Case report

A case of neuronal intranuclear inclusion disease associated with lupus nephritis-like nephropathy

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ABSTRACT

Neuronal intranuclear inclusion disease (NIID) is a relatively new entity identified as a progressive neurodegenerative disease characterised by eosinophilic hyaline intranuclear inclusions widely observed in neuronal and somatic cells. Renal biopsy from one of our patients with NIID showed lupus nephritis-like pathology. He was treated with steroids and angiotensin-converting enzyme inhibitors and his proteinuria improved. The present case highlights that immune-mediated glomerulonephritis can be a presenting feature of NIID, which can be controlled with proper treatment.

1. Introduction

Neuronal intranuclear inclusion disease (NIID) is a rare neurodegenerative disorder characterised pathologically by presence of eosinophilic intranuclear inclusions in neuronal and glial cells [1]. In recent years, it has been found that skin biopsy also reveals intranuclear inclusions in somatic cells [2], and consequently, the number of case reports has increased. However, in most case reports, only neurologic and psychiatric symptoms are described and there is no statement regarding physical symptoms.

2. Case report

A 63-year-old man presented with dementia. Two years before admission, dizziness occurred and proteinuria was confirmed. Two months before admission, pollakisuria and urinary incontinence occurred and his movement slowed down. Neurologic examination revealed dementia and wide-based gait, and he was admitted to our hospital for further examination. Physical examination revealed blood pressure of 122/88 mmHg and body temperature of 36.7 °C. His cranial nerve functions were intact. Manual muscle testing showed normal results, though hyporeflexia and hypopallesthesia were present in both upper and lower limbs. Laboratory data revealed normal ranges for complete blood count, liver and renal functions. Urinary protein excretion was 4396.6 mg/gCr. Results of serologic testing, including antinuclear antibody, anti- ds-DNA antibody, anti-ss-DNA antibody, anti-Sm antibody, anti-RNP antibody, MPO-ANCA, PR3-ANCA, anti-SS-A antibody, and anti-SS-B antibody, were all negative. The patient's Mini-Mental State Examination score was 29. Brain magnetic resonance imaging (MRI) revealed moderate cerebral and cerebellar atrophy, dilatation of the lateral ventricle, and high-intensity areas in cerebral white matter on T2-weighted imaging (Fig. 1A) and high signal intensity in the corticomedullary junction on diffusion-weighted imaging (Fig. 1B). Cerebrospinal fluid examination revealed no pleocytosis or protein elevation and normal glucose level. Nerve conduction studies showed normal results. Skin biopsy revealed intranuclear inclusions in adipocytes (Fig. 2), compatible with NIID. Renal biopsy was performed, which revealed mild mesangial proliferative glomerulonephritis (Fig. 3A, B). Immunofluorescence microscopy revealed granular staining of mesangial lesions for IgG, IgM, C3, and C1q, and no detectable staining for IgA and C4 (Fig. 3C). Electron microscopy detected electron-dense deposits in paramesangial lesions (Fig. 3D). Based on these findings, we considered that he had mesangial proliferative glomerulonephritis-like lupus nephritis. After renal biopsy, oral prednisolone 20 mg daily was started and his proteinuria improved to incomplete remission level. One year after discharge, he was found to have no remarkable changes and prednisolone was tapered to 10 mg daily. Unfortunately, the patient's dementia and incomplete remission level of proteinuria continued.

3. Discussion

NIID is considered to be a heterogeneous disease with highly variable clinical manifestations, including neuropathy, cerebellar ataxia, and dementia [3]. Previous investigators proposed that NIID can be categorised into 3 subgroups: infantile, juvenile, and adult [1]. In adult-
onset NIID, most cases are diagnosed at 60 to 70 years of age [4].

Since it was first reported in 1980 [5], NIID has been a pathologic entity usually diagnosed by postmortem histologic examination and considered to be an extremely rare disease because only 30 cases were reported until the 2000s [4]. However, nuclear inclusions in visceral organs also have been reported [1]. Recently, skin biopsy has been reported to be useful for antemortem diagnosis of NIID because of nuclear inclusions in adipocytes, fibroblasts, and sweat gland cells in cutaneous tissue [2,3]. Consequently, the number of case reports of NIID diagnosed by characteristic findings on MRI and skin biopsy are increasing.

While there are many detailed reports on the neurologic and psychiatric symptoms of NIID, descriptions of organ disorders are hardly recognised in previous reports. Renal biopsy confirmed that our case had lupus nephritis–like glomerulopathy. However, the typical findings suggesting systemic lupus erythematosus (SLE), such as antinuclear antibodies, were not observed. Thus, this glomerular lesion was considered to be associated with NIID. As described above, whether NIID causes organ disorders is not clear from the previous literature. In the future, according to accumulation of NIID cases, accumulation of knowledge on organ disorders, as in our case, is desired.

Previous investigators described ‘antinuclear antibody–negative lupus nephritis’, which is characterised as having renal-limited or renal and extra-renal manifestations of SLE with negative serologies and may present as full-house nephropathy on renal biopsy with immunofluorescence, compatible with lupus nephropathy [6]. It also has been reported that in clinical practice, absence of antibodies does not rule out SLE, as up to 5% of patients with SLE may be seronegative, and diagnosis is made by clinical and pathologic presentation alone [7]. Previous investigators speculated that as a cause by which antinuclear antibody–negative lupus nephritis occurs, antibodies may be absent due to urinary losses in severe nephrotic syndrome [8]. However, this entity is still unclear and further examination is required. Clinicians should pay attention to evaluation of the physical symptoms of NIID and subsequent follow-up.

Disclosure statement

The authors have declared no conflicts of interest.
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