SCLC and anti-GABABR encephalitis: A retrospective analysis of 60 cases in China

Chunguo Jiang1 | Min Zhu1 | Dan Wei2 | Hongyan Duan3 | Yuhui Zhang1 © | Xiaokai Feng1 ©

1Department of Respiratory and Critical Care Medicine, Beijing Institute of Respiratory Medicine and Beijing Chaoyang Hospital, Capital Medical University, Beijing, China
2Department of Respiratory and Critical Care Medicine, NO. 215 Hospital of Shaanxi Nuclear Industry, Xianyang, China
3Department of Respiratory and Critical Care Medicine, People’s Hospital of Wudang District, Guiyang, China

Correspondence
Yuhui Zhang and Xiaokai Feng, Department of Respiratory and Critical Care Medicine, Beijing Institute of Respiratory Medicine and Beijing Chaoyang Hospital, Capital Medical University, 8 Gongti Nanlu, Chaoyang District, Beijing, 100020, China.
Email: zhangyhcy@163.com and fengxiaokai2020@163.com

Abstract
Background: Anti-gamma aminobutyric acid B receptor (anti-GABABR) encephalitis is a rare autoimmune neurological syndrome observed in lung cancer patients. More research on the clinical characteristics of small cell lung cancer (SCLC) and anti-GABABR encephalitis should be carried out to improve diagnosis and treatment.
Methods: We retrospectively investigated the clinical characteristics, auxiliary examination results, and treatment responses in patients with SCLC and anti-GABABR encephalitis at Beijing Chaoyang Hospital from January 2010 to December 2020. The study also retrospectively analyzed cases of SCLC and anti-GABABR encephalitis well documented in China.
Results: A total of 60 cases of SCLC and anti-GABABR encephalitis were analyzed in the study, two in our hospital, and 58 previously reported in the literature. The male:female ratio was 3:1, with a median age at presentation of 61 years (range: 40–81 years). Twenty-eight patients initially presented with seizures, four with cognitive disorder, and three with psychiatric symptoms. The major symptoms were epileptic seizures (n = 56; 96.9%), cognitive impairment (n = 47; 81.0%), psychiatric disorders (n = 45; 77.6%), and conscious disturbance (n = 32; 55.2%). Fifty-five patients underwent immunotherapy, and 23 patients underwent oncologic treatment in the literature. After a median follow-up duration of 8.8 (range, 0.5–37.0) months, nine patients showed good outcomes (modified Rankin Scale score, mRS ≤2), eight patients showed poor prognosis (mRS > 2), and 18 patients died.
Conclusions: The clinical characteristics of SCLC and anti-GABABR encephalitis are seizures, cognitive impairment, and psychiatric disorders which affect middle-aged to elderly men in China. The long-term prognosis is relatively poor.

Keywords
anti-GABABR encephalitis, limbic encephalitis, small cell lung cancer

INTRODUCTION

Limbic encephalitis (LE) is a rare neurological syndrome which selectively affects limbic system structures including the hippocampus, insular cortex, amygdaloid nucleus and cingulate gyrus. Patients often present with amnesia, psychological and behavioral disorder and epileptic seizures.1 LE is an immune-mediated response associated with antineuronal antibodies, including neuronal nuclear antibody 1 (Hu), Ma2, amphiphysin, collapsin response mediator protein-5 (CRMP5),2 voltage-gated potassium channel (VGKC) complex, N-methyl-d-aspartate receptor (NMDAR), and gamma aminobutyric acid B receptor (GABABR). Anti-GABABR encephalitis is a newly described form of autoimmune encephalitis associated with antineuron cell surface antigen antibodies.3 Patients usually present with early and...
prominent seizures, cognitive impairment, psychiatric disorders, and conscious disturbance. In paraneoplastic cases of the disease, these patients usually harbor an underlying tumor, and small cell lung cancer (SCLC) is the most frequent neoplasm. 4–7

Only a few cases of SCLC and anti-GABABR encephalitis have been reported to date, and the clinical manifestations and prognosis have yet to be investigated systematically. 8 In this study, we analyzed the clinical manifestations, auxiliary examination results, treatment strategies, and prognoses in patients with SCLC and anti-GABABR encephalitis in China, to improve the understanding of this relatively rare disorder.

METHODS

This observational retrospective study enrolled patients diagnosed SCLC and anti-GABABR encephalitis at Beijing Chaoyang Hospital from January 2010 to December 2020. Clinical information was obtained from hospitalization reports. The modified Rankin Scale (mRS) 9 was used to define favorable (score 0–2) and poor (score 3–6) functional outcomes. The study was approved by the Ethics Committee of Beijing Chaoyang Hospital, Capital Medical University (No. 2016-ke-79). We also retrospectively collected cases of SCLC and anti-GABABR encephalitis in China, include Chinese National Knowledge Infrastructure (CNKI), Wanfang, Vip, Pubmed. Only reports on cases at first spinal tap. An elevated leukocyte count was demonstrated in 31 cases (60.8%) (>8 cells/μl), and treatment responses, were analyzed. Statistical analyses were performed using SPSS 25.0 software (IBM-SPSS Inc.). Continuous variables were expressed as median (range and interquartile range). Categorical variables were described using frequencies (percentage, %).

RESULTS

Patients at our hospital

Two patients with SCLC and anti-GABABR encephalitis were recruited at our hospital. One patient was a 59-year-old woman who presented with memory deficit. Results of blood tests indicated that anti-GABABR antibody and anti-SOX1 antibody were positive. Pathological examination confirmed a diagnosis of SCLC, and she received platinum-based chemotherapy, intravenous immunoglobulins (IVIg), and antiepileptic drugs. The other patient was a 76-year-old man who presented with cognitive disorder. GABABR antibody was detected in the serum. He was diagnosed with SCLC in the right lung and received platinum-based chemotherapy. They both died 1 year later after diagnosis.

Patient characteristics

A total of 58 cases were reported in the literature between January 2010 and December 2020. 10–15 More details of the 60 patients (including the 2 patients at our hospital) are summarized in Table 1. The average age at presentation was 61 (range, 40–81) years, with a male/female ratio of 3:1. Twenty-eight patients initially presented with seizures, four with cognitive disorder, and three with psychiatric symptoms. The main symptoms were epileptic seizures (n = 56; 96.9%), cognitive impairment (n = 47; 81.0%), psychiatric disorders (n = 45; 77.6%), and conscious disturbance (n = 32; 55.2%). Ten patients exhibited sleep disorders, and 14 patients developed respiratory failure. A total of 55.0% were smokers. The median interval from symptom onset to diagnosis was 49 (range, 1–365) days. The patient characteristics are summarized in Table 2.

Laboratory tests

GABABR antibodies were detected in both serum and CSF samples in 38 patients, solely in serum in six patients, and solely in CSF in 10 patients; however, the detailed GABABR antibody test results of the other six patients was not clearly recorded in the literature (Table 3). Additional antibodies were identified; four had anti-Hu, two had anti-Yo, two had NMDAR, and one each had anti-amphiphysin, anti-SOX1, anti-ganglioside (GM1). Antinuclear antibody (ANA) positivity was observed in the serum samples of four patients, and five patients had antithyroid peroxidase (TPO) antibodies. Tumor marker neuron specific enolase (NSE) positivity in the serum was observed in eight patients. The CSF pressure was high (>180 mmH2O, 60 mmH2O–310 mmH2O) in 12 (35.3%) cases at first spinal tap. An elevated leukocyte count was demonstrated in 31 cases (60.8%) (>8 cells/μl, range, 0–174 cells/μl) and an elevated protein level was noted in 29 cases (67.4%) (>40 mg/dl; range, 15.0–96.8 mg/dl).

Radiological examination and EEGs

There were 28 cases with lung localization reports following chest computed tomography (CT) scan. Thirteen cases (46.4%) had a lung mass on the right lung, and a lung mass was detected in 10 patients (35.7%) on the left lung, as well as hilar and mediastinal lymph node metastasis. Nine patients underwent positron emission tomography-computed tomography (PET-CT), and a hypermetabolic lung mass with lymphatic metastasis was revealed in six patients. All patients were diagnosed with SCLC following pathological biopsy and immunohistochemistry.

Brain magnetic resonance imaging (MRI) examination was performed in 47 cases and was unremarkable in
12 (25.5%) patients. MRI demonstrated an involvement of the limbic system in 28 (59.6%) cases. The distribution was restricted to the left temporal lobe, insula and hippocampus in eight cases, right in four cases, and bilateral involvement was shown in 16 patients. Contrast enhancement of the adjacent meninges was observed in two patients. The lesions appeared hypointense on T1-weighted imaging (T1WI) and hyperintense on T2-weighted imaging (T2WI)/fluid-attenuated inversion recovery (FLAIR), and diffusion-weighted imaging. PET-CT of two patients detected hypermetabolism in the temporal lobe and hippocampus. Figure 1 shows the chest CT and brain MRI images of one patient.

A total of 34 cases reported EEG examinations. Temporal epileptiform discharges were confirmed in eight (23.5%) cases. Focal or global slow waves were observed in 15 (44.1%) patients, and 11 patients (32.4%) showed approximately normal EEG results. The detailed results of imaging and EEGs are presented in Table 3.

### Table 1: Summary of the literature review on SCLC and anti-GABABR encephalitis

| First author | Institution | Year | Journal | n |
|--------------|-------------|------|---------|---|
| Linjia Guo   | Beijing Shijitan Hospital, Capital Medical University | 2015 | Journal of Apoplexy and Nervous Diseases | 1 |
| Jiakai He    | Xuanwu Hospital, Capital Medical University | 2015 | Chinese Journal of Neurology | 1 |
| Jieping Lu   | Anhui Provincial Hospital | 2016 | Chinese Journal of Nervous and Mental Diseases | 1 |
| Haitao Ren   | Peking Union Medical College Hospital | 2016 | Chinese Journal of Neurology | 1 |
| Lei Qiao     | Peking Union Medical College Hospital | 2016 | Chinese Journal of Neurology | 1 |
| Jun Zhang    | Xuanwu Hospital, Capital Medical University | 2016 | Chinese Journal of Neurology | 2 |
| Ying Shi     | Affiliated Hospital of Hebei University | 2017 | Chinese Journal of Nervous and Mental Diseases | 2 |
| Chao Zhao    | Tangdu Hospital, the Fourth Military Medical University | 2017 | China Medical Herald | 1 |
| Guiyang Sun  | The First Affiliated Hospital of Zhengzhou University | 2017 | Chinese Journal of Neurology | 3 |
| Cancan Wang  | Zhengzhou University People’s Hospital | 2017 | Chinese Journal of Neuromedicine | 2 |
| Song Qiao    | Zhejiang Hospital | 2017 | International Journal of Neuroscience | 3 |
| Xueping Chen | West China Hospital, Sichuan University | 2017 | Neurological Research | 3 |
| Songbin Pan  | Wuhan First Hospital | 2018 | Chinese Journal of Nervous and Mental Diseases | 1 |
| Ying Wang    | The First Affiliated Hospital of Dalian Medical University | 2018 | Journal of Dalian Medical University | 1 |
| Junyan Liu   | The First Affiliated Hospital of Harbin Medical University | 2018 | Chinese Journal of Nervous and Mental Diseases | 1 |
| Qinlan Xu    | Beijing Tiantan Hospital, Capital Medical University | 2018 | Journal of Neurology and Nervous Diseases | 4 |
| Junzhao Cui  | Second Hospital of Hebei Medical University | 2018 | International Journal of Neuroscience | 5 |
| Qing Liu     | Xuanwu Hospital, Capital Medical University | 2019 | Journal of Clinical Neurology | 1 |
| Junjie Dai   | Ningbo City Medical Treatment Center Lihuili Hospital | 2019 | Chinese General Practice | 5 |
| Jingfang Lin | West China Hospital, Sichuan University | 2019 | Frontiers in Neurology | 3 |
| Yue Qiu      | Huashan Hospital Affiliated to Fudan University | 2020 | Chinese Journal of Clinical Neurosciences | 1 |
| Minrui Dong  | The First Affiliated Hospital of Zhengzhou University | 2020 | Chinese Journal of Neuroimmunology and Neurology | 5 |
| Benhai Yao   | Affiliated Hospital of Zunyi Medical University | 2020 | Chinese Journal of Neuroimmunology and Neurology | 1 |
| Yi Li        | Second Hospital of Hebei Medical University | 2020 | Journal of Clinical Neurology | 1 |
| Lina Li      | Shenzhen Hospital, University of Hong Kong | 2020 | Chinese Journal of Neurology | 4 |
| Haibing Zhu  | The First Affiliated Hospital of Gannan Medical College | 2020 | Chinese Journal of Geriatric Heart Brain and Vessel Diseases | 2 |
| Xiuhe Zhao   | Qilu Hospital, Shandong University | 2020 | Experimental and Therapeutic Medicine | 2 |

Abbreviations: GABABR, gamma aminobutyric acid B receptor; SCLC, small cell lung cancer.

### Table 2: Clinical features of patients with SCLC and anti-GABABR encephalitis

| Characteristics                  | No. of cases | Proportion (%) |
|----------------------------------|--------------|----------------|
| Sex, M                           | 44           | 75.9           |
| Age, years, median (range)       |              |                |
| 40–49                            | 7            | 12.1           |
| 50–59                            | 15           | 25.9           |
| 60–69                            | 28           | 48.3           |
| ≥70                              | 8            | 13.8           |
| Smoker                           | 11           | 55.0           |
| Symptoms of LE, n (%)            |              |                |
| Epileptic seizures               | 56           | 96.6           |
| Cognitive impairment             | 47           | 81.0           |
| Psychiatric disorders            | 45           | 77.6           |
| Conscious disturbance            | 32           | 55.2           |

Abbreviations: GABABR, gamma aminobutyric acid B receptor; LE, limbic encephalitis; M, male; SCLC, small cell lung cancer.
Treatment and prognosis

Fifty-five patients underwent first-line immunomodulatory therapy and 34 cases were treated with a combination of corticosteroids and IVIg, nine cases with corticosteroids alone, and 12 cases with IVIg alone, respectively (Table 4). Two patients were given at least one course of plasma exchange, and rituximab was administered in two patients. Twenty-three patients received treatment for the malignancy described in the literature. Furthermore, 31 patients received antiepileptic drugs or medication for psychiatric symptoms.

After a median follow-up duration of 8.8 (range, 0.5–37.0) months, 26 (52.0%) patients showed different degrees of recovery. Nine patients had experienced good outcomes (mRS ≤2), and the epileptic symptoms were well controlled. Eight patients showed poor prognosis (mRS >2), and there were no relapses on limbic symptoms observed during the follow-up periods. In addition, 18 patients died due to tumor progression or chemotherapy-related infection.

DISCUSSION

Anti-GABABR encephalitis cases have been reported in the literature since 2010, yet numerous studies only report a small number of cases. Anti-GABABR encephalitis is often seen in SCLC. Our study provides the first detailed description of SCLC and anti-GABABR encephalitis, clinical characteristics, long-term prognoses, and anticancer treatment response rates of SCLC and anti-GABABR encephalitis in China. To the best of our knowledge, this is the largest case series of patients with this relatively rare disease currently available in the literature. However, as the disease information obtained from case reports was incomplete, this may have led to incomplete data analysis.

GABABRs are G-protein-coupled receptors belonging to typical inhibitory synaptic proteins in neurons, widely
distributed in the central nervous system, including the cerebral cortex, hippocampus, thalamus, and cerebellum.\textsuperscript{18} They play critical roles in neurotransmitter transmission and synapse stabilization, and are primarily involved in learning, memory, and cognitive function.\textsuperscript{19,20} The pathological features are believed to be immune-mediated, and include microscopic perivascular lymphocytic infiltration, neuronal cell loss, and reactive microglial proliferation of limbic structures. Around half of patients with anti-GABABR encephalitis have a final diagnosis of SCLC or neuroendocrine tumors.\textsuperscript{7} Clinicians should eliminate the possibility of SCLC in patients with high anti-GABABR antibody levels. The detection of a tumor is usually established after the development of neurological symptoms.\textsuperscript{8} Therefore, once a clinical diagnosis of anti-GABABR encephalitis is confirmed, screening for lung cancer is important. Long-term regular follow-up for tumor screening is recommended, even if no tumor is discovered at the time of presentation.\textsuperscript{21} Similarly, in patients with SCLC accompanied by symptoms associated with LE, it is necessary to detect anti-GABABR antibody. GABABRs may be expressed in lung cancer tissues.\textsuperscript{14}

Our study suggests that Chinese patients with SCLC and anti-GABABR encephalitis have similar clinical features as described in previous studies. This disease mostly affects middle-aged to elderly men.\textsuperscript{3–5,8} Seizures are the initial and most prominent presentation. Indeed, seizures have been recognized as one of the major features of anti-GABABR encephalitis.\textsuperscript{3,8} It should be considered as a possible diagnosis in middle-aged and older patients with refractory new-onset epilepsy. In the present study, almost all patients presented with typical limbic epilepsy, and had symptoms including seizures, cognitive dysfunction, confusion, personality changes, and psychiatric symptoms.\textsuperscript{3} When these symptoms occur in combination with seizures, anti-GABABR encephalitis should be suspected, and comprehensive screening for antineuronal autoantibodies and tumors in both serum and CSF is essential. A strong suspicion might enable earlier diagnosis and lead to a better long-term outcome.

All the patients in our study had tested positive for anti-GABABR antibodies in serum and/or CSF. Consistent with previously reported cases, some patients also expressed additional antineuronal antibodies in the serum, most commonly, anti-Hu, anti-Yo, NMDAR, SOX1, ANA, and TPO antibodies. The proportion of additional antineuronal antibodies was previously reported to be in the range of 7\%-40\%.\textsuperscript{3–5,16} These additional antibodies may very well reflect the disease association with autoimmunity or latent tumors, such as SOX1 antibodies associated with SCLC,\textsuperscript{6} and are frequently associated with poor prognosis.\textsuperscript{4} It has been suggested that testing for antineuronal antibodies should be considered in all patients with anti-GABABR encephalitis. The effects of these antibodies on anti-GABABR encephalitis patient treatment response and prognosis require further investigation.

As for brain MRI, unilateral or bilateral medial temporal lobe and hippocampal changes were revealed in 28 patients, which is in accordance with the results of most prior studies.\textsuperscript{5} Brain MRI did not provide unique or specific information useful for the diagnosis of anti-GABABR encephalitis, and 12 (25.5\%) patients showed negative MRI findings in our study, which did not exclude the disease possibility and immunological testing should therefore be performed.\textsuperscript{11} As far as we are concerned, brain MRI is more useful to rule out other disorders, such as tumors, that might lead to neurological symptoms. PET-CT might be more sensitive in the diagnosis and evaluation of anti-GABABR encephalitis, especially in patients with normal MRI findings.\textsuperscript{8,22} Two patients in our study presented with hypermetabolism in the temporal lobe and hippocampus on PET-CT, and PET-CT could aid evaluations of both abnormal metabolism in the limbic system and the underlying neoplasms. More cases and research will be needed to determine the diagnostic value of PET-CT in this disease.

No agreement on the anti-GABABR encephalitis diagnostic criteria has been reached, with a high, incorrect preoperative diagnosis rate. The diagnosis requires a combination of clinical characteristic neurological syndromes, and the detection of specific anti-GABABR antibodies in the serum and/or CSF.\textsuperscript{8,23} Furthermore, one could apply the criteria used for the diagnosis of other autoimmune encephalitides to anti-GABABR encephalitis, which consists of the presence of autoantibodies in the serum or CSF and a clinical response to immunotherapy.\textsuperscript{24} Additionally, metabolic encephalopathy, neurotoxic drugs, inflammatory disorders, central nervous system tumors, and neurodegenerative disorders must be excluded.\textsuperscript{23}

For the treatment of SCLC and anti-GABABR encephalitis, immunotherapy and antineoplastic therapy have been universally applied as first-line therapies.\textsuperscript{3,4,25} Treatment with corticosteroids, IVIg and plasmapheresis, either alone or in combination, adding rituximab or cyclophosphamide as second-line therapies in refractory cases, is appropriate.\textsuperscript{26} In our research, most patients received treatment with corticosteroids and IVIg. Previous studies have demonstrated that patients who received immunotherapy at initial presentation had better outcomes and lower rates of death than those who did not.\textsuperscript{25} In comparison with traditional intracellular antigen antibody-related (e.g., anti-Hu) LE, anti-GABABR encephalitis usually shows a much better response.\textsuperscript{3,4} The seizures caused by anti-GABABR encephalitis are usually refractory to antiepileptic medications, but respond well to immunotherapy.\textsuperscript{27}

For patients with SCLC, treatment of cancer may also be necessary. In our study, 23 patients were reported to have received treatment for malignancy after diagnosis. Most patients experience improvement in neurological symptoms after systemic chemotherapy. Tumor therapy in most cases might lead to better neurological improvement than treatment with immunotherapy.\textsuperscript{28} Patients with LE might have lower performance status scores owing to neurological disorders,\textsuperscript{29} which was previously considered contraindicative for chemotherapy. Aggressive chemotherapy, despite slight reductions in tumor burden, might improve prognosis in this population.\textsuperscript{28} However,
as the description of treatment and prognosis in the literature is unclear, our study did not provide more in depth analysis for SCLC-related clinical assessment, treatment, short-term effects, and outcome. Further studies are required to provide a detailed description of SCLC and anti-GABABR encephalitis, clinical characteristics, long-term prognoses, and anticancer treatment response rates of SCLC and anti-GABABR encephalitis.

At follow-up in the present study, 18 patients had died due to tumor progression or chemotherapy-related infection. Patients with SCLC and anti-GABABR encephalitis had a relatively poor prognosis. Few studies have focused on treatment responses and prognoses in patients with SCLC and anti-GABABR encephalitis. Previous studies have revealed that most patients with anti-GABABR encephalitis without cancer responded well to immunotherapy; however, patients with tumors have been reported to have lower survival rates. The presence of status epilepticus or refractory seizures did not significantly affect survival. The prognosis might be worse for patients who were older at disease onset. A large number of additional cases with long-term follow-up data to identify the optimal treatment and prognosis for this uncommon disorder should be addressed in more detail in the future.

In conclusion, SCLC and anti-GABABR encephalitis is a relatively rare disease. This disease in Chinese patients mostly affects middle-aged to elderly men and the major manifestations are seizures, cognitive impairment, and psychiatric disorders. Patients frequently express additional autoantibodies in the serum, most commonly anti-Hu, anti-Yo, NMDAR, SOX1, ANA, and TPO antibodies. MRI results reveal unilateral or bilateral medial temporal lobe and hippocampal changes, but negative findings do not exclude the disease possibility. Clinicians should make an appropriate early diagnosis and initiate immune therapy and possible antineoplastic therapy as soon as possible. Patients with SCLC and anti-GABABR encephalitis have a relatively poor prognosis. Additional studies are needed to provide more convincing data to establish a definite diagnosis and treatment strategy for clinical practice.

ACKNOWLEDGMENTS

The authors thank physicians, nurses and patients for their participation in the study.

CONFLICT OF INTEREST

The authors have declared that no conflict of interest exists.

ORCID

Yuhui Zhang https://orcid.org/0000-0002-4373-1845
Xiaokai Feng https://orcid.org/0000-0002-1521-9545

REFERENCES

1. Vincent A, Buckley C, Schott JM, Baker I, Dewar BK, Detert N, et al. Potassium channel antibody-associated encephalopathy: a potentially immunotherapy-responsive form of limbic encephalitis. Brain. 2004;127(Pt 3):701–12.
2. Gozzard P, Woodhall M, Chapman C, Nibber A, Waters P, Vincent A, et al. Paraneoplastic neurologic disorders in small cell lung carcinoma: a prospective study. Neurology. 2015;85(3):235–9.
3. Lancaster E, Lai M, Peng X, Hughes E, Constantinescu R, Raizer J, et al. Antibodies to the GABA(B) receptor in limbic encephalitis with seizures: case series and characterisation of the antigen. Lancet Neurol. 2010;9(1):67–76.
4. Hofbäger R, Titaufar MJ, Sabater L, Dome B, Roszas A, Hegeduš B, et al. Encephalitis and GABAB receptor antibodies: novel findings in a new case series of 20 patients. Neurology. 2013;81(17):1500–6.
5. Boronat A, Sabater L, Saiz A, Dalmau J, Graus F. GABA(B) receptor antibodies in limbic encephalitis and anti-GAD-associated neurologic disorders. Neurology. 2011;76(9):795–800.
6. Dalmau J, Rosenfeld MR. Autoimmune encephalitis update. Neuro Oncol. 2014;16(6):771–8.
7. Leyboldt F, Armanagu T, Dalmau J. Autoimmune encephalopathies. Ann N Y Acad Sci. 2015;1338:94–114.
8. Kim TJ, Lee ST, Shin JW, Moon J, Lim JA, Byun JL, et al. Clinical manifestations and outcomes of the treatment of patients with GABAB encephalitis. J Neuroimmunol. 2014;270(1–2):45–50.
9. Quinn TJ, Dawson J, Walters MR, Lees KR. Reliability of the modified Rankin scale: a systematic review. Stroke. 2009;40(10):3393–5.
10. Qiao S, Zhang YX, Zhang BJ, Liu RY, Lai QL, Chen LH, et al. Clinical, imaging, and follow-up observations of patients with anti-GABAB receptor encephalitis. Int J Neurosci. 2017;127(5):379–85.
11. Chen X, Liu F, Li JM, Xie XQ, Wang Q, Zhou D, et al. Encephalitis with antibodies against the GABAB receptor: seizures as the most common presentation at admission. Neurol Res. 2017;39(11):973–80.
12. Cui J, Bu H, He J, Zhao Z, Han W, Gao R, et al. The gamma-aminobutyric acid-B receptor (GABAB) encephalitis: clinical manifestations and response to immunotherapy. Int J Neurosci. 2018;128(7):627–33.
13. Lin J, Li C, Li A, Liu X, Wang R, Chen C, et al. Encephalitis with antibodies against the GABAB receptor: high mortality and risk factors. Front Neurol. 2019;10:1030.
14. Zhao XH, Yang X, Liu XW, Wang SJ. Clinical features and outcomes of Chinese patients with anti-gamma-aminobutyric acid B receptor encephalitis. Exp Ther Med. 2020;20(1):617–22.
15. Qin W, Wang X, Yang J, Hu W. Coexistence of anti-SOX1 and anti-GABAB receptor antibodies with autoimmune encephalitis in small cell lung cancer: a case report. Clin Interv Aging. 2020;15:171–5.
16. Dogan Onugoren M, Deuretzbacher D, Haensch CA, Hagedorn HJ, Halve S, Isennmann S, et al. Limbic encephalitis due to GABAB and AMPA receptor antibodies: a case series. J Neurol Neurosurg Psychiatry. 2015;86(9):965–72.
17. Jeffery OJ, Lennon VA, Pittock SJ, Gregory JK, Britton JW, McKeon A. GABAB receptor autoantibody frequency in service seroconversion. Clin Imaging. 2015;39(1):67.
18. Benarroch EE. GABAB receptors: structure, functions, and clinical implications. Neurology. 2012;78(8):578–84.
19. Ulrich D, Bettler B. GABAB receptors: synaptic functions and mechanisms of diversity. Curr Opin Neurobiol. 2007;17(3):298–303.
20. Collingridge GL, Isaac JT, Wang YT. Receptor trafficking and synaptic plasticity. Nat Rev Neurosci. 2004;5(12):952–62.
21. Titaufar MJ, Soffietti R, Dalmau J, Gillius NE, Giometto B, Graus F, et al. Screening for tumours in paraneoplastic syndromes: report of an EFNS task force. Eur J Neurol. 2011;18(1):e19–e13.
22. Ances BM, Vitaliani R, Taylor RA, Liebeschid DS, Voloschin A, Houghton DJ, et al. Treatment-responsive limbic encephalitis identified by neuropot antibodies: MRI and PET correlates. Brain. 2005;128(Pt 8):1764–77.
23. Graus F, Titaufar MJ, Balu R, Benseler S, Bien CG, Cellucci T, et al. A clinical approach to diagnosis of autoimmune encephalitis. Lancet Neurol. 2016;15(4):391–404.
24. Zuliani L, Graus F, Giometto B, Bien C, Vincent A. Central nervous system neuronal surface antibody associated syndromes: review and guidelines for recognition. J Neurol Neurosurg Psychiatry. 2012;83(6):638–45.
25. Nosadini M, Mohammad SS, Ramanathan S, Brilot F, Dale RC. Immune therapy in autoimmune encephalitis: a systematic review. Expert Rev Neurother. 2015;15(12):1391–419.

26. Lancaster E, Martinez-Hernandez E, Dalmau J. Encephalitis and antibodies to synaptic and neuronal cell surface proteins. Neurology. 2011;77(2):179–89.

27. Dubey D, Samudra N, Gupta P, Agostini M, Ding K, van Ness PC, et al. Retrospective case series of the clinical features, management and outcomes of patients with autoimmune epilepsy. Seizure. 2015;29:143–7.

28. Shen K, Xu Y, Guan H, Zhong W, Chen M, Zhao J, et al. Paraneoplastic limbic encephalitis associated with lung cancer. Sci Rep. 2018;8(1):6792.

29. Guan HZ, Ren HT, Yang XZ, Lu Q, Peng B, Zhu YC, et al. Limbic encephalitis associated with anti-gamma-aminobutyric acid B receptor antibodies: a case series from China. Chin Med J (Engl). 2015;128(22):3023–8.

How to cite this article: Jiang C, Zhu M, Wei D, Duan H, Zhang Y, Feng X. SCLC and anti-GABABR encephalitis: A retrospective analysis of 60 cases in China. Thorac Cancer. 2022;13:804–10. https://doi.org/10.1111/1759-7714.14323