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Case Report

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Isolated central nervous system leukemiarelapse presenting as Guillain-Barré-like syndrome: A case report

Abstract

We report the clinical picture, management and outcome of a 14-year-old boy treated for acute lymphoblastic leukemia (ALL) in whom isolated central nervous system relapse manifested by a Guillain-Barré-like syndrome (GBS). While on maintenance chemotherapy for his first CNS-relapse, he developed acute progressive lower motor neuron right facial palsy and marked hypotonia and areflexia of both lower limbs with otherwise no systemic manifestations. Vincristine-induced neuropathy (VIN) was suspected but his electrophysiological evaluation revealed a proximal demyelinating polyradiculoneuropathy pattern suggestive of GBS, but his cerebrospinal fluid analysis showed increased protein and infiltration by 95% leukemic blast cells. Immunoglobulins and chemotherapy were initiated. Although GBS in children with ALL is very rare, differentiating it from VIN by electrophysiological studies and excluding CNS relapse is crucial to determine the proper treatment and ensure a better clinical outcome.

Keywords: guillain-Barré syndrome, acute leukemia, relapse, neuropathy

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Marwa Abd El-Maksoud,[1] Yasmine El Chazli,[2] Yasser Wali[2,3]

[1]Department of Pediatrics, Neurology unit, Faculty of Medicine, Alexandria University, Egypt

[2]Department of Pediatrics, Hematology/Oncology unit, Faculty of Medicine, Alexandria University, Egypt

[3]Child Health Department, Sultan Qaboos University Hospital, Muscat, Oman

Correspondence: Marwa Abd El-Maksoud, Department of Pediatrics, Neurology unit, Faculty of Medicine, Alexandria University, Egypt, Email mabdelmaksoud16@alexmed.edu.eg

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Abbreviations: GBS, guillain barre syndrome; CNS, central nervous system; VIN, vincristine-induced neuropathy; LMN, lower motor neuron; CSF, cerebrospinal fluid

Introduction

Guillain Barre Syndrome (GBS), also known as acute acquired polyradiculoneuropathy, presents with progressive ascending muscle weakness sometimes progressing to complete paralysis. Although the exact etiology is still unknown, an immune-mediated mechanism is strongly suggested. Its incidence widely ranges between 0.4 and 4 cases per 100.000 people per year.[1] Involvement of the central nervous system (CNS) in acute lymphoblastic leukemia (ALL), the most common childhood cancer, is a major clinical problem. Neurologic symptoms associated with CNS leukemia include headaches, nausea and vomiting, lethargy, and irritability and are usually due to direct infiltration by malignant cells, complications by a CNS infection or as a result of treatment adverse effects.[2] The most frequently recorded acute treatment-induced neurological sequelae are methotrexate-induced leukoencephalopathy, vincristine-induced neuropathy (VIN) and L-asparaginase-induced strokes.[2,3] We hereby report the case of a boy in whom leukemic relapse manifested by the picture of GBS.

Case description

A 14-year-old boy diagnosed as B-ALL at the age of 9 years in January 2013. His cerebrospinal fluid (CSF) analysis was free at diagnosis with no blast cells. He was treated according to the high-risk standard-arm of the modified children cancer group (CCG) 1961 protocol.[4] He achieved complete remission after the induction phase and received consequent cycles of chemotherapy punctuated with recurrent episodes of bone marrow suppression and hospital admissions for febrile neutropenia. After two years of maintenance therapy, in December 2015, he developed isolated CNS relapse presenting by headache and evidenced by the presence of blasts on his CSF, while his bone marrow was still in remission. He was shifted to the isolated CNS relapse protocol adopted from the pediatric oncology group (POG) 9412.[5] He responded well to remission induction, went into consolidation and intensification phases, and received cranial irradiation. While still on maintenance chemotherapy, in January 2018, he complained of acute onset of mouth deviation, inability to close his eyelid, and difficulty walking. Physical examination revealed acute progressive lower motor neuron (LMN) right facial palsy and marked hypotonia and areflexia of both lower limbs with normal upper limbs and otherwise no systemic manifestations. The MRI brain and orbit were free. An electrophysiological evaluation revealed a proximal demyelinating polyradiculoneuropathy pattern suggestive of GBS. The motor conduction was tested bilaterally and showed delayed motor conduction velocity, decreased amplitude with poor F waves for all tested peripheral nerves on both lower limbs. The right facial nerve showed a poor response compared to the left side. The sensory nerve action showed only a poor response of superficial peroneal nerve with normal somatosensory evoked potentials on both upper and lower limbs, suggesting a peripheral rather than a central lesion. The H reflex was poor with absent F waves on both sides, suggesting an acute demyelinating process. Fundus examination showed bilateral papilledema, right sided retinal hemorrhage, and excaudate. Urgent brain CT was unremarkable. His magnetic resonance imaging of the brain and orbit did not show any evidence of leukemic infiltration. Blood investigations revealed leukopenia (2930 cell/cmmµL), borderline platelet count (153.000 c/cmmµL), and hemoglobin 10.7 g/dL. His CSF analysis showed protein of 132 mg/dL, neutrophils 25 cell/cmmµL, lymphocytes 2705 cell/cmmµL with 95% blast cells, while his bone marrow examination was negative for leukemic infiltration. Intravenous immunoglobulin (IVIG) was initiated at (0.4 mg/kg/dose for 5 five days), but he actually received only 3 three doses as he developed a severe anaphylactic reaction during the third infusion. Re-induction chemotherapy for isolated CNS relapse was concomitantly initiated using dexamethasone,

vincristine, L-asparaginase, mitoxantrone, and intrathecal therapy.[6] The child improved gradually, with the recovery of facial palsy within 2 two weeks and complete recovery of walking within 2 two months.

Discussion

This report describes a 14-year-old boy with a second isolated CNS relapse, which presented by acute progressive ascending paresis of both lower limbs with right-sided facial palsy while on maintenance therapy for B-ALL first CNS relapse. The differential diagnosis at presentation with peripheral neuropathy was VIN or GBS. Nerve conduction velocity examination after the onset of neurologic symptoms is mandatory, as the absent F waves indicate a proximal nerve conduction block caused by an acute demyelinating process allowing us to rule out acute VIN.

Peripheral neuropathy in the form of sensory-motor axonal polyneuropathy is a common adverse effect of vincristine that manifests in 30% to 50% of treated patients and is sometimes severe enough to cause complete paralysis .[7] Whereas VIN is considered a relatively common cause of peripheral neuropathy in children with ALL receiving chemotherapy,[8] only a few published reports describe acute inflammatory demyelinating polyradiculoneuropathy (AIDP) in these patients. Nine patients were reported so far in the literature, including; six children who developed GBS during induction;[7,9–11] two were in remission, [7,12] and only one child presented with GBS as the initial presentation of underlying ALL.[13]

Although the clinical and electrophysiological studies of the presented patient were consistent with the AIDP subtype of GBS, a CSF analysis, which is mandatory not only to fulfill ""Brighton diagnostic criteria" " for GBS but also because of the possibility of CNS-relapse in a known patient with ALL.[14] It revealed the presence of blast cells indicating leukemic infiltration due to CNS relapse. The overlap of the GBS and CNS relapse might explain the clinical improvement of the child after the reinduction chemotherapy and IVIG.

Guillain-Barré syndrome is a common cause of acute flaccid paralysis and is strongly believed to be an autoimmune-mediated disease mostly triggered by infections. Molecular mimicry between microbial and nerve antigens has a major role, especially with Campylobacter jejuni infection, although GBS occurs in less than 1 in 1000 infected people.[15] GBS had also been reported in association with various hematologic conditions, including Hodgkin and non-Hodgkin lymphoma and ALL in adults.[16–18]

The pathophysiologic basis for AIDP in children with ALL remains unclear. Several explanations for its pathogenesis have been proposed. Immunosuppression secondary to intensive chemotherapy could pave the way to infectious triggers of AIDP.[12] Neoplasms may also trigger AIDP in a manner similar to some viral infections.[19] However, the exact mechanism, including the microbial or neoplastic and host factors, by which the immune response is shifted towards unwanted autoreactivity, is still not well understood.[20] A paraneoplastic demyelinating sensorimotor neuropathy has been also suggested.[13]

In conclusion, although GBS in children with ALL is very rare, differentiating it from VIN by electrophysiological studies, and excluding underlying leukemia relapse, especially the isolated CNS type, is crucial to determine the proper diagnosis, treatment, and improve the clinical outcome.

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Conflicts of interest

The authors declare that they have no conflict of interest.

Ethics approval

Ethical approval was waived by the local Ethics Committee of University A in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

Authors' contribution

Marwa Abd El-Maksoud and Yasmine El Chazli were responsible for clinical diagnosis, management and follow up of the index case. The first draft of the manuscript was written by Marwa Abd El-Maksoud and Yasmine El Chazli and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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