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LETTER TO THE EDITOR

Anti-$GABA_B$ Receptor Encephalitis Presenting with Atypical Corticobasal Syndrome in a Patient with Parkinson's Disease

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Anti-$GABA_B$ receptor ($GABA_BR$) encephalitis commonly presents with seizures and limbic encephalitis and, rarely, rapidly progressive dementia. Here, we report a patient with Parkinson's disease (PD) who developed anti-$GABA_BR$ encephalitis leading to a presentation of an atypical corticobasal syndrome.

A 65-year-old woman with PD for 5 years (diagnosed in another center) was referred for worsening tremors and cognitive difficulties. At presentation 5 years earlier, she had bilateral resting tremors of her hands (left > right) associated with bradykinesia. She responded well to 125 mg levodopa four times daily but developed mild to moderate peak-dose dyskinesia a year before presentation to our center. She had not been on any other anti-Parkinson medications or neuroleptics. Two months prior to her presentation to our center, she reported a marked deterioration in her parkinsonism symptoms with frequent falls and worsening tremors in her left hand. She developed memory difficulties with visual hallucinations 2 weeks prior to presentation. She had difficulty using her left hand as it would 'shake', especially on action. On examination, there was markedly asymmetric parkinsonism; her left hand was rigid and dystonic with superimposed stimulus-sensitive action myoclonus. The left leg was also markedly rigid. Brain CT showed white matter hypodensities in the right frontotemporal area. Brain MRI showed multifocal cortical and subcortical T2 and FLAIR hyperintensity in the right superior frontal and rectus gyri, both cingulate gyri (right more than left), the right hippocampus and the right temporal lobe. The affected cortex was thickened with subjacent subcortical white matter edema, with mass effect. There was no hemorrhage or enhancement following gadolinium administration. Mild restricted diffusion of the cortex with T2 shine-through of the white matter was observed (Figure 1).

CSF opening pressure was 20 cm H_2O, the CSF protein level was 382 mg/L, the CSF glucose level was 3.74 mmol/L and the CSF/serum glucose ratio was 0.76. CSF HSV PCR DNA and TB PCR DNA were negative. ANA and anti-dsDNA were negative. An autoimmune encephalitis screen was negative for anti-NMDAR, anti-CASPR2, anti-AMPA 1 and 2, anti-DPPX 1, and anti-LGI1 antibodies but positive for anti-$GABA_BR$. CT of the thorax, abdomen, and pelvis was negative for malignancy. She received intravenous ceftriaxone and acyclovir for 7 days and intravenous methylprednisolone 500 mg daily for 3 days. With treatment, the left-hand myoclonus and parkinsonism improved, and she was able to walk with assistance. She was discharged on prednisolone 40 mg, azathioprine 50 mg daily and levodopa. A repeat MRI was planned in 6 weeks.

At the time of readmission, the patient presented with worsening left-hand tremor, gait difficulties, visual hallucinations and recurrent falls despite compliance with medications. On examination, she appeared restless with similar neurological findings: asymmetric parkinsonism, with prominent dystonia of the left

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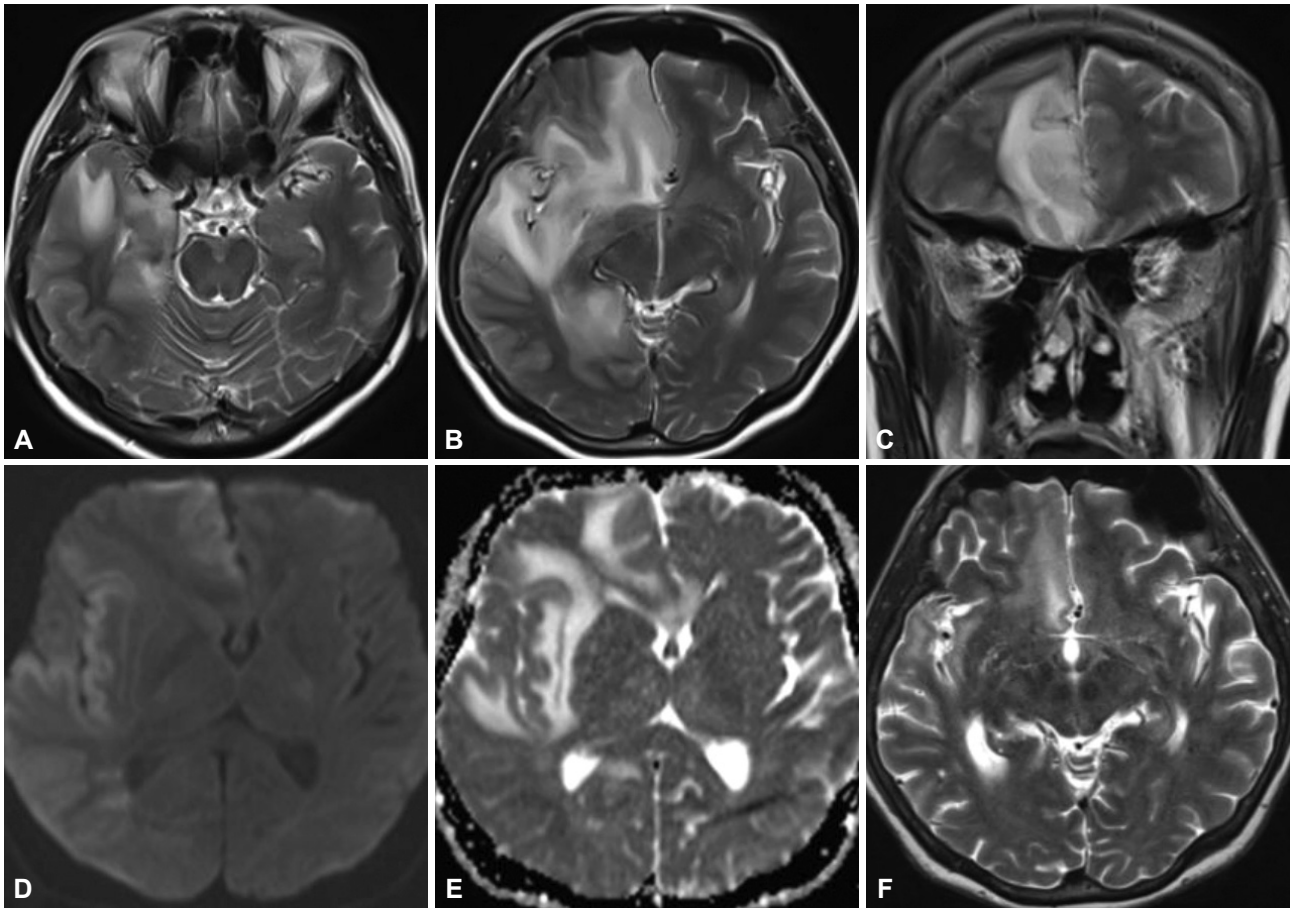

Figure 1. MRI of the brain at presentation demonstrated multifocal cortical and subcortical white matter T2 hyperintensity in the right hippocampus and right middle and superior temporal gyri (A and B), both cingulate gyri (R > L), the right superior frontal and rectus gyri (B and C) and the right insular cortex (B), with mild restricted diffusion of the cortex and T2 shine-through within the subcortical white matter on DWI (D) and the corresponding ADC map (E), without hemorrhage (not shown) or postcontrast enhancement (not shown). Follow-up MRI 6 weeks later demonstrated decreased T2 hyperintensity in the cortex and subcortical white matter of the original lesions (F).

hand with superimposed stimulus-sensitive action myoclonus as well as an alien hand phenomenon. There was a diffuse goiter. Further investigations confirmed hyperthyroidism, with elevated T4 and T3 levels (T4: 28.4 pmol/L, T3: 6.65 pmol/L) and low TSH levels (TSH < 0.01 μIU/mL). The anti-thyroid globulin and anti-thyroid peroxidase antibodies were normal. She was started on carbimazole and propranolol, with improvement in her symptoms. The oral prednisolone and anti-Parkinson medications were maintained. A repeat MRI 2 weeks later showed a reduction in the T2 hyperintense signal and cortical and white matter edema, indicating a treatment response. Unfortunately, no EEG was performed during either admission.

Our patient developed rapidly progressive atypical corticobasal syndrome (CBS) 5 years after the diagnosis of PD, which prompted further investigations, leading to the diagnosis of anti-$GABA_BR$ encephalitis. In clinical practice, it is not uncommon to revise an initial diagnosis of PD to other Parkinson plus (PP) syndromes, as some of the typical features of the PP syndromes may have been missed or not apparent, especially early in the disease course. However, a diagnosis of corticobasal degeneration from the outset was perhaps unlikely, as the patient had levodopa-responsive parkinsonism with later occurrence of levodopa-induced dyskinesia, typical of PD. Our patient fulfilled the criteria for possible secondary CBS with new-onset cognitive difficulties and dystonia of the left hand with superimposed myoclonus.[1] The brain MRI abnormalities within the right frontotemporal region also correlated with the clinical findings. The CBS phenotype has been reported in other rapid encephalopathy syndromes, such as Hashimoto's encephalitis[2] and Creutzfeldt-Jakob disease (CJD).[3] To our knowledge, this is the first report of anti-$GABA_BR$ encephalitis presenting with an atypical CBS. Interestingly, a recent clinical-pathological review of 32 cases of anti-$GABA_BR$ encephalitis showed that 13% of their patients presented with rapidly progressive dementia, suggestive of CJD.[4] Patients with progressive dementia were older and did not have underlying malignancies.[4] Seizures were uncommon in this group, while

myoclonus was common.[4] Similarly, another review of 28 patients with anti-GABA$_B$R encephalitis reported that older patients aged ≥ 45 years were more likely to present with cognitive and behavioral difficulties, whereas seizures were the most common presenting symptom in patients under 45 years of age.[5] Movement disorders have been described in 14.3% of patients with anti-GABA$_B$R encephalitis, the most common being myoclonus and ataxia.[4,5] Rarer clinical presentations of anti-GABA$_B$R encephalitis, limited to single case reports, include recurrent syncope,[6] and amyotrophic lateral sclerosis.[7]

It is possible that the pre-existing diagnosis of PD in our patient contributed somewhat to the CBS phenotype. However, the right frontotemporal brain MRI abnormalities were suggestive of a new insult and correlated with the clinical syndrome of CBS. MRI abnormalities in anti-GABA$_B$R encephalitis are variable, ranging from 25–45%.[4,5] Frequently observed changes include unilateral or bilateral T2/FLAIR white matter hyperintensities in the mesial temporal lobes and rarely atrophy or hypointensity of the mesial temporal lobe.[4,5] Normal MRI findings despite clinical and EEG progression have also been reported.[6] Anti-GABA$_B$R encephalitis has a high mortality, especially if associated with underlying malignancy, commonly small-cell lung carcinoma.[4] Immune-mediated therapies, such as intravenous steroids, intravenous immunoglobulins and plasma exchange, with disease-modifying therapies are used with reasonable success.[4,5] Our patient initially responded to intravenous steroids but deteriorated again due to hyperthyroidism. Although steroid therapy was not repeated, our patient improved following the treatment of hyperthyroidism with carbimazole and beta blockers. This case, therefore, highlights the importance of investigating an unexplained and rapid clinical deterioration in a patient with PD even if the symptoms overlap with PP syndrome and further expands the clinical spectrum of anti-GABA$_B$R encephalitis.

Conflicts of Interest

The authors have no financial conflicts of interest.

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None.

Author Contributions

Conceptualization: Norlinah Mohamed Ibrahim. Data curation: Noor Sharizat Abdullah, Norlinah Mohamed Ibrahim, Tan Hui Jan, Rabani Remli, Shahizon Azura Mohamad Mukari. Formal analysis: Norlinah Mohamed Ibrahim, Noor Sharizat Abdullah, Rabani Remli, Shahizon Azura Mohamad Mukari. Investigation: Noor Sharizat Abdullah, Rabani Remli, Tan Hui Jan, Norlinah Mohamed Ibrahim, Shahizon Azura Mohamad Mukari. Methodology: Noor Sharizat Abdullah, Norlinah Mohamed Ibrahim, Shahizon Azura Mohamad Mukari, Tan Hui Jan.

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REFERENCES

1. Armstrong MJ, Litvan I, Lang AE, Bak TH, Bhatia KP, Borroni B, et al. Criteria for the diagnosis of corticobasal degeneration. Neurology 2013;80:496-503.
2. Sheetal SK, Mathew R, Peethambaran B. Hashimoto's encephalopathy as a treatable cause of corticobasal disease. Ann Indian Acad Neurol 2016;19:285-286.
3. Lee W, Simpson M, Ling H, McLean C, Collins S, Williams DR. Characterising the uncommon corticobasal syndrome presentation of sporadic Creutzfeldt-Jakob disease. Parkinsonism Relat Disord 2013;19:81-85.
4. van Coevorden-Hameete MH, de Bruijn MAAM, de Graaff E, Bastiaansen DAEM, Schreurs MWJ, Demmers JAA, et al. The expanded clinical spectrum of anti-GABA$_B$R encephalitis and added value of KCTD16 autoantibodies. Brain 2019;142:1631-1643.
5. Lin J, Li C, Li A, Liu X, Wang R, Chen C, et al. Encephalitis with antibodies against the GABA$_B$ receptor: high mortality and risk factors. Front Neurol 2019;10:1030.
6. Kitazaki Y, Ikawa M, Yamaguchi T, Enomoto S, Kishitani T, Shirafuji N, et al. Autoimmune encephalitis associated with anti-gamma-aminobutyric acid B receptor antibodies mimicking syncope. Intern Med 2020;59:843-847.
7. Schumacher H, Meyer T, Prüss H. GABA$_B$ receptor encephalitis in a patient diagnosed with amyotrophic lateral sclerosis. BMC Neurol 2019;19:41.