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Case Report / Olgu Sunumu

A Cause of Status Epilepticus in Turkey: Isoniazide Intoxication

Eda Kilic Coban[1], Vasfiye Burcu Dogan[2], Ali Dirik[3]

[1]Neurologist, Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, 3rd Department of Neurology, Istanbul - Turkey
[2]Neurologist, Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, 2nd Department of Neurology, Istanbul - Turkey
[3]Anesthesiologist, Esenler Ozel Guney Hastanesi, Department of Anaesthesiology and Reanimation, Istanbul - Turkey

ABSTRACT

A cause of status epilepticus in Turkey: Isoniazide intoxication

In Turkey, isoniazide (INH) is widely used for the prophylaxis and treatment of tuberculosis. Acute overdose of INH may cause metabolic acidosis, repetitive seizures and coma. A 17 year old patient was admitted to our emergency clinic with generalized convulsive status epilepticus. Her initial laboratory studies revealed hyperglycemia, leucosytosis, metabolic acidosis, hypopotasemia and high creatinin kinase (CPK) levels. Her seizures continued under standard anticonvulsive therapy. As acute toxic exposure of INH was suspected, piridoxin infusion was started. Her seizures ended. She became awake, alert and responsive. On the third day, serum transaminase and CPK levels increased. As a conclusion, INH is widely used for treatment of tuberculosis in our country. That's why INH toxicity should be suspected in any patient with refractory seizures, hyperglycemia and metabolic acidosis.

Key words: Isoniazide, metabolic acidosis, status epilepticus

ÖZET

Ülkemizde bir status epileptikus nedeni: İzoniazid zehirlenmesi

Tüberküloz profilaksisi ve tedavisinde ülkemizde yaygın olarak kullanılan izoniazidin (INH) yüksek dozda alımı metabolik asidoz, nöbet ve koma ile sonuçlanabilir. On yedi yaşında, öncesinde nöbet öyküsü olmayan kadın hasta, acil nöroloji polikliniğimize jeneralize konvülsif status epileptikus tablosu ile başvurdu. Hastanın kan tetkiklerinde hiperglisemi, metabolik asidoz, hipopotasemi, lökositoz ve kreatinin kinaz yüksekliği saptandı. Standart antikonvülsan tedaviye nöbetlerinin yanıt vermemesi ve şüpheli izoniazid (INH) zehirlenmesi öyküsünün alınması üzerine yapılan piridoksin infüzyonu sonrası hastanın nöbetleri sona erdi. Nöbet tekrarı olmayan hastada takibinin 3. gününde karaciğer enzimlerinde ve kreatinin kinazda artış gözlendi. Sonuç olarak, ülkemizde tüberküloz nedeni ile INH kullanımı yaygındır. Bu nedenle, durdurulamayan nöbetlerle acil nöroloji polikliniklerine başvurmuş hastalarda, metabolik asidoz ve koma birlikteliğinde izoniazid zehirlenmesi mutlaka akla gelmelidir.

Anahtar kelimeler: İzoniazid, metabolik asidoz, status epileptikus

Address reprint requests to / Yazışma adresi:
Neurologist Eda Kilic Coban
Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery,
3rd Department of Neurology, Istanbul - Turkey

Phone / Telefon: +90-286-263-5951/1451

E-mail address / Elektronik posta adresi:
eda_coban@yahoo.com

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INTRODUCTION

High dose intake of isoniazide (INH), which is used widely for tuberculosis profilaxy in Turkey, may lead to metabolic acidosis, seizures and coma. The drug reduces production of gamma aminobutiric acid (GABA) by inhibiting glutamic acid decarboxylase, a pyridoxal phosphate dependent enzyme, and causes seizures (1). These seizures do not respond to routinely used antiepileptic drugs and can only be stopped with parenteral pyridoxine treatment and early diagnosis is important to prevent cases which can result in death.

CASE

Seventeen years old female patient who did not have a history of seizures applied to our emergency neurology service with generalized convulsive status epilepticus. The patient had tonic clonic type seizures. She was unconcious and her Glasgow coma score

was 9/15. Other than a pulse of 120/minute, her vital signs were stable. There was no finding in physical examination. Neurological examination revealed letargy, spontaneous movement of extremities and bilateral extensor plantar reflexes. First laboratory examination in emergency conditions revealed hyperglycemia, leukocytosis, high creatine kinase and low potassium (Glucose: 380 mg/dL, WBC: 29600/mm^3, CK: 225 IU/L, K: 3.4 mEq/L. Arterial blood gases: pH: 7.01, pO_2: 106, Pco_2: 41 mmHg, $HC0_3$: 7.0 mmHg). The patient had metabolic acidosis. When the seizures continued after 10 mg diazepam infusion, phenytoin replacement was done. It was learned that sister of the patient, who did not have a history of any illness and drug use, was treated for tuberculosis. Lack of treatment response to antiepileptics, accompanying hyperglycemia, leukocytosis and metabolic acidosis and history of isoniazide use in the family led us to think ingestion of isoniazid for suicide. Emergency medicine unit was consulted and seizures stopped after pyridoxine infusion. However, the patient was referred to intensive care unit since coma continued. Metabolic values returned to normal at the third day of hospitalization. Glasgow coma score raised to 15. History from the patient affirmed ingestion of high dose isoniazid for suicide. However, the patient was consulted with gastroenterology service for increased liver enzymes. After supportive treatment, all biochemical parameters returned to normal at the first week of treatment and the patient was discharged without recurrence of seizures.

DISCUSSION

Lethal INH poisoning occurs when serum INH level exceeds 30 microgram/mL (1). Classical triad of poisoning are unstoppable epileptic seizures, metabolic acidosis due to hyperglycemia and coma. Laboratory findings of hyperglycemia, glucosuria, and high anion gap metabolic acidosis may mimic diabetic ketoacidosis at the first place. In fact, we found similar laboratory findings in our case. Acute ingestion of drug in doses higher than 35 mg/leads to epileptic seizures (2) and these seizures are resistant to standard anticonvulsant treatment and even to barbiturates. In our case, seizures continued after diazepam and phenytoin loading. Phenytoin infusion is stopped since INH poisoning was suspected and INH and phenytoin interacts. Pyridoxine replacement was planned after getting in touch with the emergency medicine clinic.

Unfortunately, measuring INH serum level in cases with suspected INH overdose does not help for treatment and diagnosis since it takes a long time to have the results. Besides, there is a weak correlation between systemic effects and drug levels. Therefore, controlling metabolic acidosis due to INH toxicity plays a key role in management of seizures (3).

Prydoxine is the standard antidote of INH. Amount of necessary prydoxine is the same as ingested INH dose by the patient. When the ingested INH dose is not known, 5 gram pyridoxine can be administered by intravenous route (4,5). In resistant seizures, dose can be repeated in every 20 minutes. Although INH induced epileptic seizures are resistant to standard anticonvulsants, alternate use of pyridoxine and benzodiazepines may also lead to synergistic effect. Therefore, alternate use of diazepam and pyridoxine can be used for continuing seizures. Pyridoxine also has a role in reversing coma. It is not only effective in treating INH induced seizures, but also improves mental status due to high dose of the drug. Higher doses than the ones used to control seizures may be necessary to improve conciousness (6). Although intravenous pyridoxine is an effective antidote for INH overdose induced seizures, the drug has very few indications and it may be difficult to find it. Therefore, emergency services must keep intravenous pyridoxine (3).

During follow-up, increased liver and lactate dehydrogenase enzymes along with cratine kinase heralds emerging rabdomiolysis. Rabdomiolysis is an unfrequent but potentially lethal complication of INH poisoning. Although exact mechanism is not known, direct toxic effects of the drug and/or its metabolites or severe muscle breakdown due to seizures are blamed (7). In our patient, during intensive care follow up enzymes are elevated and returned to normal in following days spontaneously.

INH is used commonly in developing countries like our country, which continue to struggle with tuberculosis. Similar to the literature, INH poisoning is becoming more frequent among young adults also in our country (8). In patients admitted with unstoppable seizures, when metabolic acidosis and coma accompany, isoniazid poisoning must be kept in mind at any rate. Even if INH poisoning is not definite in the history, pyridoxine must be administered as antidote.

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