

Guillain-Barré Syndrome with Acute Lymphoblastic Leukemia

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Guillain-Barré syndrome (GBS) is rarely reported in children with acute lymphoblastic leukemia and may be difficult to differentiate from vincristine induced neuropathy. We report two children with acute lymphoblastic leukemia on induction chemotherapy who developed GBS. The diagnostic issues and potential pathogenic mechanisms underlying GBS in pediatric patients with ALL are discussed.

Keywords: *Acute Lymphoblastic Leukemia, Chemotherapy, Guillain-Barré Syndrome, Vincristine.*

There is substantial evidence for autoimmune cause for Guillain-Barré syndrome (GBS), the most frequent cause of acute flaccid paralysis [1]. GBS has been reported in association with hematologic malignancies like non-Hodgkin lymphoma, chronic lymphocytic leukemia and acute lymphoblastic leukemia (ALL) in adults. There are only few reports of GBS in children with ALL [2,3]. Differentiation from other neuropathies is important from the therapeutic point of view [3,4]. We report two cases of GBS in children on induction chemotherapy for ALL and discuss the clinical and electrophysiological features and potential mechanisms of pathogenesis.

CASE REPORT

Case 1: A 6-year-old boy was evaluated for fever, pallor, cervical lymphadenopathy and hepatosplenomegaly. Bone marrow aspiration and flow cytometry was suggestive of T-cell acute lymphoblastic leukemia. His CSF did not show blasts. He was started on induction chemotherapy with prednisolone, vincristine, daunorubicin and L-asparaginase. In the fifth week, he developed symmetrical and gradually progressive proximal and distal weakness of upper and lower limbs, progressing to dense quadriplegia over a period of 3 days. Weakness of facial muscles was noticed on third day. He did not have any sensory symptoms. The tendon reflexes were depressed initially and totally disappeared by the third day.

Electrophysiological evaluation done on fourth day of illness was suggestive of a motor axonopathic polyradiculoneuropathy. The common peroneal nerves were bilaterally unexcitable. Stimulation of the tibial, median and ulnar nerves resulted in compound muscle

action potentials (CMAPs) with marked reduction of amplitude bilaterally; conduction velocities were normal. F waves were not elicitable from peroneal nerves; F waves from other nerves showed prolonged latency. The sensory nerve action potentials (SNAPs) were normal from all the tested nerves. Correlating the clinical and electrophysiological findings, acute motor axonal neuropathy (AMAN) – a subtype of GBS was diagnosed. He was given a course of intravenous immunoglobulin (IVIg) (0.4 g/kg/day) for 5 days. CSF was re-examined on the eighth day which showed: glucose-55 mg/dL; protein-163 mg/dL; cell count-2 lymphocytes/mm³. No blasts were detected in the CSF. The weakness began to improve on the third day of treatment with immunoglobulin. Eight weeks later, he had normal power of all the limbs and was ambulant normally. He is presently on chemotherapy.

Case 2: A 2-year-old boy was evaluated for fever, pallor and hepatosplenomegaly. Bone marrow flow cytometry was diagnostic of precursor B acute lymphoblastic leukemia with co-expression of CD 13 and CD33. His CSF did not show blasts. He was started on induction chemotherapy with prednisolone, vincristine, daunorubicin and L-asparaginase. In the third week of chemotherapy, he developed fever, cough and loose stools and was started on broad-spectrum antibiotics and antifungals. One week later, he developed rapidly progressive ascending areflexic weakness of the limbs; within 24 hours, he had paralysis of respiratory muscles necessitating emergency endotracheal intubation and mechanical ventilation. His nerve conduction study showed marked reduction of CMAPs from all upper and lower limb nerves tested. None of the F waves was elicitable. Conduction velocities and distal motor latencies were relatively preserved. All the SNAPs

were elicited normally. Repetitive nerve stimulation from ulnar and facial nerves did not result in any decremental response. He was started on IVIg and he showed signs of improvement in the form of voluntary movements of the limbs, on the fourth day. However, he succumbed to sepsis.

Neither of the children had any known family history of hereditary neuropathies or foot deformity. The parents were evaluated retrospectively for evidence of hereditary neuropathies and they were normal.

DISCUSSION

We report two patients who developed GBS during treatment for ALL. The pattern and evolution of the neurological syndrome and electrodiagnostic features in both children were consistent with AMAN variant of GBS [5]. The CSF study was supportive of the diagnosis in the first child but could not be repeated after the onset of polyneuropathy in the second case because of severe thrombocytopenia and coagulopathy.

Guillain-Barre syndrome is an acute immune polyneuropathy and demyelinating and axonal subtypes are described [1]. There are only very few reports of GBS in children with ALL [2,3,6]. Out of the five cases so far reported, three were from a single centre [3]. Autoimmune disorders are known to occur in ALL [7,8]. Depletion of the regulatory T cells which suppress auto-reactive T cells, either resulting from ALL or intensive chemotherapy has been postulated as the mechanism underlying immune thrombocytopenia in ALL[7]; similar mechanisms may underlie the genesis of acute immune neuropathies in ALL. The immunological vulnerability of the peripheral nervous system could be increased in lymphoproliferative disorders; known infective triggers could precipitate an immune neuropathy in this setting. The association between GBS and ALL could be coincidental or causal. However, the occurrence of immune neuropathy in immunocompromised children is interesting. Improvement of GBS with immunotherapy (before remission of ALL) is not unexpected as GBS is an autoimmune disorder, not directly related to the hematologic malignancy.

An important consideration in children with ALL developing neuropathy while on chemotherapy is vincristine-induced neuropathy. But the clinical and electrodiagnostic findings will be distinct for vincristine induced neuropathy, [9] which is a toxic, “dying-back” neuropathy with prominent sensory involvement [10]. Vincristine may also cause a fulminant neuropathy with severe weakness in patients with Charcot-Marie-Tooth disease; the clinical and electrophysiological features in our cases were not supportive of this. Critical illness

polyneuropathy could be considered in critically ill ALL patients; however, our patients did not satisfy the definition for “critical illness” (no multi-organ failures / mechanical ventilation) prior to onset of neuro-muscular illness.

It has been recently suggested that GBS in ALL is probably more common than expected[3]; a high index of suspicion is needed for differentiation from other neuropathies. Electrophysiological studies guide to the correct diagnosis. The differentiation is important to initiate timely immunomodulatory therapies for GBS and avoid unnecessary withdrawal of vincristine, which could worsen the outcome of ALL.

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