



GUILLAIN-BARRE' SYNDROME AS THE INITIAL MANIFESTATION OF PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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ABSTRACT

Background: Various neurological manifestations of pediatric systemic lupus erythematosus (pSLE) have been reported. However, Guillain-Barré syndrome (GBS) as the initial presentation has rarely been documented. We report a case of the acute motor axonal neuropathy (AMAN) subtype of GBS as the first presentation of pSLE.

Case presentation: A previously healthy 11-year-old girl was admitted for a viral upper respiratory tract infection. Subsequently, she developed acute progressive weakness and respiratory failure. Nerve conduction velocity findings were compatible with the AMAN subtype of GBS. Further investigations revealed proteinuria, hematuria, elevation of Antinuclear antibody(ANA) levels, anti-dsDNA, and a decrease in complement components. Pediatric SLE was diagnosed using the The Systemic Lupus Collaborating Clinics (SLICC) criteria. The GBS did not improve after intravenous immunoglobulin therapy, plasmapheresis (PE), or pulse methylprednisolonebut gradually improved after the third cycle of intravenous cyclophosphamide, with complete recovery at 4 months after the treatment.

Conclusion: To our knowledge, this is the first and youngest case of pSLE in which the patient presented with GBS and achieved complete recovery following immunosuppressive therapy. Our findings suggest intravenous pulses of cyclophosphamide to be the most effective treatment in the case of GBS and SLE.

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INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease with heterogenous multisystem involvement. Neuropsychiatric manifestations are not uncommon and can occur at any stage of the disease. However, Guillain-Barré syndrome (GBS) as an initial presentation has rarely been reported.[1, 2] Here, we report a child who presented with GBS as the initial manifestation of pediatric SLE (pSLE).

Case presentation

An 11-year-old Thai girl with no past medical history was admitted for a viral upper respiratory tract infection. After 24 hours of hospitalization, she had generalized weakness with neckpain. Physical examination revealed flaccid weakness of all extremities and hyporeflexia. Other physical examinations were unremarkable except a discoid-like rash on her right pinna (Figure 1). Three hours later, she developed dysarthria and impending respiratory failure. Her blood pressure was high. We secured her airway using intubation and transferred her to the pediatric intensive care unit (PICU). Acute flaccid paralysis was the primary issue in this patient. The differential

diagnosis included acute transverse myelitis, GBS, and acute disseminated encephalomyelitis. Initial laboratory tests revealed a normal complete blood cell count. Serum electrolytes and renal function test results were all within normal limits except urinary analysis showed hematuria and proteinuria (urine protein, 3+). A lumbar puncture (LP) was performed 48 hours after the onset of weakness and the cerebrospinal fluid (CSF) profile revealed 31 mg/dL protein, 72 mg/dL glucose (blood sugar 120 mg/dL), and no cells. CSF examination findings for infection, NMO-IgG, and oligoclonal band were all negative. Magnetic resonance imaging (MRI) of the whole spine and brain was unremarkable. Nerve conduction velocity (NCV) tests and electromyography (EMG) were also performed. The sensory nerve conduction study (NCS) disclosed normal distal latencies and sensory nerve action potential (SNAP) amplitudes of the bilateral superficial radial and sural nerves. The motor NCS revealed an absent response in bilateral tibial, peroneal, and right ulnar nerves. These findings were consistent with the acute motor axonal neuropathy (AMAN) subtype of GBS.

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Table 1 Summary of previous case reports of GBS and SLE

Case report	Age/sex	Onset	Treatment	outcome
Hsu <i>et al.</i> [10]	28/F	At presentation	Immediate PE, steroid PE * 5 times+ IVIG (0.4mg/Kg) * 5d with no response then IVCY 500mg/m * 5 times +MPS 60mg/d *4wk	Nearly complete recovery after 2 weeks Improve after 4 weeks Full recovery after 4 months
Santiago-Casas <i>et al.</i> [7]	20/F	At presentation	MPS 1gm * 3d ->IVIG 0.4mg/Kg *5d ->IVCY 500mg/m *6d	Complete resolution after 6th IVCY
Santiago-Casas <i>et al.</i> [7]	34/F	1 month after dx SLE	IVIG 0.4mg/Kg *5d with no response then IVCY 750mg/m ² /month*6d + prednisolone at day 30	Improve at day 45 Fully recovery after 6 months
Van Larrhoyen <i>et al.</i> [5]	20/F	At presentation	IVIG 0.4mg/Kg *5d with no response then IVCY 100mg + MPS 1gm *4d, PE at d14 * 5d	Improve after 3rd session of PE Fully recovery after 5th PE
Bingisser <i>et al.</i> [15]	17/F	4 months after dx SLE	PE total * 13d then IVIG 0.4mg/Kg *3d then MPS 1gm. * 3d	Complete recovery after 5 months
Miyagawa <i>et al.</i> [12]	13/F	6 years afeter dx SLE	PE* 8d then MPS 1 gm* 3d then IVCY 1 gm *1d	Nearly complete recovery (no time mentioned)
Vaidya <i>et al.</i> [14]	23/M	At presentation	ACTH * 10d then Prednisolone 80 MKD	Improve at 2 months Complete recovery at 4 months
Millette <i>et al.</i> [16]	23/F	At presentation	IVIG 0.4mg/Kg * 5 d then AZA, MPS and IVCY ànot improve then CSF filtration	Improve after CSF filtration 10 days (50 d after onset)
Stahl <i>et al.</i> [13]	56/F	4 months after dx SLE	IVCY 500 mg weekly *4d IVIG 0.4 mg/Kg *5d	Complete recovery 10 days after IVIG (after IVCY treatment 6 weeks)
Lewis <i>et al.</i> [11]	26/M	5yr after diagnosis SLE	MPS 1 gm/d *10d/ IVCY 1 gm/month	Walk with aid after 3 months
Yildiz <i>et al.</i> [9]	47/F	20 years after dx SLE	IVIG 0.4 mg/Kg MPS 1 gm * 5 d	Nearly complete recovery 2 weeks after treatment

Abbreviation:

ACTH: Adrenocorticotropic hormone;

AZA: Azathioprine;

CSF: Cerebrospinal fluid;

Dx: Diagnosis;

d: Day;

F: Female;

M: Male;

MPS: Methylprednisolone;

IVCY: Intravenous Cyclophosphamide;

IVIG: Intravenous Immunoglobulin;

PE: Plasma exchange;

SLE: Systemic Lupus Erythematosus

**Figure 1** Discoid rash

Because the discoid-like rash on her pinna was notable and the abnormal urinary analysis findings, we decided to further investigate for SLE. She had positive ANA (1:1280), anti-ds DNA antibody, and low C3 and C4 levels. Pediatric SLE was diagnosed using the SLICC criteria.[3] We began to manage the patient's condition with IVIG 1 g/kg for 2 days as per the standard treatment of GBS, followed by plasmapheresis for three sessions and pulse methylprednisolone for 3 days. However, her clinical condition was worsening. On day 13 after hospitalization, she was totally paralyzed, including the facial muscles, and her pupils did not react to light. At that time, intravenous cyclophosphamide (IVCY) pulse therapy was given. Her clinical condition gradually improved after the 3rd dose of IVCY and full recovery 4 months after the treatment was achieved.

DISCUSSION

We report a case of Guillain-Barré syndrome in pediatric SLE which occurred at the onset of the disease. The prevalence of SLE in patients with GBS has been reported to lie between 0.6–1.7% and it usually occurred during the course and not the onset of the disease. [1] The exact pathogenesis of GBS and SLE is not well understood. Previous studies have reported that both cell-mediated and humoral-mediated processes might play the role in this association.[4] The concept of autoantibodies in SLE reacting with specific myelin sheath antigens causing acute inflammatory demyelinating polyneuropathy has also been proposed.[5] Recently, some emerging concepts of a process linked with SLE pathogenesis and type I – interferon production has been investigated in animal models mimicking GBS.[6] Therefore, immunosuppressive agents seem to be effective options but no standard treatment guidelines have yet been established. The previous reports have been reviewed and summarized in Table 2.[5, 7-16]

From previous case reports, we found that half of the patients presented with GBS as an initial symptom of SLE and most of the patients nearly or fully recovered after treatment. The recovery time had a wide range from 2 weeks to 6 months. Varying responses to different treatment modalities have been noted. Concerning the association of GBS and SLE, the efficacy of standard IVIG in GBS alone is insufficient. Only one case was reported that responded well to second course of IVIG.[17] Most of the cases were well controlled with immunosuppressive agents that are used in lupus treatments. Similar to the patient in our case, her clinical condition failed to respond to intravenous immunoglobulin and plasmapheresis, the standard GBS regimens, but markedly improved after the third cycle of intravenous

cyclophosphamide, thus resulting in complete recovery at 4 months after treatment.

CONCLUSION

To our knowledge, we reported the first and youngest case of pSLE in which the patient presented with GBS and achieved complete recovery through intravenous cyclophosphamide pulse therapy. We recommend that the most effective treatment in the setting of pSLE and concurrent GBS is intravenous cyclophosphamide pulses rather than the standard treatment used for GBS.

Abbreviations

pSLE: pediatric Systemic lupus erythematosus; SLE: Systemic lupus erythematosus; GBS: Guillain-Barré syndrome; AMAN: Acute axonal motor neuropathy; ANA: Antinuclear Antibodies; SLICC criteria: Systemic Lupus Collaborating Clinics criteria; PE: Plasmapheresis; PICU: Pediatric intensive care unit; LP: Lumbar puncture; CSF: Cerebrospinal fluid; MRI: Magnetic resonance imaging; NCV: Nerve conduction velocity; EMG: electromyography; NCS: Nerve conduction study; SNAP: sensory nerve action potential, IVIG: Intravenous immunoglobulin; IVCY: Intravenous cyclophosphamide

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