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Anti-GQ1b IgG antibody syndrome: a case report

Sindrom anti-GQ1b IgG protutijela: prikaz bolesnika

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Case report

Anti-GQ1b antibody syndrome is a term used for describing different conditions that are believed to have a common underlying autoimmune mechanism and positive anti-GQ1b IgG antibodies in serum. The aim was to present challenges in diagnosis and treatment of a young 31-year old patient with overlapping Guillain-Barré syndrome and Miller Fisher syndrome who was treated with plasma exchange and intravenous immunoglobulins (IVIg) which gradually resulted in almost full neurological recovery.

Prikaz bolesnika

Sindrom anti-GQ1b protutijela pojam je koji se koristi za opis različitih stanja za koja se smatra da imaju zajednički predležeći autoimuni mehanizam nastanka i pozitivna anti-GQ1b protutijela u serumu. Cilj ovog rada bio je prikazati izazove u dijagnostici i liječenju mladog 31-godišnjeg bolesnika s preklapajućim Guillain-Barréovim sindromom i Miller Fisherovim sindromom koji je liječen plazmaferezom i intravenskim imunoglobulinima (IVIg) te postupno rezultirao punim neurološkim oporavkom.

Introduction

Studies have shown that serum samples from patients with Miller Fisher syndrome (MFS), Guillain-Barré syndrome (GBS), Bickerstaff's brainstem encephalitis (BBE) and acute ophtalmoparesis often have positive anti-GQ1b antibodies [1].

These results might suggest that there is a common underlying mechanism in the pathogenesis of these diseases. The importance of these findings lies in the fact that it could bring us closer to understanding the etiological mechanisms behind these conditions, as well as to expand the well known and effective therapy used for GBS to other related disorders [1].

The aim of this case report was to present challenges in diagnosis and treatment of a young patient with overlapping GBS and MFS syndrome.

Case report

Patient information and clinical findings

A 31-year-old man presented in our emergency department due to the sudden onset of binocular diplopia. One week prior to the symptom onset he had diarrhea. Other past medical history didn't reveal any significant diseases other than psoriasis.

The physical examination was unremarkable, while the neurological examination revealed diplopia with suspected right abducens nerve palsy and right ptosis with preserved pupil function. Other than that, the patient didn't have any sensory or motoric deficits nor signs of respiratory insufficiency.

The examination was followed by the computed tomography (CT) of the brain which was unremarkable. Full blood count, serum electrolytes, urea and liver en-

zymes profile were normal. After the initial diagnostics were performed, the patient was admitted to the Department of Neurology.

During the first days after hospitalization, the clinical state continued to worsen with the progression of neurological deficit affecting multiple cranial nerves presenting in dysphagia, dysarthria, bilateral facioparesis and bilateral ophthalmoplegia, the absence of myotatic reflexes, paresthesias in the hands and feet, tetraparesis (muscle strength in the left arm and in both legs 1/5, muscle strength in the right arm 2/5). First signs of dysautonomia were observed on the 4th day after the admission when the patient developed urinary retention. Later on, he manifested other signs of autonomic dysfunction that included bradycardia, orthostatic hypotension and excessive sweating.

Diagnostic assessment

Initial negative CT scan in the emergency department was followed with intrahospital magnetic resonance (MR) of the brain and the magnetic resonance angiography (MRA) of the brain vessels on the second day after the admission. Neither showed any significant pathological findings.

The lumbar puncture was performed on the third day of the admission that showed increased protein level (0,61 g/L) with normal cell counts (2 cells) and normal CSF glucose levels.

Electroneurography performed on day 7 of the illness revealed moderate loss of motoneurons in all examined muscle groups. Neurographic analysis showed low amplitude sensory nerve action potentials (SNAP) in all sensory nerves, left ulnar nerve conduction block, absent F waves of both ulnar nerves and right peroneal nerve, as well as the absence of the H reflex and reduced nerve conduction velocity of motor fibers of the left ulnar nerve and both peroneal nerves.

Serum tests for antiganglioside antibodies were sent for analysis and came positive for anti-GD1b and anti-GQ1b.

Therapeutic interventions

Considering the clinical presentation of overlapping Miller Fisher and Guillain-Barré syndrome, treatment with plasma exchange was initiated. Despite the treatment, the clinical state continued to worsen to the state of the respiratory arrest on the 6th day of the hospitalisation due to which the patient was urgently intubated and mechanically ventilated.

In total, five plasma exchanges were given on alternate day schedule which gradually resulted in the separation of the patient from the mechanical ventilation. However, there was no other clinical improvement and since the slight progress of the motoric deficit in the arms was observed, therapy with intravenous immunoglobulin (Octagam) was indicated in dose 2g/kg over 5 days.

Follow-up and Outcomes

During the hospitalisation, intensive physiotherapy and speech therapist treatment were continuously implemented. The first signs of recovery were observed one month after admission in the reduction of facial palsy, ptosis, ophthalmoplegia, dysarthria and in the improvement of the muscle strength in the right (3/5) and in the left arm (2/5) and in both legs (3/5). Three months after the admission, the patient was discharged from the hospital and referred to stationary rehabilitation.

The first follow-up after the discharge from the hospital was two months later. The neurological exam revealed significant improvement with residual gait ataxia, dysarthria and slight weakness of the proximal musculature of both arms (motor strength in the upper extremities 3/5, motor strength in the lower extremities 4/5).

On the second follow-up, four months after the discharge, the patient was independently mobile, without speech disturbances and with the residual mild motoric deficit of the left arm (motor strength 3/5).

Discussion

The typical presentation of a patient with MFS includes a triad of symptoms: ophthalmoplegia, ataxia and areflexia. MSF is considered to be a variant of GBS since one-fourth of the patients with MFS will develop some kind of muscular weakness [2]. Furthermore, the antibodies against GQ1b that are present in most cases of MFS, can also be found in patients with GBS that present with ophthalmoplegia [1, 3, 5]. In addition, BBE, that represents features of MFS with accompanying encephalopathy and hyperreflexia, also has been associated with anti-GQ1b antibodies that can be found in up to 66 % of the cases and can respond well to intravenous immunoglobulin (IVIG) and plasma exchange [1, 4, 5].

This issue has been recognized and the term anti-GQ1b IgG antibody syndrome was formed in order to explain the nosological relationship between these conditions [2].

In overlapping cases, such as MFS and GBS, or MFS and BBE, the clinical features may cause confusion so that making a correct diagnosis can be challenging for clinicians, especially when taking into consideration that various forms of overlapping syndromes are increasingly reported [5].

In our case, the patient initially showed symptoms of MFS that progressed to GBS in the first week of the symp-

toms onset. Since there were no signs of consciousness disturbances and his electroencephalography (EEG) and brain MR were normal, we have ruled out Bickerstaff brainstem encephalitis from the diagnosis.

There are no early predictors that could be used to differentiate which patient initially diagnosed as MFS will later on develop MFS-GBS overlap syndrome. It has been noticed, however, that the progression occurs within one week from the disease onset, as it was in our case [6].

No randomized controlled trial has been performed investigating the efficacy of IVIg or plasma exchange in MFS or MFS-GBS overlap syndrome [7]. However, it is considered that extrapolating GBS data to the population of MFS patients whose disease course is complicated is justified [7].

Our patient was initially treated with plasma exchange. However, since there was no adequate response after five plasma exchanges and the slight worsening of symptoms was observed, we have indicated therapy with intravenous immunoglobulin that eventually led to almost full recovery. The trial of the combination of both treatments is already present in clinical practice for over 25 years [8]. The rationale for this treatment in patients with insufficient clinical response might be that these treatments probably have different immunomodulatory effects that may influence the treatment efficacy in individual patients [9].

The optimal management for most severe cases of GBS remains uncertain [8]. On-going studies are trying to investigate if it is justified to switch to another immunomodulatory therapy or repeat treatment in patients who deteriorate after receiving first-line immunomodulatory therapy [10]. Currently known data show no difference in outcomes of patients that received either PE, IVIg or PE followed by IVIg [10].

Regarding the treatment with PE after IVIg, there was one study that reported that patients who received treatment with IVIg followed by PE had worse outcomes than patients that received IVIg alone [11]. These results could be explained by PE washing out IVIg and in that way preventing therapeutic effects of IVIg [11].

This suggests that current clinical practice requires further investigations to clinical predictors of early deterioration and to define the treatment modalities in patients with anti-GQ1b overlapping syndromes.

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