

Isoniazid induced childhood diabetes: A rare phenomenon

Abstract

Drugs raise blood glucose concentrations via two broad mechanisms: By reducing insulin biosynthesis or secretion, or by reducing tissue sensitivity to insulin. Until date, there have been very few reported cases of isoniazid induced diabetes. We are presenting a case report of 6-year-old child with isoniazid induced diabetes who was misdiagnosed initially as a case of type 1 diabetes mellitus. We hereby stress that before diagnosing a patient with diabetes-type 1 or 2, a detailed history of drug intake for any such drugs, which can cause hyperglycemia has to be taken. Clear cut knowledge/cognizance of all such culprit drugs is therefore required.

Key words:

Drug induced diabetes, insulin therapy, type 1 diabetes

Introduction

Drug induced diabetes/worsening of hyperglycemia in previously diagnosed diabetic patients, is a problem recently recognized by the World Health Organization and American Diabetes Association. They define drug-induced diabetes as a separate etiologic category.^[1] The diabetogenic properties of drugs are important for two main reasons. First, polypharmacy is a common necessity in managing patients with diabetes; clear understanding of the potential hyperglycemic effects of drugs is therefore helpful in anticipating and avoiding deterioration in glycemic control.^[2,3] Second, various drugs can induce diabetes in previously normoglycemic individuals; this state is usually reversible and not insulin-dependent, but it can become permanent. Drugs can raise blood glucose concentrations through two broad mechanisms: By reducing insulin biosynthesis or secretion, or by reducing tissue sensitivity to insulin.^[2,3] We are presenting a case report of 6-year-old female child with isoniazid induced diabetes (following pulmonary tuberculosis) that was previously misdiagnosed as type 1 diabetes.

Case Report

A 6-year-old female child presented to our Outpatient Department for the evaluation of type 1 diabetes, she was the

only child of family with no family history of diabetes, she weighed 18 kg, and her height was 115 cm. She was diagnosed as a case of sputum positive pulmonary tuberculosis 3 months back and started on anti-tubercular medication consisting of isoniazid, rifampicin, ethambutol, pyrazinamide, and streptomycin. She was on regular medication, and no other medication was prescribed besides the above mentioned drugs. After 2 months of anti-tubercular treatment, patient complained of polyuria, polyphagia, and polydipsia and during the routine evaluation, patient was found to have high blood sugar and she was diagnosed with type 1 diabetes mellitus by a local physician, she was put on biphasic insulin therapy by the same physician. But on taking detailed history we found out that she had never developed diabetic ketoacidosis.

Blood sugar levels of the patient at the time of presentation were: Prebreakfast –324 mg/dl, and Predinner –287 mg/dl.


Clinical history, anthropometry, and biochemical investigations were done following admission to endocrinology ward. Routine biochemical investigations, hemogram, urine routine/microscopy, liver function test, renal function tests were normal.

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The anthropometry showed no weight loss, normal weight for age and height for age, thereby indicating that the disease process was not chronic [Table 1].

Biochemical investigations showed absence of autoimmune markers such as anti-glutamic acid decarboxylase antibody, insulin auto antibody, anti-thyroid peroxidase antibody, and normal anti-tissue transglutaminase antibody, indicating that the patient was not a case of type 1 diabetes. Elevated level of C-peptide (stimulated value), slightly elevated value of insulin indicating that patient's endogenous insulin secretion was preserved. Her homeostasis model assessment for insulin resistance index was calculated and it was within normal limits-indicating that there was no insulin resistance [Table 1].

Following the treatment modification (by withdrawal of isoniazid), patient's glycemic control was achieved, her glycemic control is maintained till date, and presently patient is free from insulin therapy and she is on regular and close follow-up.

Discussion

Many therapeutic drugs can predispose to/precipitate diabetes, especially in the presence of risk factors, and these can also deteriorate the control of preexisting diabetes. The cause of deterioration of glycemic control may be an increase in insulin resistance, change in insulin secretion, or both. These drugs are classified into the widely used weakly diabetogenic drugs like anti-hypertensives and statins, and the strongly diabetogenic drugs used for special indications like steroids, antipsychotics. A range of immunosuppressive agents, antibiotics can also cause hyperglycemia by their mechanism of action.

Among antibiotics, hyperglycemia is most consistently attributed to the fluoroquinolones.^[3] Occasionally, isoniazid (INH) is also implicated in causing hyperglycemia by blocking specific steps of Krebs cycle requiring NAD⁺ and also by stimulating glucagon secretion.^[4,5] Among patients using isoniazid, oral glucose tolerance test could show hyperglycemia in both diabetic and nondiabetic patients. Furthermore, the insulin requirement of diabetic patients may increase while on isoniazid treatment.^[6]

Drug-induced or drug-associated hyperglycemia, irrespective of patient's diabetic status, should be suspected in patients newly started or maintained on any of the drug categories shown in Table 2. This case report shows the diagnostic importance of drug induced diabetes, as it can be mislabeled as type 1 or type 2 due to lack of evidence/cognizance. Therefore, it is very important to exclude the drugs which can cause hyperglycemia as their side effect, and it is also very important to take a detailed history, anthropometry, and do the biochemical investigations accordingly.

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Table 1: Summary of history/examination, investigations and response to treatment

| | | |
|--|----------------------------|--|
| Blood sugar at the time of diagnosis of tuberculosis | | RBS: 110 mg/dl FBS: 74 mg/dl |
| DKA at presentation | Clinical history | Absent |
| Drug known to cause hyperglycemia | | Present |
| Insulin requirement | | Minimal |
| History of weight loss | Anthropometry | Absent |
| Weight for height | | Normal |
| Height for age | | Normal |
| Anti-GAD antibody, IAA | Biochemical investigations | Absent |
| Anti TPO antibody, anti tTG antibody | | Normal |
| Fasting insulin level | | 12 μ IU/ml (normal: 3-14 μ IU/ml) |
| Stimulated C-peptide level | | 3.0 ng/dl (normal: 1.2-3.4 ng/ml) |
| FBS | | 84 mg/dl |
| FBS \times fasting insulin/405 | HOMA-IR index | 2.49 (normal < 3) |
| Blood sugar on 5 th day of isoniazid withdrawal | Treatment modification | RBS: 124 mg/dl FBS: 89 mg/dl |
| At 1 st month | | RBS: 108 mg/dl FBS: 81 mg/dl |
| At 3 rd month | | RBS: 114 mg/dl FBS: 92 mg/dl |

DKA: Diabetic ketoacidosis, IAA: Insulin auto antibody, TPO: Anti thyroid peroxidase antibody, HOMA-IR: Homeostasis model assessment for insulin resistance, RBS: Random blood sugar, FBS: Fasting blood sugar, GAD: Glutamic acid decarboxylase, tTG: Tissue transglutaminase

Table 2: Drugs that cause or exacerbate hyperglycemia

| Potentially potent effects | Minor or no effects |
|---|--|
| Glucocorticoids | Oral contraceptives |
| Oral contraceptives | Progestogen - only pills |
| High - dose estrogen | Levonorgestrel in combination pills |
| | Loop diuretics |
| Thiazide diuretics (especially high dosages) | |
| Non - selective β - adrenoceptor antagonists | |
| Calcium - channel blockers | |
| β 2 - adrenoceptor agonists | α 1 - adrenoceptor antagonists |
| Salbutamol | Growth hormone (physiologic doses) |
| Ritodrine | Somatostatin analogs |
| Antipsychotics | Androgen deprivation therapy for prostate cancer |
| HIV protease inhibitors | Selective serotonin reuptake inhibitors |
| Indinavir, nelfinavir, ritonavir and others | Nicotinic acid, Lamivudine, Isoniazid |
| Others | |
| Pentamidine, Gatifloxacin, Streptozocin (streptozotocin), Diazoxide, Ciclosporin (cyclosporine), Tacrolimus | |
| Interferon - α , L - asparaginase | |

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