CONVULSIVE REACTION IN A TWO-YEAR-OLD CHILD FOLLOWING THE ACCIDENTAL INGESTION OF AN OVERDOSAGE OF ISONIAZID

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ISONIAZID has proved to be of considerable value in the treatment of tuberculosis. However, it has caused a wide variety of untoward reactions, the most common of which have been those involving the central nervous system. This is the report of a 2-year-old boy who suffered a convulsive reaction following the accidental ingestion of a large amount of isoniazid. To our knowledge, there has been only 1 similar case reported in the literature.

CASE REPORT

History

S. K., a 26-month-old white male, was admitted to the hospital because of several generalized convulsions in the preceding hour. The mother had tuberculous pleurisy with effusion in 1938. The father had pulmonary tuberculosis with cavitation in 1933 for which pneumothorax was induced from 1934 to 1939 and a lobectomy performed in 1940. Since 1942 neither parent showed signs of active tuberculosis.

The patient was one of twins born 3 weeks prematurely by breech presentation. Birth weight was 1,955 gm. He breathed and cried spontaneously. The neonatal period was uneventful, development was entirely normal and there were no serious illnesses or convulsions.

Because of the family history of tuberculosis, the patient and 3 siblings were vaccinated on June 18, 1954 with 1/16 ml. of Rosenthal’s B.C.G. vaccine (dry freeze), intradermally. Tuberculin tests preceding vaccination were negative and became positive by September 11, 1954. Because the patient had a continuously draining ulcer at the site of vaccination and a large, tender, fluctuant axillary lymph node, treatment was started with streptomycin sulfate 250 mg. twice weekly and 50 mg. of isoniazid t.i.d. on August 4. On September 11, the streptomycin sulfate was reduced to 125 mg. twice weekly, but the isoniazid was continued at the original dosage. This regimen of therapy was maintained until admission to the hospital on November 1.

About 1 hour before admission, the patient vomited several times while riding in the car with his mother. Shortly after this, the mother noted that he seemed less alert and responsive than usual. He then had 3 generalized clonic convulsions in rapid succession, following which he became unconscious. He was brought immediately to the hospital.

Physical Examination

He was found to be unresponsive and his color was poor. There were mild clonic movements of the extremities, blinking of the eyes and twitching of the lips. Weight, 10 kg.; temperature 36°C.; pulse, 100; respirations 28; blood pressure 90/60. The ocular fundi were normal. Deep tendon reflexes were absent. The skin revealed numerous small scattered cavernous hemangiomas which had been present since birth. The remainder of the examination was normal.

Laboratory Findings

Hemoglobin 11.8 gm.; leukocytes, 14,900/mm.³, mature polys 84 per cent, immature polys 3 per cent, myelocytes 1 per cent, lymphocytes 11 per cent. Eosinophils 1 per cent. Urine: negative for albumin, sugar and cells or casts. Serological test for syphilis: negative. Cerebrospinal fluid: Crystal clear; Pandy test negative; protein 7, sugar 117, chloride 128 mg./100 ml.; 2 erythrocytes/mm.³; culture, sterile.

Course

The patient received 48 mg. of phenobarbital, intramuscularly, upon arrival at the hospital followed in 15 minutes by 10 ml. of paraldehyde, rectally, following which all twitching and involuntary movements ceased.

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During the stay of 48 hours in the hospital, there were no more convulsions. He received parenteral fluids in the form of half-normal saline in 5 percent glucose during the first 24 hours after admission. He remained quiet and asleep for 18 hours and then gradually awakened. Within 36 hours after admission he seemed normal and lively. He was discharged on November 3 with a completely negative physical examination.

**Further observations**

On the morning following admission, the mother found an empty bottle from which she estimated 25 to 30 50-mg tablets of isoniazid were missing. This information was relayed immediately to the hospital, so that a 24-hour urine collection for analysis was obtained from the morning of November 2 to November 3. Washings from the snow suit on which he had vomited were also obtained. Quantitative analyses for isoniazid were as follows: 24-hour urine specimen: 212.1 mg. of isoniazid; Specimen of vomitus in tap water washings from snow suit: 693.8 mg. of isoniazid; Total isoniazid recovered: 905.9 mg.

It was estimated that the patient had ingested approximately 1500 mg of isoniazid of which possibly 500 to 800 mg had been absorbed, the rest being lost in vomitus. This would amount to an absorption of roughly 50 to 80 mg./kg. of body weight in a relatively short period.

An electroencephalogram obtained under sedation with Seconal® 11 days after the ingestion of isoniazid showed a normal sleep pattern for his age. He has been followed regularly for 12 months and is apparently an entirely normal child showing no residua.

**DISCUSSION**

Convulsions have been produced in experimental animals and in humans by the intramuscular or intravenous administration of isoniazid, and also reported in adult patients with tuberculosis receiving the conventional dosages of this drug. These patients had epilepsy or a history of convulsions in the past. Reilly and co-workers reported that isoniazid lowered the convulsive threshold for photic stimulation in a group of schizophrenic adult patients.

It has been shown that the barbiturates (pentobarbital and phenobarbital) are exceedingly effective in controlling isoniazid convulsions in experimental animals and in humans. The effects of pyridoxine and isoniazid are somewhat antagonistic, and the administration of pyridoxine has proved to be of value in alleviating some of the toxic reactions caused by isoniazid. However, it appears that pyridoxine is not as effective in controlling isoniazid convulsions as are the barbiturates. It has been reported that diphenylhydantoin is of no value in the control of isoniazid convulsions.

From a survey of the literature one may conclude that the risk associated with the oral administration of the usual dosages of isoniazid to patients without convulsive tendencies is not great. However, those patients who have a history of convulsive disorders should be given daily doses of phenobarbital throughout the entire period of isoniazid therapy.

Because isoniazid is excreted almost entirely in the urine, patients with poor kidney function being given isoniazid should also be protected from convulsions by maintenance doses of phenobarbital.

**REFERENCES**

ARTICLES  


SUMMARIO IN INTERLINGUA

Reaction Convulsive in un Infante Bienne post le Ingestion Accidental de un Dosage Excessive de Isoniazido

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