LETTER TO EDITOR (VIEWERS CHOICE)

CHEMOTHERAPY INDUCED DIABETIC KETOACIDOSIS IN A CHILD

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An 11 years old girl with acute lymphoblastic leukemia (ALL) with relapse was on chemotherapy since 9 years of age was admitted for maintenance chemotherapy with Inj Vincristine, L asparaginase, Adriamycin and injectable steroids. Child received 3 doses of L asparaginase, 2 doses of Vincristine and one dose of Inj Adriamycin after hospitalization. On the seventh day of therapy, child became drowsy with vomiting, dehydration and tachypnea. Investigations revealed blood sugar of 485 mg/dl, urea of 179 mg/dl and creatinine of 1.7 mg/dl. Serum sodium was 134 meq/dl and potassium was 4.8 meq/dl. Repeat blood sugar was 614 mg/dl. Urine revealed ketonuria and glycosuria. Arterial blood gases showed wide anion gap metabolic acidosis. Child was started on diabetic ketoacidosis (DKA) treatment protocol. IV infusion of insulin was continued for 24 hours and switched over to subcutaneous 8 hourly short acting insulin. Child was stabilized with twice daily insulin after 36 hours. Other investigations such as blood culture showed no growth, X-ray chest was normal, ultrasound abdomen revealed normal pancreas with mild hepatomegaly. Serum amylase was 246 IU/l, SGOT was 112 IU/l, SGPT was 110 IU/l and bilirubin was 2.2mg/dl. Complete blood count revealed thrombocytopenia with anemia and leucopenia. She was discharged on split mixed regimen requiring 1.2units/kg/day. She showed a good pancreatic beta cell reserve in terms of fasting and stimulated C peptide levels at 3 weeks of hyperglycemia (fasting C peptide was 1.1 pmol/ml and stimulated c peptide was 3 pmol/ml). Insulin was stopped at 4 weeks and child continued to be in normoglycemia thereafter.

Hyperglycemia can result from perturbation of the hormones involved in glucose regulation, such as insulin or glucagon, or from dysfunction of the organs involved in glucose homeostasis. Given the effects of glucocorticoids on glucose metabolism, the most frequent pharmacological cause of insulin resistance and hyperglycemia in cancer therapy is the administration of high-dose glucocorticoids, usually in combination with chemotherapeutic or antiemetic regimens. Hyperglycemia may occur as a complication during induction therapy with L-asparaginase and steroids. (1) Hyperglycemia and glycosuria without ketonemia occurs in 1-14% of patients treated with L-asparaginase, an effect that is reversible upon discontinuation of the drug. Insulin therapy is frequently required, but close monitoring of blood glucose is necessary to avoid hypoglycemia after cessation of L-asparaginase. (2) Inhibition of insulin or insulin receptor synthesis, leading to a combined insulin deficiency/resistance syndrome, is the presumed mechanism of the L-asparaginase effect. (3) Leukemic process itself can cause impairment of glucose tolerance and the diabetogenic effect of L-asparaginase is not manifested in all patients. L-asparaginase complications which are not dose dependent can be life threatening. (4)

Pancreatitis, which occurs in 1-2% of L-asparaginase-treated patients, provides yet another mechanism for the development of transient or permanent diabetes mellitus. The incidence of pancreatitis rises when L-asparaginase is combined with other drug therapy such as doxorubicin, vincristine, and prednisone. Our patient had been on all the four drugs. Close monitoring during L-asparaginase therapy for hyperglycemia will enable prompt recognition and early correction of the metabolic imbalance. (5) Periodic evaluation of blood glucose in children on these drugs is essential to identify and treat this life threatening complication. The occurrence of DKA does not warrant alteration of ALL treatment. (6)

REFERENCES

1. Gillette PC, Hill LL, Starling KA, Fernbach DJ. Transient diabetes mellitus secondary to L-asparaginase therapy in acute leukemia. J Pediatr 1972; 81:109-111
2. Yeung SC, Chiu AC, Vassilopoulou-Sellin R, Gagel RF. The endocrine effects of nonhormonal antineoplastic therapy. Endocr Rev 1998; 19:144-172
3. Carpentieri U, Balch MT, Hyperglycemia associated with the therapeutic use of L-asparaginase: possible role of insulin receptors. J Pediatr 1978 ; 93: 775-778
4. Cetin M, Yetgin S, Kara A, Tuncer AM, Gunay M, Gumruk F, Gurgey A. Hyperglycemia, ketoacidosis and other complications of L-asparaginase in children with acute lymphoblastic leukemia. J Med. 1994; 25: 219-229.
5. Iyer RS, Rao SR, Pai S, Advani SH, Magrath IT. L-asparaginase related hyperglycemia. Indian J Cancer. 1993 ;30: 72-76
6. Roberson JR, Raju S, Shelso J, Pui CH, Howard SC, Howard SC. Diabetic ketoacidosis during therapy for pediatric acute lymphoblastic leukemia. Pediatr Blood Cancer. 2008; 50: 1207-1212.

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