Original Article

Brain MRI Study in Thai Patient with Neuromyelitis Optica

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Background: Neuromyelitis optica spectrum disease [NMOSD] is an inflammatory disease of the central nervous system involving optic nerve, spinal cord, and brain. Asymptomatic brain abnormalities were recorded in some countries but the data in Thailand were limited.

Objective: To evaluate asymptomatic NMOSD brain abnormalities and their relation to clinical relapses in Thai patients.

Materials and Methods: This was a retrospective study, recruiting 27 NMOSD patients in a tertiary care center in Thailand. All patients were seropositive for aquaporin-4 IgG. Magnetic resonance imaging [MRI] of the brain was performed in every case.

Results: Twenty-four cases (88.89%) had asymptomatic hyperintensities on fluid-attenuated inversion recovery images [FLAIR]. These lesions were widespread across the brain even in areas with low density of aquaporin-4. To our knowledge, a fornix lesion was reported for the first time in a patient with acute optic neuritis. By using linear regression analysis, no significant correlation between annual relapse rate [ARR] and the number of asymptomatic FLAIR hyperintensities was established (coefficient 0.02, 95% confidence interval -0.0009 to 0.04, $p = 0.06$).

Conclusion: Asymptomatic FLAIR hyperintensities on brain MRIs are frequently found in NMOSD. They may not correlate with clinical relapses. Further cohort studies are required. To our knowledge, this is the first report of a fornix lesion in a NMOSD patient presented with acute optic neuritis.

Keywords: Neuromyelitis optica spectrum disease, Optic neuritis, Transverse myelitis, Aquaporin-4 IgG, Asymptomatic brain abnormalities, Fornix lesion

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Neuromyelitis optica spectrum disease [NMOSD] is an inflammatory disease of the central nervous system predominantly involving optic nerve and spinal cord[1]. Aquaporin-4 immunoglobulin G [AQP4-IgG] plays an important role in the pathogenesis of NMOSD and is highly specific for this disease[2,3]. Since the discovery of the antibody, clinical manifestations outside optic nerves and spinal cord have become more widely recognized such as in area postrema syndrome, acute brainstem syndrome, acute diencephalic syndrome, and symptomatic cerebral syndromes[1,4]. Such patients have characteristic imaging findings[1,5]. Furthermore, asymptomatic brain parenchymal signal-intensity abnormalities have also been documented in several studies[6-8]. The incidence is 64.7% in South Korea[7], 79.2% in Brazil[9], 65.5% in Cuba[10], 84.8% in China[11], and 54.5% in UK[12]. It has been noted that non-specific white matter changes and normal brain magnetic resonance images [MRIs] support the diagnosis according to the 2006 diagnostic criteria[3]. The clinical course in asymptomatic patients with NMOSD-compatible MRI lesions is less understood[1]. Hence, the present study was performed to evaluate asymptomatic brain parenchymal signal-intensity abnormalities and their relation to clinical relapses in Thai NMOSD patients.

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Material and Method

NMOSD patients, who satisfied the 2015 revised NMOSD criteria, were recruited retrospectively between June 2010 and December 2012 in a tertiary care center in Thailand. All patients were seropositive for AQP4-IgG. Medical records and brain MRIs were reviewed. Brain MRIs were performed with 3.0T MR imaging Unit (Achieva, Philips Medical Systems, Best, the Netherlands) and 1.5T MR imaging Unit (Signa Twin Speed, GE Healthcare). The MRI sequences included fluid-attenuated inversion recovery [FLAIR] with and without fat suppression, T2-weighted, and T1-weighted [T1W] at pre- and post-contrast. Brain MRIs were reviewed by two neuroradiologists to obtain a consensus. They were blinded to the clinical information. The number, location, and appearance of asymptomatic signal abnormalities were assessed. The study was approved by Ethics Committee of Faculty of Medicine, Ramathibodi Hospital.

Statistical analysis

Summary statistics were presented as frequency, percentage, and mean ± standard deviation [SD]. A correlation between annual relapse rate [ARR] and the number of FLAIR hyperintensities was evaluated using linear regression analysis. Statistical analyses were performed in Stata.

Results

Twenty-seven seropositive NMOSD cases were enrolled in the present study. Age ranged from 18 to 79 years (mean 38.6, SD 14.4). There were two males (7.4%) and 25 females (92.6%). Clinical manifestations were isolated optic neuritis (ON, n = 13, 48.15%, unilateral n = 6, bilateral n = 7), isolated transverse myelitis (TM, n = 10, 37.04%), ON + TM (n = 2, 7.41%), area postrema syndrome + TM (n = 1, 3.7%), and brainstem syndrome + TM (n = 1, 3.7%). Follow-up duration ranged from 3 to 120 months (mean 49.25, SD 33.9). Clinical relapses ranged from 0 to 20 (mean 3.9, SD 5.2). ARR ranged from 0 to 2 (mean 0.6, SD 0.6). Twenty patients (74%) were treated with steroid before MRI examinations.

Of the 27 cases, 24 (88.89%) had asymptomatic hyperintensities on FLAIR images. The number of FLAIR hyperintensities ranged from 0 to 40 (mean 9.1, SD 10.4). They were located in the frontal lobe (92.59%), parietal lobe (48.15%), temporal lobe (18.52%), occipital lobe (11.11%), cortex (0%), subcortical area (62.96%), deep white matter (59.26%), periventricular region (62.96%), periependymal surfaces of the lateral ventricle (14.81%), basal ganglia (22.22%), thalamus (11.11%), corpus callosum (7.41%), fornix (3.7%), midbrain (33.33%), pons (7.41%), and medulla (11.11%) (Figure 1, 2). The patient with fornix lesion presented with acute isolated ON and did not show memory or cognitive impairment. Of the 24 cases with asymptomatic FLAIR hyperintensities, lesions were greater than 3 mm in six (25%) and smaller than 3 mm in all cases (100%). They appeared round (87.5%), irregular (25%), and oval (29.17%). These lesions were in isolation (83.33%), in cluster (4.17%), and in patches (8.33%). White matter hyperintensities perpendicular to the lateral ventricles (Figure 3) and subcortical U-fibers were shown in seven cases (29.17%). Abnormal enhancement on T1W with gadolinium was detected in two cases (8.33%) (Figure 4). By using linear regression analysis, there was no significant correlation between ARR and the number of asymptomatic FLAIR hyperintensities (coefficient 0.02, 95% confidence interval -0.0009 to 0.04, $p = 0.06$).

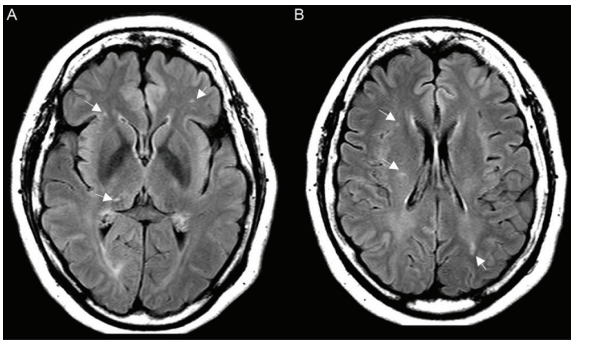

Figure 1. Axial fluid-attenuated inversion recovery MRI showed white matter hyperintensities (arrows) at the right thalamus, right external capsule, left frontal lobe (A), right corona radiata, and left parietal lobe (B).

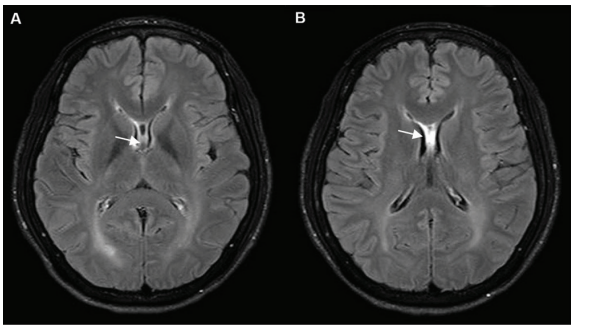

Figure 2. Axial fluid-attenuated inversion recovery MRI showed a hyperintense lesion at the fornix (arrows).

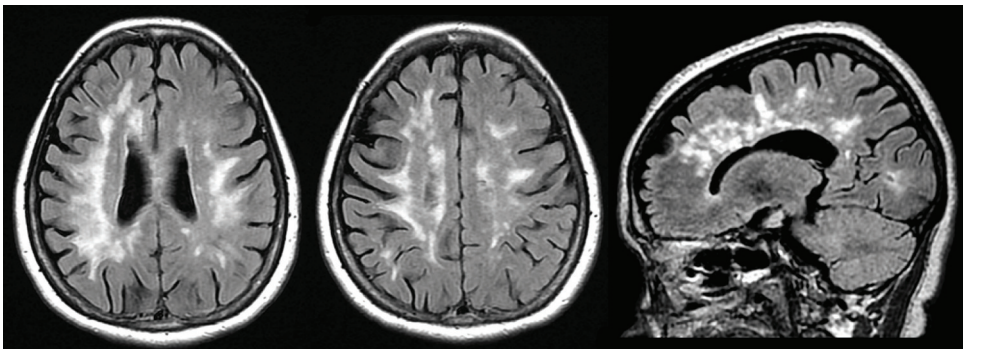

Figure 3. Axial fluid-attenuated inversion recovery MRI showed white matter hyperintensities which were perpendicular to the lateral ventricles, consistent with MS-like pattern.

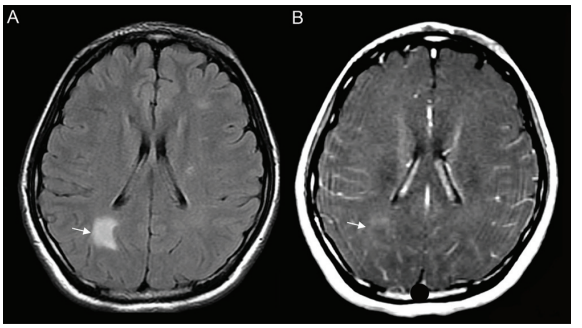

Figure 4. A) Axial fluid-attenuated inversion recovery MRI showed a focal hyperintensity at the deep white matter of the right parietal lobe (arrow). B) Post-gadolinium axial T1W MRI showed peripheral enhancement at the right parietal lobe (arrow).

Discussion

Asymptomatic FLAIR hyperintensities on brain MRIs were frequently seen in seropositive NMOSD patients. The results agree with previous studies in different populations[13,14]. The number of FLAIR hyperintensities was not associated with clinical relapses. This is inconsistent with another study that showed higher ARR in patients with abnormal brain lesions compared with those without[8]. As our study had a small sample size and was conducted in a retrospective manner, further cohort studies are required to clarify this matter.

The abnormalities were widespread across the brain even in areas with low density of aquaporin-4[5,15-17]. Most of them were small and round in the white and deep gray matter[9,16,17]. They are considered as non-specific lesions[5]. In the supratentorial region, they were located preferentially in the fronto-parietal lobes[12]. The periependymal lesions are characteristic of NMOSD and uncommon in multiple sclerosis[5]. They can be identified in both symptomatic and asymptomatic cases. Furthermore, a fornix lesion was reported for the first time in a patient presented with acute ON. Multiple sclerosis-like lesions are considered as a red flag and should be interpreted with caution[5,13,18]. White matter hyperintensities perpendicular to the lateral ventricles and subcortical U-fibers, which are parts of multiple-sclerosis features, could be observed in our study and in others[6,8,19]. However, cortical regions were spared[20,21]. In contrast to other studies[6,8], our results revealed only a few cases with abnormal enhancement and none with extensive hemispheric white matter lesions. This might be due to vanishing lesions following steroid treatments and transient functional disturbance of blood-brain barrier[22].

Conclusion

Asymptomatic FLAIR hyperintensities on brain MRIs are frequently found in NMOSD. They may not correlate with clinical relapses. Further cohort studies are required. To our knowledge, this is the first report of a fornix lesion in a NMOSD patient presented with acute ON.

What is already known on this topic?

Asymptomatic FLAIR hyperintensities on brain MRIs in patients with NMOSD in other populations.

What this study adds?

Asymptomatic FLAIR hyperintensities on brain MRIs in Thai patients with NMOSD. To our knowledge, this is the first report of a fornix lesion in a NMOSD patient presented with acute ON. By using linear regression analysis, there was no significant correlation between ARR and the number of asymptomatic FLAIR hyperintensities.

Acknowledgement

We would like to thank Mr. Nattawut Unwanatham, Department of Clinical Epidemiology and Biostatistics, Ramathibodi Hospital, for assistance with statistical analysis.

Potential conflicts of interest

None.

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รอยโรคในสมองที่ยังไม่แสดงอาการในผู้ป่วยนิวโรไมอิไลติส ออปติกา

ภัทรนันท์ แสงวิโรจน์กุล, อรนันท์ ไตรตานนท์, ปนิษฐา จินดาหรา, ธีรธร พูลเกษ, ดิษยา รัตนากร, ไพโรจน์ บุญคงชื่น, จรุงไทย เดชเทวพร, เจษฎา เขียนดวงจันทร์, พิศิษฐ์ ปรีชาวัฒน์, อนุชิต ปุญญทลังค์, เมธา อภิวัฒนกุล, จิรพร เหล่าธรรมทัศน์, สุพจน์ ตุลยาเดชานนท์

ภูมิหลัง: โรคนิวโรไมอิไลติส ออปติกา เป็นการอักเสบของระบบประสาทส่วนกลางชนิดหนึ่ง ที่มักทำให้เกิดการอักเสบของประสาทตา ไขสันหลัง และสมองอักเสบ มีการศึกษาในต่างประเทศ พบว่าผู้ป่วยโรคนี้มีรอยโรคในสมองที่ไม่แสดงอาการได้ แต่ข้อมูลในประเทศในยังมีไม่มากนัก

วัตถุประสงค์: เพื่อศึกษารอยโรคในสมองที่ไม่แสดงอาการ ในผู้ป่วยนิวโรไมอิไลติส ออปติกา ชาวไทย

วัสดุและวิธีการ: การศึกษานี้เป็นการศึกษาแบบย้อนหลัง ได้รวบรวมผู้ป่วยนิวโรไมอิไลติส ออปติกา 27 ราย ผู้ป่วยทุกคนมี อควา พอริน โฟร์ แอนติบอดี ในเลือด และได้รับการถ่ายภาพสมองด้วยคลื่นแม่เหล็ก

ผลการศึกษา: ผลปรากฏว่าพบรอยโรคในสมองที่ไม่แสดงอาการ ในผู้ป่วย 24 ราย (88.89%) ในการถ่ายภาพสมองด้วยคลื่นแม่เหล็กแบบแฟลร์ รอยโรคเหล่านี้กระจายทั่วสมอง แม้แต่ในตำแหน่งที่มี อควา พอริน โฟร์ น้อย นอกจากนี้การศึกษานี้ได้รายงานรอยโรคที่ฟอร์นิกส์เป็นครั้งแรก ในผู้ป่วยที่มาด้วยเส้นประสาทตาอักเสบ จำนวนรอยโรคดังกล่าวไม่มีความสัมพันธ์กับจำนวนครั้งของการอักเสบ (coefficient 0.02, 95% confidence interval -0.0009 to 0.04, p = 0.06)

สรุป: รอยโรคในสมองที่ไม่แสดงอาการ เกิดขึ้นบ่อยในผู้ป่วยนิวโรไมอิไลติส ออปติกา จำนวนรอยโรคอาจไม่สัมพันธ์กับจำนวนครั้งของการอักเสบ เนื่องจากการศึกษานี้เป็นแบบย้อนหลัง การศึกษาแบบต่อเนื่องไปในอนาคตน่าจะให้ข้อมูลได้ดียิ่งขึ้น