

Case report of the treatment and experience of mental disorders due to chronic viral encephalitis

Mingming Zheng,^{1,2,3} Ran Bi,⁴ Yezhe Lin,⁵ Cuizhen Zhu,^{1,2,3} Daomin Zhu^{1,2,3}

To cite: Zheng M, Bi R, Lin Y, *et al.* Case report of the treatment and experience of mental disorders due to chronic viral encephalitis. *General Psychiatry* 2021;**34**:e100340. doi:10.1136/gpsych-2020-100340

Received 16 July 2020
Revised 12 October 2020
Accepted 29 November 2020

ABSTRACT

Viral encephalitis is a common clinical condition. Its clinical manifestations are variable and include neurological symptoms and psychiatric abnormalities, which makes clinical diagnosis and treatment difficult. To date, there are only a few reported cases on mental symptoms of chronic viral encephalitis. We present a case of a 16-year-old male patient who was previously hospitalised and diagnosed with schizophrenia and treated with aripiprazole 15 mg/day but failed to respond. The patient was then given antiviral therapy and recovered after 2 weeks. Clinicians should be aware of the possibility that chronic mental disorders could be caused by viral encephalitis. In the future, diagnosis of chronic functional mental disorders should include viral encephalitis in the differential diagnosis.

INTRODUCTION

Viral encephalitis (VE) is an infectious disease of the central nervous system (CNS), which refers to inflammation involving the meninges and brain parenchyma.¹ Studies have shown that the annual incidence of VE is approximately 3.5/100 000 to 7.4/100 000.² The clinical manifestations vary as different parts of the CNS are involved. The prognosis is generally good, but a few cases with sudden onset and rapid progress either end up with various neurological sequelae or result in death. VE is one of the diseases that has immense public health importance around the world.³ The clinical manifestations of mental disorders caused by VE, including neurological and/or psychiatric symptoms, are complicated. The majority of cases are sporadic and consist of young and middle-aged people with acute or subacute onset and a history of infection. No seasonality has been observed.

In clinical practice, it is necessary for the clinician to master and carefully identify the symptoms of mental disorders caused by VE to reduce the rate of misdiagnosis and improve the efficiency of diagnosis. At present, there are only a few reported cases of psychiatric symptoms due to chronic VE; the purpose of this case report is to remind the clinician

to include VE in the differential diagnosis of chronic functional mental disorders.

CASE HISTORY

Case description

The patient is a 16-year-old boy having symptoms of paranoid ideation, anxiety, fear and hallucination for a period of 3 months. He was diagnosed with schizophrenia at the local psychiatric hospital and treated with aripiprazole 15 mg/day since 6 June 2019. After 14 days of treatment, the patient developed symptoms of stiff limbs, difficulty in limb moving and flushing. The patient was later admitted to our hospital owing to 3 months of paranoid ideation, auditory hallucinations, headache and 3 days of limb rigidity. Physical examination showed facial flushing, uncoordinated gait, increased muscle tone and Babinski sign presented on the right side. These are important positive signs, which may hint the diagnosis of organic brain disease. Clinicians should be aware of the possibility that chronic mental disorders could be caused by physical disease.² The auxiliary examination revealed that the patient's blood routine, biochemical analysis, electrocardiogram (ECG), brain topography, electroencephalographic (EEG) and brain MRI were normal, and the serum drug concentration of aripiprazole was 22.48 µg/L. Psychiatric examination found that patient had auditory hallucinations, loosening of association, delusion, inattention and lack of self-insight. The patient was then diagnosed with schizophrenia again and treated with haloperidol 1.25 mg intramuscular injection two times per day and promethazine 12.5 mg intramuscular injection two times per day. However, the patient's symptoms of anxiety and fear worsened in 2 days, alongside agitated and violent behaviour. Treatment was adjusted to haloperidol 2.5 mg intramuscular injection two times per day and promethazine 25 mg intramuscular injection two times per day. After 2 days,



© Author(s) or their employer(s) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Department of Sleep Disorders, Affiliated Psychological Hospital of Anhui Medical University, Hefei, Anhui, China

²Hefei Fourth People's Hospital, Hefei, Anhui, China

³Anhui Mental Health Center, Hefei, Anhui, China

⁴Schulich Interfaculty Program in Public Health, Western University, London, Ontario, Canada

⁵Department of Psychiatry, University of Rochester Medical Center, Rochester, NY, USA

Correspondence to

Dr Cuizhen Zhu;
zhucuzhenhi@163.com

Dr Daomin Zhu;
Hfsyzdm7778@163.com

the patient's agitated behaviour improved, but he developed symptoms of unsteadiness while standing, sweating and headaches. In addition, there was no improvement of the psychiatric symptoms, and tolerance to low-dose antipsychotic drugs remained poor.

After communicating with the family members, we performed cerebrospinal fluid (CSF) examination, which revealed that the number of white cell count in CSF was $0.07 \times 10^9/L$. Combined with the previous symptoms of headache, flushing, increased muscle tone and Babinski sign presented on the right side, these results were consistent with CNS infection. Thus, antipsychotic treatment was discontinued and a ganciclovir 0.3 g intravenous injection, two times per day, was given instead.

After 2 weeks of antiviral treatment, CSF examination was carried out again and revealed the CSF leucocyte count to be $0 \times 10^9/L$. The patient's headache disappeared, muscle tone returned to normal and Babinski sign was absent on the right side. His psychiatric symptoms including auditory hallucinations and delusions disappeared as well, and self-insight was present. Case discussion modified the diagnosis as 'mental disorder caused by viral encephalitis'. Then, antiviral treatment was discontinued and mecobalamin 0.5 mg, three times per day, was started. After 3 weeks of observation in the hospital, the patient recovered and was discharged.

After 1 month, the patient revisited the hospital for follow-up appointment. Physical examination, laboratory test and mental examination were normal. Three months later, the patient reported normal social function and excellent academic performance in a telephone follow-up.

Diagnosis of mental disorders caused by VE

The patient's symptoms met the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria applicable to VE. We established the diagnosis of suspected mental disorders caused by VE, excluding anaemia and iron deficiency, diabetic neuropathy, vitamin B₁₂ and folic acid deficiency, according to laboratory test results. The patient's renal function (urea nitrogen and creatinine), thyroid function (thyroid stimulating hormone, serum free triiodothyronine 3 (FT3), FT4, triiodothyronine (T3) and thyroxine (T4)), liver function (aspartate aminotransferase, alanine aminotransferase, bilirubin, direct bilirubin and γ -glutamyl transpeptidase) and brain MRI were all within normal ranges. The patient had no previous history of smoking, alcohol drinking, drug or caffeine abuse.

Clinical treatment of mental disorders caused by VE

According to the treatment principle of CNS infection, the primary management is the aetiologic treatment. At the same time, the symptomatic treatment is used to alleviate pathological changes of the brain tissues and restore brain function, and specific treatments such as antiviral medication can be given to reduce intracranial pressure and cerebral oedema, control convulsions and fever and

improve brain metabolism.³ Antipsychotic drugs were discontinued due to the prominent extrapyramidal side effects. After treatment with the antiviral ganciclovir, the patient's psychiatric and physical symptoms disappeared. Finally, the patient recovered and was discharged home after 2 weeks.

DISCUSSION

According to the patient's clinical manifestations, laboratory test results, treatment process and patient's outcome, this case met the DSM-5 criteria applicable to VE. Previous studies have suggested that mental disorders caused by VE often present with abnormal EEG, brain MRI and CSF examination. However, in this case, no apparent abnormality was detected in EEG, brain MRI and CSF examination, only a slight increase of white cells can be seen in CSF. Due to the extrapyramidal side effects, the antipsychotic treatment was discontinued, and then the extrapyramidal symptoms improved, which was consistent with 'other drug-induced movement disorders' (ICD-10-CM Code G25.79) (<https://icd.codes/icd10cm/G2579#>).

The improvement of the patient's condition with antiviral treatment is in line with the characteristics of VE. The clinical process supported the diagnosis of mental disorders caused by VE. Owing to equipment limitation, CSF immunological examination was not performed. It has been shown that severe insult to the central immune system may trigger different diseases; CSF immunological examination can provide aetiological diagnosis and aid in precise treatment.⁴ The proportion of mental disorders caused by VE is 70%, but most of the patients' medical history reports are not accurate, and the infection history and the history of disease progression could only be obtained after repeated questioning. The precursor symptoms are often ignored as well.⁵ The study discovered that about 81% of patients with VE have varying degrees of mental disorders and mental symptoms are seen in various stages of the disease course.⁶ These symptoms are easily confused with schizophrenia, and the misdiagnosis rate is as high as 45%. The symptoms of organic mental disorders caused by VE mainly include cognitive dysfunction, attention disorder, perceptual disorder, thinking content change and mood and personality change. It is different from functional mental disorders, in that, it is accompanied by different levels of disorders of consciousness.⁷ However, the early presentation of disturbance of consciousness in some patients cannot be readily recognised; in addition, the prominent mental symptoms cover up other symptoms of VE.⁸

The characteristics of VE, mainly seen in young adults, are sporadic and of no obvious seasonality. The onset of disease is usually acute or subacute. Although the aetiologies of acute and chronic encephalitis are different, it is difficult to distinguish the two diseases by clinical symptoms, which requires neurological examination and CSF analysis to establish clinical diagnosis. According to our observation, some psychiatrists do not pay enough

attention to the neurological examination, meanwhile some neurological symptoms are often obscure or not manifested. Most of them have a history of infection. The psychiatric symptoms of this disease are diverse and complex, mostly uncoordinated psychomotor excitability or suppression, often accompanied by auditory hallucinations, illusions, victimised delusions and relationship delusions. At present, there are only a few reported cases of chronic VE with prominent mental symptoms.

The patients in this study presented with a chronic onset, with psychiatric symptoms as the prominent manifestation. No typical signs of infection, such as fever, headache and nerve injury, were found in the early stages of the disease, thus led to misdiagnosis. This case suggests that physicians should take VE into consideration when diagnosing chronic functional mental disorders. At present, since only a few reports on mental disorders caused by chronic VE are available, this case provides new insights for doctors to diagnose similar cases in the future.

Contributors MZ was responsible for the study design, literature searches and manuscript writing. CZ was involved in evolving the ideas, editing and manuscript writing. DZ and YL were involved in editing the manuscript. RB was involved in editing and submitting the manuscript. All authors have contributed to and have approved the final manuscript.

Funding This case report was funded by Shanghai Key Laboratory of Psychotic Disorders Open Grant (grant number: 13dz2260500).

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

- 1 Shao N, Li F, Nie K, *et al.* Taqman real-time RT-PCR assay for detecting and differentiating Japanese encephalitis virus. *Biomed Environ Sci* 2018;31:208–14.
- 2 Yang H, Xu H, Li Q, *et al.* Study of brain morphology change in Alzheimer's disease and amnesic mild cognitive impairment compared with normal controls. *Gen Psychiatr* 2019;32:e100005.
- 3 Orlovska-Waast S, Köhler-Forsberg O, Brix SW, *et al.* Cerebrospinal fluid markers of inflammation and infections in schizophrenia and affective disorders: a systematic review and meta-analysis. *Mol Psychiatry* 2019;24:869–87.
- 4 Wang Y, Hu Z, Ju P, *et al.* Viral vectors as a novel tool for clinical and neuropsychiatric research applications. *Gen Psychiatr* 2018;31:e000015.
- 5 Tyler KL. Acute viral encephalitis. *N Engl J Med* 2018;379:557–66.
- 6 Casella G, Tontini GE, Bassotti G, *et al.* Neurological disorders and inflammatory bowel diseases. *World J Gastroenterol* 2014;20:8764–82.
- 7 Roohi-Azizi M, Azimi L, Heysiattalab S, *et al.* Changes of the brain's bioelectrical activity in cognition, consciousness, and some mental disorders. *Med J Islam Repub Iran* 2017;31:307–12.
- 8 Bechter K. Encephalitis, mild encephalitis, neuroprogression, or Encephalopathy-Not merely a question of terminology. *Front Psychiatry* 2018;9:782.



Cuizhen Zhu obtained a master's degree in psychiatry from the West China Medical College of Sichuan University, China, in 2011, and a doctorate degree in psychiatry from Shanghai Jiao Tong University School of Medicine in China in 2018. She is currently an attending doctor and is working at the Department of Science and Education of the Anhui Mental Health Center, China. Her main research interests include pain, depression, and intestinal flora.