The underlying mechanism of Guillain-Barré syndrome in a young patient suffered from Japanese encephalitis virus infection: a case report

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Case Report

Keywords: Guillain-Barré syndrome, Japanese encephalitis virus, Vaccination, Pathogenesis

Posted Date: May 31st, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1689342/v1

Abstract

Background: The presentation of Guillain-Barré syndrome (GBS) suffered from Japanese encephalitis virus (JEV) is uncommonthoughthe clusters of GBS cases were observed in Chinain 2018. The underlying mechanism was not clarified especially in individuals with JE vaccination in childhood.

Case presentation: Here we reported a patient suffered from acute flaccid paralysis (AFP) involvement with four extremities and respiratory muscles, while showed normal images by brain and spine magnetic resonanceimaging (MRI). Electrophysiology examination displayed slowed conduction speed of motor nerves and declined amplitude of evoked velocity. GBS was finally considered related to JEV verified by both positive anti-JEV immunoglobulin M antibody and positive immunoglobulin G antibody in serum. Unfortunately, he died after declining mechanical ventilator and intravenous immunoglobulin at 36th day of illness onset. We also made a review of related cases reported previously and discussed the underlying mechanism.

Conclusion: JEV infection-associated GBS was an unusual clinical appearance. We should pay attention to the atypical manifestations of JEV infection and explore possible pathogenesis behind particular individuals.

Background

Japanese encephalitis (JE) is responsible for 30,000–50,000 cases every year and 25–30% mortality[1]. JE is a mosquito-borne zoonotic disease mainly occurring in eastern and southern Asia, caused by the Japanese encephalitis virus (JEV). The prevalence of JE has already obviously decreased by vaccination in China. The genotype 1 of JEV is currently circulating in China. The typical clinical manifestation include fever, headache, vomiting, neurological symptoms, coma, convulsions, and respiratory failure[2]. Most of cases with JEV-associated acute flaccid paralysis (AFP)met the case-definition of Guillain-Barré syndrome (GBS), whilea small number of cases werethought to have viral myelitis[3]. Here we reported a young man suffered from JEV, who was featured by GBS after several days fever. The underlying mechanism is worth further study.

Case Presentation

A 18-year young man, firstly complained muscle weakness of bilateral lower limbs, followed by fever, dizziness and muscle weakness of the neck and bilateral upper limbs. At 5th day of illness onset (on October 3,2018), he felt dyspnea without convulsion and impaired consciousness and was referred to the emergency room of our hospital. He abruptly presented deteriorate respiratory distress and adopted invasive ventilator in emergency room of our hospital on October 3,2018. The brain magnetic resonance imaging (MRI) was normal (Fig. 1C).Blood tests revealed elevated white blood cell counts (11.79 x 10^9/L) and neutrophils count (9.56 x 10^9/L). Positive anti-JEV immunoglobulin(Ig) M antibody(EEB-IgM, Enzyme immunoassay test kit, Shanghai B&C Biological Technology Company) was detected in serum. Unexpectedly, high level anti-JEV IgG antibody (JE detect ™IgG, ELISA, InBios) was also be detected in serum. The cerebrospinal fluid (CSF) showed elevated the leukocyte counts (49×10^6/L, lymphocytic pleocytosis) and protein level (814 mg/L, normal range:100–600mg/L), while anti-JEV IgM for CSF sample was undetected. He was from a rural area in Liaoning province of China where JEV is epidemic in the summer of 2018. He has a definite history of twice JE vaccination in childhood scheduled at eight-months old and at two years old respectively. He adopted methylprednisone (500mg per day) followed by reduced dosage treatment.

Ten days later, his condition partly improved. He refused to continue invasive ventilator though he still had respiratory disturbance with elevated PaCO2 58.0mmHg and decreased PaO2 72.0mmHg (at intranasal oxygen therapy of 10L/min). Despite clear consciousness, proper cognition and functional bladder or bowel, he had markedly disturbances in coughing, articulation and swallowing with disappeared pharyngeal reflex and disabled soft palate movement, which indicated the injured cranial nerves(bulbar paralysis). He could only use pectoral type breathing without any thoracic breathing, which suggested the respiratory myoparalysis. We examined weakened muscle power in left upper limb (grade 4/5), right upper limb (grade 2/5) and bilateral lower limb (grade 2/5), which were already better than before. His muscle tone of four extremities was decreased. Deep tendon reflexes were decreased without pathological reflex and sensations disturbance.

Auscultation showed purring sound in bilateral lungs. Lung computed tomography (CT) indicated consolidation in the lower lobe of the right lung (Fig. 1A). Blood test showed negative antibodies for Epstein-Barre virus, herpes simplex virus, varicella-zoster virus, cytomegalovirus and human immunodeficiency virus. At 24th day of illness onset, both repeated brain MRI and spine MRI showed normal (Fig. 1D, 1E). He did not accept lumbar puncture again. The detection for anti-gangliosides antibodies was unavailable in our hospital. At 27th day of illness onset, electrophysiology examination showed abnormal discoveries including prolonged latency of H reflex in bilateral tibial nerves, declined amplitude of evoked velocity in right median nerve and slowed motor conduction in the right tibial nerve, while the sensory nerves conduction were normal.JEV infection-associated GBS was considered, which matched with Brighton criteria level 1. He declined intravenous immunoglobulin and mechanical ventilator. Despite the application of broad-spectrum antibiotics and sputum clearance with bronchoscopy, he developed progressive dyspnea, deteriorated carbon dioxide retention and respiratory acidosis (PaCO2 120 mmHg; PH 7.185). Lung CT indicated aggravated consolidation in the lower lobe of bilateral lung, mainly in the right lung (Fig. 1B). As a result of refusing mechanical ventilator again and tracheotomy, the patient died on the 36th day of illness onset.

We made a literature review of a total of 85 cases of JEV-associated AFP reported previously (Table 1), 73 cases were considered as GBS. There were 4 cases with reported a history of previous JE vaccination.

Table 1
Clinical features in patients with acute flaccid paralysis caused by Japanese encephalitis virus

Case numbers	Reference number/ year of publication	Age(yr)	Gender (M/F)	Area of report	Clinical presentations	Encephalitis	Brain MRI	JE vaccination	Treatment	Outcome D/S/N
21	[4]/1994	6–58	18/3	India	GBS	No	NM	NM	GC or MV	4/15/2
1	[5]/2014	23	1/0	China	GBS	No	Normal	No	IG + GC	S
1	[13]/2015	14	1/0	India	GBS	Yes	Abnormal	NM	IG + MV	S
1	[3]/2007	22	1/0	Taiwan	AFP	No	Normal	Yes	GC + MV	S
12	[12]/1998	3–15	9/3	Vietnam	AFP including GBS(1)	Yes(4)	NM	NM	No MV	S
1	[14]/2021	43	0/1	China	GBS	Yes	Abnormal	NM	IG + GC + MV + PAIA	S
47	[8]/2020	*59 (24–63)	26/21	China	GBS	39	NM	Yes(2)	IG(28) + GC(47) + MV(44)	S
1	PR	18	1/0	China	GBS	No	Normal	Yes	GC + MV	D
GBS,Guillain-Barre syndrome; AFP, acute flaccid paralysis										
NM, not mentioned; PR, present report										
D,died;S,survived; N,no follow up										
IG,immunoglobulins; GC,glucocorticoid; MV,mechanical ventilator; PAIA,protein A immunoadsorption										
*Median age (IQR)										

Discussion And Conclusion

JEV infection was an important etiology of GBS in endemic regions[4]. Most patients of JEV-associated GBS reported previously had not received the JE vaccination before[5].Our patient is quite similar to the case who also had received JE vaccination in childhood reported by Chung CC, et al[3]. The high ratio of IgG to IgM has a possible hint of distinction between rapid seroconversion of IgM and IgG due to acute infections and IgG antibodies deriving from previous vaccine virus. All available vaccines belong to the JEV genotype 3 strain. A partial cross-protection between JEV genotype 1 strain and JEV genotype 3 strain[1, 6]and the inferior protective efficacy due to inadequate neutralizing antibodies level probably explain why JE vaccination could not provide a complete protection.

Although Liaoning province had a low prevalence of JE[7], there was a outbreak consisted of 69 cases with a 30.4% fatality rate in the summer of 2018, which was identical to the prevalence of JEV infection in the north of Ningxia in 2018[8]. JEV genotype 1 was the pathogen in this outbreak. None of children cases was reported, which indicated the JEV vaccine is still effective. Our patient was confirmed the JEV infection by positive anti-JEV IgM antibody in serum, which is a sensitive, specific and an early indicator of JEV infection. His characteristic clinical manifestation included weakness of four extremities and respiratory myoparalysis accompanied with several cranial nerves involvement. Electrophysiology examination suggested decreased evoked potential amplitude of motor nerves and slowed conduction speed of motor nerves. Acute disseminated encephalomyelitis and acute transverse myelitis were excluded for normal images in the brain and spinal MRI[9–10]. Glucocorticoid-induced myopathy was also ruled out due to his muscle paralysisthe earlier than glucocorticoid application[11]. We also need to differentiate between anterior horn cell myelitis[3, 12] and GBS[4, 13–14]. Viral myelitis tends to have a fever and a moderate pleocytosis in the CSF, while GBS typically presents a prodromal infection 1–2 weeks ago and analbuminocytologic dissociation in the CSF. However, anterior horn cell myelitis was not supported by his normal MRI of the spinal cord and slowed motor nerves conduction speed. Therefore, GBS was finally considered. Molecular mimicry, antiglycolipid autoantibody and immune complexes were implicated in the pathogenesis of GBS, which is the acute or subacute demyelination of peripheral nerves fibers and axonal degeneration[15–16]. The mortality of GBS is 2–10%[17]. The underlying mechanism for the clusters of GBS cases in 2018 was unclear [8]. In our case, the presence of high level anti-JEV IgG in early serum provided the possibility that

antibody-dependent enhancement (ADE) between pre-existing antibody targeting genotype 3-derived JE vaccine and subsequent genotype 1 virus infection may play a role in the development of GBS[18].

In summary, JEV combined with GBS showed an increasing trend in recent years. Rapid diagnosis and early application of intravenous immunoglobulin or plasma exchange will be beneficial to GBS while glucocorticoid is not recommended[17–19]. JEV genotype 1 is currently circulating in China[20]. The longevity and titres of protective antibody responses induced by JE vaccine depend on the type of vaccine, the number of doses and immune status of hosts. Up to now, there is no standardized protocol for neutralization test and the commercial kit for neutralizing antibodies detection is unavailable. Therefore, the protective role of genotype 3-derived JE vaccine in preventing genotype 1 virus infection needs additional attention.

Abbreviations

AFP: acute flaccid paralysis; JE: Japanese encephalitis; GBS: Guillain-Barré syndrome; MRI: magnetic resonance imaging; JEV: Japanese encephalitis virus; CSF: cerebrospinal fluid; CT: computed tomography; Ig: immunoglobulin；ADE: antibody-dependent enhancement;

Declarations

Ethics approval and consent to participate:

Not applicable.

Consent to publication:

The patient has provided written informed consent for the publication of this report.

Availability of data and materials:

All data generated or analyzed during this study are included in this published article.

Competing interests:

The authors declare that they have no competing interests.

Funding:

This work was supported by the science and technology foundation of Shenyang (China) of Ying Wen (18-014-4-30) in the First Affiliated Hospital of China Medical University. Ying Wen made the conception and design of the work and the fund supports patients to complete antibody testing

Authors' Contributions

WY and YJ made the conception and design of the work. LS helped to collect the data of the case. LS, W-JY and WY wrote the manuscript. All authors carried out final approval of the version to be published.

Acknowledgements:

The authors extend their sincere thanks to all participants in diagnosing and treating this case.

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Figures

Figure 1

The radiographs in this case

A. At 19th day of illness onset, lung CT indicated consolidation in the right lung.

B. At 24th day of illness onset, lung CT indicated aggravated consolidation in the lower lobe of bilateral lung adjacent to the pleura, mainly in the right lung.

C.At 5th day of illness onset, brain MRI (T2 weighted image) was normal.

D. At 24th day of illness onset, enhanced brain MRI was normal.

E. At 24th day of illness onset, spine MRI (T2 weighted image) was normal.