Cyclophosphamide Induced Hypomania in a Pediatric Bone Marrow Transplant Patient

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Background

- Patients are at risk of developing graft-versus-host disease (GVHD) following bone marrow transplant (BMT).
- Alkylating agents, which are used in BMT and cancer therapy, such as cyclophosphamide, busulfan, and ifosfamide have been associated with neuropsychiatric side effects.
- Cyclophosphamide is an immunosuppressant used in BMT conditioning regimens to prevent GVHD.
- Previous research has investigated cyclophosphamide's association with neurotoxic effects via inflammation, apoptosis and hippocampal alterations.
- Less is known about the psychiatric adverse effects of cyclophosphamide. There is a case report of an adult woman who experienced mania while taking cyclophosphamide following a renal transplant.[1]
- We present a case of a pediatric patient with hypomania following single dose of cyclophosphamide in the post-BMT period.

Neurotoxicities Associated with Cyclophosphamide
Dizziness
Blurred Vision
Encephalopathy
Sensation of Heat
Cognitive Impairment

Case Presentation

- 15-year-old male with autosomal dominant-STAT 3 deficiency and Hyper-IgE syndrome and prior depressive episode who presented for myeloablative conditioning and matched sibling donor allogenic fresh BMT.
- Family history is significant for depression in his brother.
- Hospital course was complicated by lower and upper GI bleed requiring ICU care.
- Cyclophosphamide was initiated on post-BMT day 3.
- On day 4, psychiatry was consulted for evaluation of acutely disordered behaviors in an otherwise alert and oriented patient.
- Patient exhibited hypomanic symptoms, including psychomotor agitation, pressured speech, racing and tangential thoughts, grandiosity, increased goal-directed activities, and decreased sleep.
- Cyclophosphamide-induced neurotoxicity was suspected, and the medication was discontinued.
- Olanzapine 5mg was administered, with moderate improvement. Scheduled olanzapine 2.5mg continued for one week.
- Symptoms gradually remitted and patient's mood stabilized.

Case Timeline

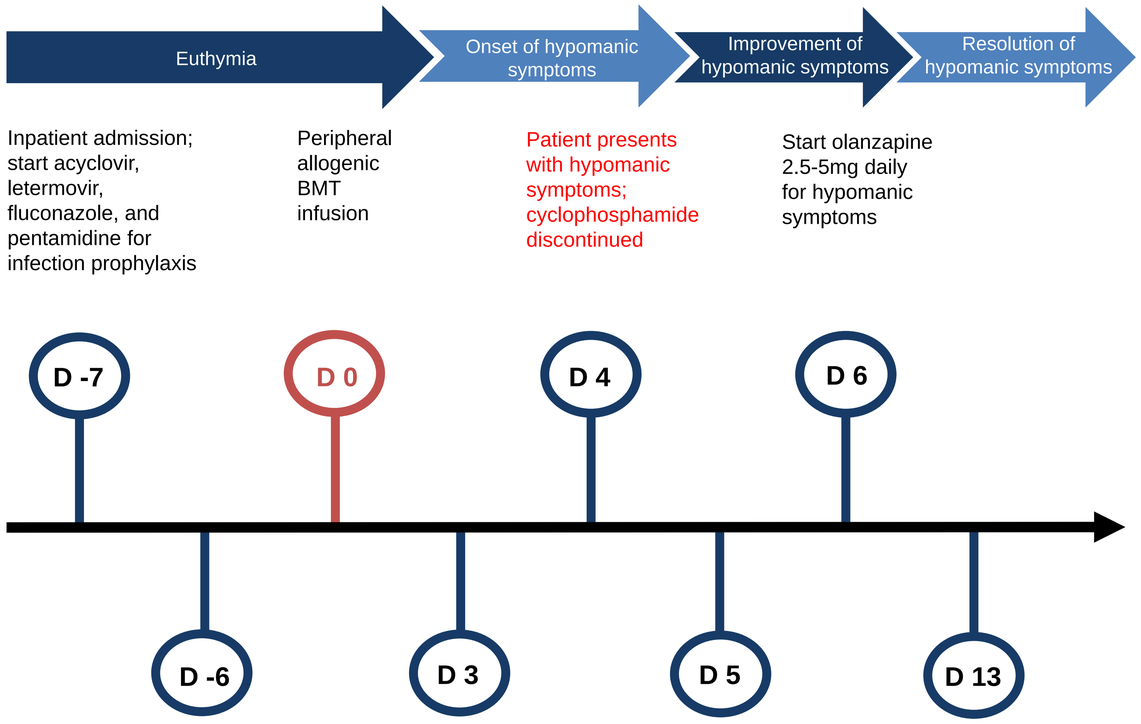

Figure 1: Timeline of Events

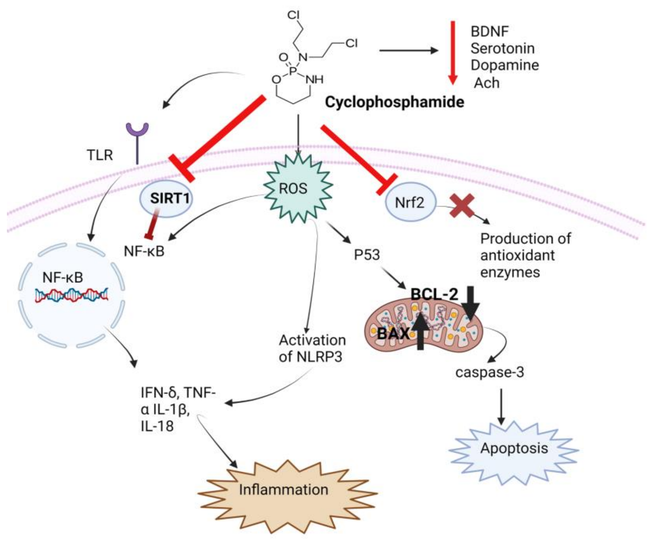

Figure 2: Mechanisms of Cyclophosphamide Induced Neurotoxicity[3]

Recommendations

- Consultation liaison (CL) psychiatrists should be aware of commonly used alkylating agents, such as cyclophosphamide, and their potential CNS neurotoxicities.
- Thorough assessments of patients, including family psychiatric histories, are important to identify patients at risk of developing potential neuropsychiatric adverse effects.
- Management strategies should include discontinuation of offending agents, pharmacologic treatments for acute symptoms, communicating with primary teams and education for patients and their families.

Discussion

- To our knowledge, this is the first pediatric case documenting acute behavioral activation following a single dose of cyclophosphamide.
- Quick resolution of symptoms upon cyclophosphamide discontinuation and treatment with a second-generation antipsychotic suggests a potential relationship between the drug and observed behavioral changes.
- Additional risk factors, including the patient's history of depression, adolescent age, stress of illness and transplant, and severity of medical complications, may have contributed to the observed psychiatric symptoms.
- Acute cyclophosphamide-induced hippocampal alterations may have precipitated a hypomanic state, supported by existing research on the relationship between hippocampus dysfunction and hypomanic symptoms. [2-4]

Conclusion

- Pediatric patients can be susceptible to adverse effects of alkylating agents such as cyclophosphamide.
- Further studies are needed to investigate the neuropsychiatric side effects of cyclophosphamide in pediatric patients.

References

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