with the finding of serum AVPcAb in a patient with SLE over-

lapping with dermatomyositis. CDI was diagnosed based on the results of 5% NaCl loading test and presence of nocturia without psychogenic polydipsia. It was not likely that pulsed steroid therapy caused CDI by thrombosis, since anterior pituitary function was normal. Interestingly, the disappearance of AVPcAb and restoration of normal post-pituitary function after IV CYC and steroid therapy suggest that induction of remission of autoimmune CDI is possible when a residual amount of AVP granules are still present at the onset of the disease.

Another important observation is that AVPcAb were found (titer 1:8) in one of 6 patients with active SLE without CDI, but in none of the patients with inactive SLE nor in the normal controls. It has been recently reported that AVPcAb could be a good marker for CDI in patients with endocrine autoimmune diseases without CDI[11]; in particular, during 5 years of followup, 4 AVPcAb-positive patients with normal posterior pituitary function developed partial or complete CDI. Our results suggest that AVPcAb can be detected not only in patients with active SLE and CDI, but also in those without CDI. Since AVPcAb-positive patients with active SLE are usually treated with aggressive immunosuppressive therapy, the possible development of clinical CDI could be avoided by the treatment interrupting autoimmune mechanisms leading to the clinical disease.

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