Fasting Hypoglycemia Associated with Hyperinsulinemia in a Child with Acute Lymphoblastic Leukemia (ALL) and 6-mercaptopurine (6-MP) therapy

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Background: Symptomatic fasting hypoglycemia has been reported as an uncommon side effect in patients with ALL on maintenance therapy with purine analogs. The exact mechanism of the hypoglycemic effect of the antimetabolic therapy remains unclear. The association of 6-MP therapy with hypoglycemia and hyperinsulinemia has not been described previously.

Case: A 6 9/12 y/o girl with pre-B ALL and 6-MP therapy presented with fasting hypoglycemia. She was also having symptoms of reactive hypoglycemia post breakfast. Paradoxically, she was having hyperglycemia during dexamethasone pulses. Her height was 120.5 cm (53%); weight 33.3 kg (98%) and BMI 22.9 kg/m2 (99%). It was assumed that hypoglycemia was related to 6-MP, and dosing was changed from evening to morning. Unfortunately, hypoglycemia persisted. She was admitted for a fasting study, few days before scheduled dexamethasone pulse, to rule out other etiologies. She developed hypoglycemia with lab glucose of 45 mg/dl. Critical sample was obtained. Insulin level was inappropriately elevated for the degree of hypoglycemia; beta-hydroxybutirate was not completely suppressed but was not elevated as seen in ketogenic hypoglycemia. Subsequently it was recommended to continue 6-MP in the morning and to increase protein with meals, avoid concentrated sweets, and add cornstarch to bedtime snack. Unfortunately, hypoglycemia was occurring more frequently. Furthermore, she was symptomatic during hypoglycemia, and it was impeding quality of life. 6-MP therapy was discontinued for seven days to evaluate if hypoglycemia would resolve. Within three days, hypoglycemia resolved, with no hypoglycemic symptoms. Subsequently, split dosing of 6-MP was recommended and she experienced relief from hypoglycemia.

Conclusion: Association of 6-PM therapy with severe hypoglycemia and hyperinsulinemia has not been described previously. Although the exact mechanism of hypoglycemia remains unclear and is likely multifactorial, our findings indicate the possibility of associated hyperinsulinemia. Further, large scale studies are needed to further delineate exact etiology.

Abstract

Case report

Results

Fasting Study

Critical Sample

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Conclusions

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References