A 7-year-old boy with dysphagia and proximal muscle weakness

A previously well 7-year-old boy (weight 23.8 kg, 0.34 standard deviation score [SDS] and height 125.2 cm, 0.65 SDS) with a 6-month history of Type 1 diabetes presented with blurred vision, droopy eyelids and slurred speech. He had good glycemic control with basal bolus regime. He developed chicken pox 2 days prior to presentation.

His symptoms deteriorated rapidly with progressive difficulty in swallowing fluids and chewing food. His weakness was fluctuating; it became more pronounced through the day and improved with rest.

Physical examination revealed vesicular rash of chicken pox. Neurologically, he presented with bilateral ptosis with complete ophthalmoplegia leading to diplopia and positive Cogan’s lid twitch sign (presence of upper lid twitch upon looking straight ahead after looking down for 15 seconds). Over the next 48 hours, he developed generalized weakness with painless fatigability of the bulbar and limb musculature with resultant dysphonia, dysphagia and proximal weakness leading to an unsteady gait. He had negative Romberg’s sign and normal deep tendon reflexes.

Investigations revealed a normal blood count, inflammatory markers, liver and renal function. Brain magnetic resonance imaging was normal. Neostigmine test was inconclusive. Nerve conduction study was not tolerated. A therapeutic challenge led to dramatic improvement and solidified the diagnosis.

DIAGNOSIS: SERONEGATIVE MYASTHENIA GRAVIS

The differential diagnosis of this child’s presentation included viral cerebellitis, Miller Fisher syndrome and myasthenia gravis (MG). Viral cerebellitis tends to occur typically 5 to 10 days after an infection, classically following varicella. Children with viral cerebellitis usually present with ataxia as the main feature, and dysarthria or nystagmus. In our patient, the neurological symptoms occurred during the infection and the main symptom was dysphagia that is not characteristic of viral cerebellitis. Miller Fisher syndrome is characterized by clinical triad of ophthalmoplegia, ataxia and areflexia. Symptoms may be preceded by viral illness. Presence of reflexes and negative anti-ganglioside Q1b antibodies made the diagnosis of Miller Fisher syndrome unlikely in our patient.

He was diagnosed with MG following objective assessment by the paediatric neurologist and physiotherapist. Diagnosis is based on classical clinical features and the dramatic response to a trial of pyridostigmine 15 mg 5 times per day. There was marked improvement of symptoms within the first three doses. At 3 months’ follow-up, he continued to do well despite parents stopping medication as they ran out of it. Antibodies to acetylcholine receptor (AChR), anti-ganglioside Q1b and anti muscle-specific kinase (MuSK) were negative. Chest computed tomography for evidence of thymoma and further investigations for multiple antibodies were not done as they were felt unnecessary given the response to therapeutic challenge.

MG is a rare autoimmune condition affecting the neuromuscular junction. It has been proposed that infections trigger the onset of disease in those with a genetic predisposition to autoimmunity but the exact etiology remains unknown.

There is a genetic predisposition for MG. Coexistence of another autoimmune disorder in MG patients is a recognized event. Coexistence of Type 1 diabetes and MG has been reported in six patients (1–6). Recent findings show that polymorphisms in CTSL2 gene could possibly be the candidate gene for early onset myasthenia gravis and diabetes (7). The CTSL2 gene encodes the cysteine protease cathespin V involved in human cortical thymic epithelial cells and involvement of the protease in autoimmunity has been suggested. It is thought that the overexpression of cattlespin V causes an imbalance of the positive and negative selection mechanism in thymus leading to an increased number of autoreactive cells in the periphery.

MG can occur on its own or triggered by viral infections. Measles, Epstein Barr virus, West Nile virus and Varicella Zoster (VZ) virus induced MG has been reported in the past. It is proposed that viral proteins could have antigenic peptides that mimic the AChR.

VZ triggered MG is a distinct subgroup of MG. Reviewing our case and previous reported cases (8,9), we conclude that they tend to affect prepubertal children and are AChR antibody negative. They respond well to pyridostigmine and usually have a mild disease course without respiratory muscle involvement (10). Saha A et al., reported a 3-year-old boy with post-varicella ocular MG who had a dramatic response to pyridostigmine. He was well at 6 months without recurrence of symptoms. Felice KJ et al. reported a 5-year-old boy with MG following VZ infection. He had oculobulbar weakness. He was started on pyridostigmine and tapered off after 4 years. He continued to do well at 1 year after discontinuation of pyridostigmine. In both cases, the AChR antibody was negative and no other treatment required apart from pyridostigmine.

This report adds to the literature of reported patients with comorbid MG and another autoimmune disorder, specifically Type 1 diabetes and illustrates the ‘transient’ course of MG in children following VZ infection.

CLINICAL PEARLS

1. Two or more autoimmune conditions can coexist and they are likely to have a common genetic root.
2. Myasthenia gravis can occur on its own or triggered by viral infections. Viral proteins could have antigenic properties that mimic the acetylcholine receptor (AChR).
3. Prepubertal children with myasthenia gravis are often seronegative without antibodies to acetylcholine receptor (AChR) or muscle-specific kinase (MuSK).
Sivagamy Sithambaram MBBS, MRCPCH
Department of Oncology and Metabolism, University of Sheffield, Sheffield, UK
Department of Paediatrics, Doncaster and Bassetlaw Hospitals NHS Trust, Doncaster, UK

Neeta Tripathi MBBS, DCH, MRCPCH
Department of Paediatrics, Doncaster and Bassetlaw Hospitals NHS Trust, Worksop, UK

Jaya Sujatha Gopal-Kothandapani MBBS, DCH, MRCPCH
Department of Oncology and Metabolism, University of Sheffield, Sheffield, UK
Department of Paediatrics, Doncaster and Bassetlaw Hospitals NHS Trust, Worksop, UK

Santosh Mordekar MBBS, DCH, MD(paed), MRCP(paed), FRCPCH
Department of Paediatric Neurology, Sheffield Children's Hospital, Sheffield, UK

References