Case Report

Neuromyelitis Optica with Hypothalamic Involvement: A Case Report

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Current diagnostic criteria of neuromyelitis optica (NMO) includes presence of acute optic neuritis (ON) and myelitis with at least two of the three supportive criteria, which consist of spinal cord magnetic resonance image (MRI) lesion extending over 3 vertebral segments, brain MRI lesion, which does not meet the diagnostic criteria for multiple sclerosis, and NMO-IgG seropositive status. A 34 year-old woman presented with two episodes of acute demyelinating processes in the central nervous system within three years. Firstly, she presented with a 2-week history of neck pain, oscillopsia, vertigo, and weakness. MRI of the brain revealed a high signal change at cervicomedullary junction. She responded to a short course of high-dose corticosteroid. One year after the first presentation, she developed bilateral optic neuritis. High dose corticosteroid therapy was prescribed for this attack. After the second episode, she received long-term azathioprine. Two weeks before admission, she developed hypersomnia and confabulation. General physical examination was unremarkable. Neurological examination revealed visual acuity (VA) of 20/200 in both eyes. Optic fundi were normal. MRI of the brain demonstrated hypersignal intensity lesions at the hypothalamus, tuber cinereum, medial aspect of thalami, dorsal midbrain, and occipital periventricular white matter in T2 weighted and FLAIR images. Cerebrospinal fluid (CSF) analysis revealed a white blood cell count of 33 cells/mm^3 (100% lymphocytes), protein of 34 mg/dL, CSF sugar of 55 mg/dL, and blood sugar of 100 mg/dL. Oligoclonal band was negative. Two weeks after admission, she developed quadriparesis, pain, and proprioceptive sensory loss below the 6th thoracic level. She also had urinary retention and constipation. MRI of the whole spinal cord showed multi-level hypersignal intensity lesions on T2 weighted and FLAIR images involving medulla, cervicomedullary junction and all segments of the spinal cord. She was diagnosed as NMO. Hypothalamic and brainstem involvement demonstrated in this patient were uncommon but rather pathognomonic for NMO. The authors proposed that the involvement of hypothalamus and brainstem be included in the criteria for diagnosis of NMO.

Keywords: *Neuromyelitis optica, Hypersomnia, Confabulation, Hypothalamic, Brain stem*

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Clinical presentation in NMO may be similar to opticospinal form of multiple sclerosis (OSMS) that commonly occurs in Asian populations especially in Japan[1]. Early and accurate diagnosis of NMO is important because its clinical course, prognosis and response to intervention are different from classical MS. Various cardinal features which can be used to differentiate NMO from classical MS include clinical presentations, MRI of the brain and spinal cord, CSF profiles[2,3]. Recently, immunopathologic characteristic of NMO *i.e.* highly specific serum antibody NMO-IgG/aquaporin-4-water-channel specific antibody has been discovered[4-7]. The current diagnostic criteria for NMO proposed by Wingerchuck includes presence of acute optic neuritis and myelitis with at least two of the three supportive criteria, which consist of spinal cord magnetic resonance image (MRI) lesion extending over three vertebral segments, brain MRI lesions, which do not meet the diagnostic criteria for multiple sclerosis, and NMO-IgG seropositive status[2].

Hypothalamic involvement is rare but rather pathognomonic feature of NMO. Moreover, MRI abnormalities in the hypothalamic area are correlated with highly expressed Aquaporin-4 (AQP4) antibody in these regions of the brain[8,9]. The authors presented a case of NMO with hypothalamic involvement characterized by insomnia and confabulation during an attack of NMO.

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Case Report

Four years ago, a 34-year-old Thai woman firstly presented with a 2-week history of neck pain, oscillopsia, vertigo, and weakness. Physical examination revealed bilateral vertical nystagmus and mild spastic quadriparesis. MRI of the brain depicted a high signal change at cervicomedullary junction. She responded to a short course of high-dose methylprednisolone and had a full neurological recovery within five months.

One year after the first presentation, she developed blurred vision in both eyes. Physical examination revealed a visual acuity (VA) of 20/70 in right eye and 20/100 in left eye. Optic fundi were normal. She still had vertical nystagmus. Visual evoked potential (VEP) study showed demyelinating process in both eyes. Blood tests, including erythrocyte sedimentation rate (ESR) and antinuclear antibody (ANA) were within normal limit. Cerebrospinal fluid (CSF) examination revealed normal cell counts and biochemistry. Oligoclonal band was absent. MRI of the brain revealed non-enhancing high signal lesions at dorsal midbrain, pulvinar of thalami, medial aspect of thalami, massa intermedia, optic chiasm and both optic tracts in T2 weighted and FLAIR sequences. Disappearance of a previous lesion at the cervicomedullary junction was documented. The provisional diagnoses of recurrent MS were made. She responded to a short course of high-dose methylprednisolone and VA became 20/30 in both eyes within 5 months. Long-term azathioprine 100 mg/day had been prescribed.

Two years after the first presentation, she presented with memory impairment, confabulation, hypersomnolence and blurred vision in both eyes for two weeks before admission. General observations disclosed a poor attention woman who fell asleep easily even during the conversation. She had excessive daytime sleepiness and prolonged nighttime sleep. General physical examination was unremarkable. Neurological examination revealed a conscious woman with good orientation to time, place, and person. Thai minimental status examination (TMSE) score was 28/30 (impaired recent memory and calculation). VA of 20/200 was detected in both eyes and optic fundi were normal. MRI of the brain demonstrated hypersignal intensity lesions at the hypothalamus, tuber cinereum, medial aspect of thalami, dorsal midbrain and occipital periventricular white matter changes bilaterally in T2 weighted and FLAIR images (Fig. 1, 2). Blood tests, including ESR, ANA, anti-double strand DNA, lupus anticoagulant, anticardiolipin IgG, IgM were within normal limit. Antibody tests (anti-SS-A and anti-SS-B) were negative. CSF analysis revealed white blood cell count of 33 cells/mm^3 (100% lymphocytes), protein of 34 mg/dL, CSF sugar of 55 mg/dL and blood sugar of 100 mg/dL. Oligoclonal band was again reported negative. VEP revealed demyelination and axonopathy of right visual pathway and demyelination of left visual pathway. A course of pulse methylprednisolone was repeated with no improvement.

Two weeks after this admission, she developed quadriparesis, pain, and proprioceptive sensory loss below the 6^{th} thoracic level as well as urinary retention and constipation. MRI showed multi-level hypersignal intensity lesions on T2 weighted and FLAIR images involving medulla, cervicomedullary junction and all segments of the spinal cord. Central gray matter of the spinal cord was predominantly involved (Fig. 3). The presented patient was then diagnosed as NMO according to Wingerchuck's criteria. Plasmapheresis was prescribed due to severe neurological deficits, progressive course,

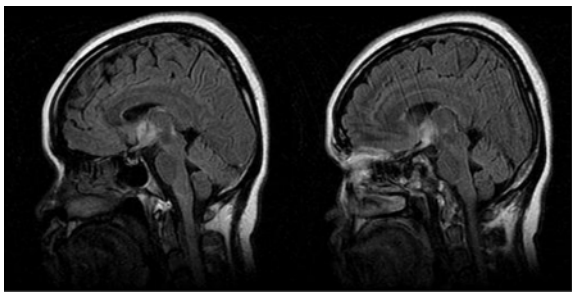

Fig. 1 MRI demonstrated hypersignal intensity lesions at hypothalamus T2 weighted and FLAIR images

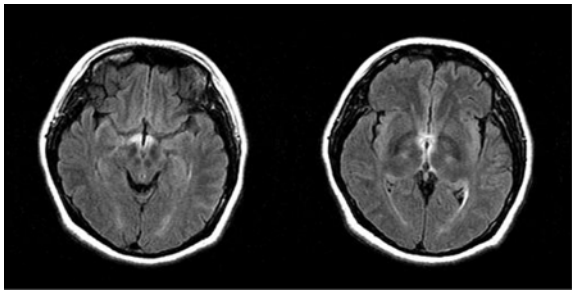

Fig. 2 MRI demonstrated hypersignal intensity lesions at hypothalamus, tuber cinereum, medial aspect of both thalami, bilaterally in T2 weighted and FLAIR images

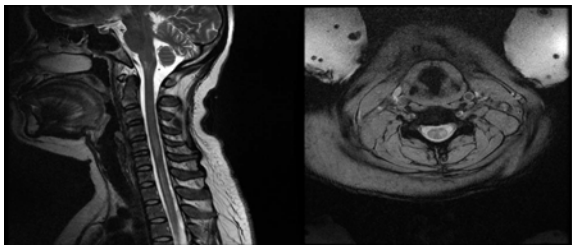

Fig. 3 T2 weighted and FLAIR images hypersignal intensity lesions involving medulla, cervicomedullary junction. Axial images demonstrated involving central gray lesions

and corticosteroid non-responsive. After two months, urinary retention and constipation were partially improved but quadriparesis was persisted. One year after the last attack, she expired from severe sepsis.

Discussion

This patient presented with recurrent optic neuritis and myelitis. Her MRI of the spinal cord showed extensive longitudinal lesions extended more than three vertebral segments and MRI of the brain did not meet the criteria for diagnosis of classical MS. She fulfilled a diagnostic criterion for NMO[2]. She had a rather benign course at the beginning but the overall natural history finally turned to be progressive severe and fatal.

NMO was originally considered to be a monophasic syndrome consisting of acute, severe myelitis and bilateral optic neuritis occurring within one month. Subsequent and recent studies discovered a wider spectrum of NMO, which included patients with less severe clinical attacks, unilateral ON, symptoms separated by weeks or years, or recurrent exacerbations. Characteristics associated with a relapsing course include female sex, older age at onset, longer time interval between index events, and presence of systemic autoimmunity (*e.g.* positive anti-DNA antibodies, systemic lupus erythematosus, Sjogren syndrome and autoimmune thyroiditis). Patients who had a relapsing course usually had clusters of severe relapses of either optic nerves or spinal cord within three years. Most relapsing patients developed severe disability in a stepwise manner. The present case followed this pattern of this type of clinical course. In contrast, characteristic features of monophasic disease include rapidly sequential index events (bilateral ON and myelitis occurring within 1 month) and followed by a moderate degree of recovery[3,10].

Patients with NMO have a specific autoantibody that differentiate them from patients with typical forms of relapsing-remitting MS[4-7]. Serum autoantibody marker, NMO-IgG, demonstrated a 73% sensitive and 90% specific for discrimination of OSMS and NMO[2]. The target antigen for NMO-IgG is the water channel aquaporin-4. AQP4 is predominant water channel in the brain and plays an important role in brain water homeostasis. AQP4 is abundantly detected in 1) optic nerve, 2) brain (hypothalamic, midbrain, periventricular regions), and 3) spinal gray matters demonstrated by immunohistochemical studies. This AQP4 highly expressed regions in the brain are the common target for demyelination in NMO and correspond with regions of abnormal MRI affected by NMO[8].

NMO with hypothalamic involvement is occasionally reported in the literature. The clinical features included somnolence, hypothermia, and endocrinopathies[8,11,12]. However, some patients may be asymptomatic[9]. MRI usually demonstrates hypersignal intensity at hypothalamus and optic chiasma in FLAIR and T2 weighted sequences. In the presented patient, hypothalamic involvement was asymptomatic in the second attack and became symptomatic in the third attack. Her symptoms characterized by recent memory impairment, confabulation, and hypersomnolence. MRI in the presented case was similar to the previous reported cases[11]. NMO with hypothalamic involvement is rare but be pathognomonic diagnosis for the diagnosis of NMO. Since AQP4 highly expressed regions corresponded with regions of abnormal MRI affected by NMO, it may be considered as a surrogate disease marker where NMO-IgG autoantibodies are not available[8,9].

In NMO, acute spinal cord MRI lesions usually occupied more than three vertebral segments and entire spinal cords involvement may be encountered. Most lesions were located predominantly in the central gray matter and corresponded to abundant AQP4 located in the spinal gray matters[13]. In the present case, gray matter involvement occupied nearly the whole spinal cord and compatible with previous reported cases.

Treatments of NMO are based on evidence from case series studies[2,14]. First-line therapy for acute attacks is intravenous methylprednisolone for five days. Plasmapheresis should be considered when clinical syndrome progress or severe syndrome fails to improve in spite of corticosteroid infusion[14]. The present case had a mild attack in the early clinical course, which responded to methylprednisolone,

but progressive severe terminal attacks resisted this treatment. Even plasmapheresis was not helpful.

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โรคนิวโรมัยอิลัยติสออบติกาที่มีรอยโรคที่ต่อมใต้สมองร่วมด้วย

กุสุมา สามารถ, กัมมันต์ พันธุมจินดา

นิวโรมัยอิลัยติสออบติกา (เอ็นเอ็มโอ) เป็นโรคที่เกิดจากการอักเสบและมีอาการเสื่อมของปลอกหุ้มมัยอิลินของเส้นประสาทตาคู่ที่ 2 และ ไขสันหลัง ปัจจุบันการวินิจฉัยโรคนี้ต้องประกอบด้วยการอักเสบของเส้นประสาทตาคู่ที่ 2 ร่วมกับการมีรอยโรคที่ไขสันหลังซึ่งตรวจพบโดยการตรวจคลื่นแม่เหล็กไฟฟ้า โดยที่รอยโรคต้องมีความยาวมากกว่า หรือ เท่ากับความยาวของกระดูกไขสันหลังอย่างน้อย 3 ข้อ ติดต่อกันขึ้นไป อีกทั้งการตรวจคลื่นแม่เหล็กไฟฟ้าที่สมองไม่เข้ากับรอยโรคของมัลติเปิ้ลสเคอโรสีส (เอ็มเอส) นอกจากนี้การวินิจฉัยต้องอาศัยการตรวจพบแอนติบอดีที่เฉพาะเจาะจงต่อโรคนี้ (เอ็นเอ็มโอไอจีจี) ผู้ป่วยหญิงไทยโสดอายุ 34 ปี เกิดภาวะมีการเสื่อม ของปลอกหุ้มมัยอิลิน 2 ครั้ง ในระยะเวลาประมาณ 3 ปี แรกสุดมีอาการปวดบริเวณต้นคอ มองเห็นภาพสั่นเวียนศีรษะ แขนขาทั้งสองข้างอ่อนแรง อาการเกิดในระยะเวลา 2 สัปดาห์ ผลการตรวจแม่เหล็กไฟฟ้าพบมีรอยโรคที่บริเวณก้านสมอง การรักษาในครั้งนี้ผู้ป่วยรับยาสเตียรอยด์หลังจากนั้น 1 ปีต่อมา มีอาการตามัวทั้งสองข้าง ได้รับการวินิจฉัยว่า มีเส้นประสาทตาคู่ที่ 2 อักเสบเฉียบพลันในช่วงอาการกำเริบครั้งนี้ได้รับการรักษาโดยยาสเตียรอยด์ตามด้วยยากดภูมิคุ้มกันเพื่อป้องกันการกลับเป็นซ้ำ จนกระทั่ง 2 สัปดาห์ก่อนมาโรงพยาบาล ผู้ป่วยมีอาการหลับมากผิดปกติและพูดจาสับสนลักษณะคล้ายพูดโกหก การตรวจร่างกายทั่วไปไม่พบความผิดปกติที่ชัดเจนการตรวจร่างกายทางระบบประสาทพบว่ามีการมองเห็นผิดปกติทั้งสองข้าง ปฏิกิริยาตอบสนองของรูม่านตา และจอประสาทตาอยู่ในเกณฑ์ปกติ ผลการตรวจคลื่นแม่เหล็กไฟฟ้าที่สมองพบรอยโรคที่ต่อมใต้สมอง ธาลามัส ก้านสมอง และรอยโรครอบ ๆ โพรงสมอง ผลการตรวจน้ำไขสันหลังพบว่ามีเม็ดเลือดขาว 33 ตัว ต่อลูกบาศก์มิลลิเมตร ผลการตรวจน้ำตาลและโปรตีนในน้ำไขสันหลังอยู่ในเกณฑ์ปกติ ตรวจไม่พบโอลิโกโคลนอลแบน ในน้ำไขสันหลังขณะรักษาอยู่ที่โรงพยาบาลได้ประมาณ 2 สัปดาห์ ผู้ป่วยมีอาการแขนขาอ่อนแรงทั้งสองข้าง ชาตั้งแต่ปลายเท้าถึงบริเวณไขสันหลังระดับหน้าอกร่วมกับมีอาการปัสสาวะอุจจาระลำบาก การตรวจภาพรังสีไขสันหลังพบรอยโรคในไขสันหลังตั้งแต่ระดับก้านสมองยาวไปจนถึงระดับไขสันหลังส่วนปลายสุด ในผู้ป่วยรายนี้ได้รับการวินิจฉัยว่าเป็นโรคนิวโรมัยอิลัยติสออบติกาที่มีรอยโรคที่ต่อมใต้สมองร่วมด้วย