Sociedad Neurológica Argentina
Filial de la Federación Mundial de Neurología

Neurología Argentina

www.elsevier.es/neurolarg

Case Report

Bickerstaff's brainstem encephalitis with monospecific anti-GT1a antibody: A subtype of Guillain–Barre syndrome

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ARTICLE INFO

Article history:
Received 28 May 2020
Accepted 10 November 2020
Available online 3 February 2021

Keywords:
Bickerstaff's
Encephalitis
Anti-GT1a
Anti-GQ1b
Autoimmune

ABSTRACT

Bickerstaff's brainstem encephalitis is an uncommon post-infectious causing autoimmune neurological disease, which is usually associated with the GQ1b antibody. We described a young man with recent upper respiratory tract infection, who presented with sudden onset of left eye ptosis with internuclear ophthalmoplegia, staccato speech with left-sided hemiplegia but with normal deep tendon reflexes. The cerebral imaging was normal and cerebrospinal fluid analysis produced no cyto-albuminologic dissociation, negative result of tuberculosis culture and virus PCR. He was tested positive for serum GT1a IgG antibody. We discussed this case as the neurological presentation was severe, in the presence of GT1a IgG antibody.

Encefalitis troncoencefálica de Bickerstaff con anticuerpos monoespecíficos anti-GT1a: un subtipo del síndrome de Guillain-Barré

Palabras clave:
Encefalitis de Bickerstaff
Anti-GT1a
Anti-GQ1b
Autoinmune

RESUMEN

La encefalitis troncoencefálica de Bickerstaff es una enfermedad neurológica postinfecciosa autoinmune rara, que está normalmente asociada al anticuerpo GQ1b. Describimos el caso de un varón joven con infección reciente del tracto respiratorio superior, que acudió con aparición súbita de ptosis en el ojo izquierdo con oftalmoplejía internuclear, habla entrecortada con hemiplejía izquierda, aunque con reflejos tendinosos profundos normales. La imagen cerebral fue normal, y el análisis del líquido cefalorraquídeo no produjo disociación

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https://doi.org/10.1016/j.neuarg.2020.11.002

cito-albuminológica, siendo negativo el resultado del cultivo para la detección de tuberculosis y la PCR para la presencia de virus. El resultado de anticuerpos séricos GT1a IgG fue positivo. Debatimos este caso, dado que la presentación neurológica fue grave, en presencia de anticuerpos GT1a IgG.

Introduction

Miller Fisher syndrome (MFS) is recognised as a clinical triad of acute onset of external ophthalmoplegia, ataxia and areflexia.[1] Similarly, patients with Bickerstaff's brainstem encephalitis (BBE) shared features of MFS such as ophthalmoplegia and ataxia though BBE patients will have encephalopathy and hyperreflexia.[1–3] The fact that BBE and MFS share a common autoantibody i.e. BBE (GQ1b IgG) and MFS (GQ1b/GT1a IgG) suggests that they are closely related.[4] Here, we highlighted a case of BBE with unusual neurological manifestations but negative GQ1b antibody.

Clinical case

A thirty-one-year-old gentleman with normal premorbid presented with a sudden onset of headache associated with left-sided body weakness and blurred vision. He initially denied history of fever and antibiotic usage. There was no history of diarrhoea, vomiting, eye pain and photophobia. There was neither recent travel nor ill-contact.

The initial general physical examination showed that he had full conscious level, stable vital signs and normal temperature. His speech was fragmented with interrupted flow, which was suggestive of staccato speech. Neurological examinations revealed left-side upper and lower limbs were hypotonia, reduced power (Medical Research Council (MRC) muscle score of 2), preserved deep tendon reflexes, and downgoing plantar response. There was no weakness at his neck. Sensory, proprioception and vibration were intact and equal bilaterally. The cranial nerve examinations were suggestive of a left-sided pathology: a partial left-sided eyelid ptosis with internuclear ophthalmoplegia and presence of nystagmus upon lateral gaze. There was no presence of relative afferent pupil defect. Both pupils were equal and reactive to light. There were no features suggestive of Horner syndrome. The ipsilateral upper motor neuron facial nerve palsy with absent gag reflex were observed. Other cranial nerves were intact. We were not able to perform cerebellar examinations and gait due to the hemiplegia. Kernig sign and neck stiffness were absent. Other systemic examinations were unremarkable.

Routine blood tests were all within normal ranges: total white blood count 11.0×10^9/L with absolute neutrophil 5.77×10^9/L and absolute lymphocyte 4.09×10^9/L. The antinuclear antibody was 320 (negative if reference range < 80). The double-stranded DNA antibody was negative and complement (Complement 3 and 4) level were within normal range. Thrombophilia screening was negative. Screening for human immunodeficiency virus, hepatitis B and C were non-reactive. The electrocardiogram showed a normal sinus rhythm. The cerebral computed tomography (CT) with angiogram was normal, and same goes for magnetic resonance imaging (MRI) brain.

He was first treated as brainstem infarct in view of his acute presentation. We were not able to extract the history of recent infection and apart from this, there was no sign of infection clinically. Therefore, antiplatelet and statin were started, with supportive treatment such as Ryle's tube insertion and referral to rehabilitation team.

On day three of admission, his Glasgow coma scale was fluctuating and eventually dropped to 7/15 (E1V2M3). In view of this, he was intubated electively to secure his airway. After we ruled out cerebral oedema with pupils' size, repeated cerebral CT was performed which reported normal. Hence lumbar puncture was carried out which demonstrated an elevated cerebrospinal fluid (CSF) opening pressure of 32 cmH_2O, acellular, normal protein level 204 mg/L, normal CSF to serum glucose ratio (4.77 mmol/L: 6.02 mmol/L, ratio of 0.79). The CSF for cryptococcal antigen, viral PCR, acid-fast-Bacilli and culture were negative. In view of clinical suspicion, we proceeded to analyse serum for anti-GQ1b and anti-GT1a by using EUROLINE (Multiparameter line blots test from EUROIMMUN, Germany). The EUROLINE test can detect antibodies against GM1, GM2, GM3, GD1a, GD1b, GT1b, GQ1b were conducted according to manufacturer's instruction manual. The purified antigens used were mostly isolated by affinity chromatography, or antigen extracts. Unspecific positive results were ruled out as the membrane strips do not contain superfluous proteins. Multiparameter line blots analysis indicated the use of an antigen spectrum which specifically tailored in order to increase the serological detection rate. With this technique, our patient's results came back to be positive for GT1a IgG antibody and negative for GQ1b IgG antibody.

Subsequently, we managed to find out from his brother that patient just recovered from an episode of acute tonsillitis one week prior to his presentation to us. He improved clinically after five days of Immunoglobulin (dose of 0.4 g/kg/day) infusion. We manage to wean off ventilation and patient was discharged with minimal left eye ptosis and left-sided hemiparesis after a week of treatment.

Comments

Bickerstaff's brainstem encephalitis is characterised by the triad of altered conscious level, ophthalmoplegia and ataxia though some similarities were made with MFS and GBS.[1–3]

Apart from altered consciousness, other common neurological manifestations were facial weakness, superficial sense impairment, positive Babinski's sign and internuclear ophthalmoplegia.[3] Our patient had severe limb weakness (MRC 2) which is in contrast to most of the patients who presented with milder form of limb weakness (MRC 4).[3] Majority of the patients presented with either absent or reduced deep tendon reflexes,[2,3] but our patient's deep tendon reflexes were preserved.

It was described that CSF protein concentration was raised in 56% of BBE patients and cyto-albuminologic dissociation seen in 29% of BBE patients.[3] In contrast to our case where the CSF analysis showed a normal protein concentration with no cyto-albuminologic dissociation. One-third of BBE patients will present with high-intensity areas on T2-weighted images of the brainstem, thalamus, cerebellum, and cerebrum on MRI finding which is not seen in our case.[3]

The GQ1b antibody detection is 70% in patients with BBE.[3] It was observed that patients with positive GT1a antibody and negative GQ1b antibody were more often seen to have preceding history of diarrhoea, bulbar palsy and limbs weakness; while the co-existence of GQ1b antibody was the cause of the variety of clinical features such as ophthalmoplegia, ataxia and sensory impairment.[5,6] Our case did not satisfy the clinical diagnostic criteria of pharyngeal-cervical-brachial weakness (PCB). There was also report stated that the presence of GT1a antibody were rare in the population of typical case of PCB.[5]

High performance thin layer chromatography (HPTLC) should be the gold standard immunostaining in characterising IgG antibodies against gangliosides.[7] In our case, the cross-reactivity between GT1a and GQ1b antibodies were not tested using HPTLC as we used line immunoassay (test principle is enzyme immunoassay) technique.

Conclusion

The described patient's unusual presentation with preserved deep tendon reflexes, with monospecific GT1a antibody, and cerebrospinal fluid analysis did not produce cyto-albuminologic dissociation. Anti-gangliosides antibody assay is important in differentiating subtypes of Guillain–Barre syndrome, especially in an atypical presentation.

Informed consent

Written informed consent for the paper to be published (including case history and data) was obtained from the patient/guardian for publication of this paper.

Conflict of interest

None.

REFERENCES

1. Fisher M. An unusual variant of acute idiopathic polyneuritis (syndrome of ophthalmoplegia, ataxia and areflexia). N Engl J Med. 1956;255:57–65, http://dx.doi.org/10.1056/NEJM195607122550201.
2. Petty RK, Duncan R, Jamal GA, Hadley D, Kennedy PG. Brainstem encephalitis and the Miller Fisher syndrome. J Neurol Neurosurg Psychiatry. 1993;56:201–3, http://dx.doi.org/10.1136/jnnp.56.2.201.
3. Odaka M, Yuki N, Yamada M, Koga M, Takemi T, Hirata K, et al. Bickerstaff's brainstem encephalitis: clinical features of 62 cases and a subgroup associated with Guillain-Barré syndrome. Brain. 2003;126:2279–90, http://dx.doi.org/10.1093/brain/awg233.
4. Fujii D, Manabe Y, Takahasi Y, Narai H, Omori N, Kusunoki S, et al. A case of fisher-bickerstaff syndrome overlapped by Guillain-Barré syndrome. Case Rep Neurol. 2012;4:212–5, http://dx.doi.org/10.1159/000345847.
5. Nagashima T, Koga M, Odaka M, Hirata K, Yuki N. Clinical correlates of serum anti-GT1a IgG antibodies. J Neurol Sci. 2004;219:139–45, http://dx.doi.org/10.1016/j.jns.2004.01.005.
6. Kim JK, Bae JS, Kim D-S, Kusunoki S, Kim JE, Kim JS, et al. Prevalence of anti-ganglioside antibodies and their clinical correlates with Guillain-Barré Syndrome in Korea: a nationwide multicenter study. J Clin Neurol. 2014;10:94, http://dx.doi.org/10.3988/jcn.2014.10.2.94.
7. Lardone RD, Irazoqui FJ, Nores GA. Neurological disorders-associated anti-glycosphingolipid IgG-antibodies display differentially restricted IgG subclass distribution. Sci Rep. 2020:10, http://dx.doi.org/10.1038/s41598-020-70063-5.