Non Salicylate-Associated Reye Syndrome: A Case Report

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Abstract- Reye's syndrome (RS) is a rare disease, usually associated with consumption of salicylates during viral illness. In 1965, the first case of association between RS and salicylates was described in United Kingdom (UK). The incidence of RS decreased dramatically after warnings of UK and US health agencies against using aspirin in children. Patients with RS presented with neurologic compromise, cerebral edema, acute hepatitis, and liver failure-especially in the children. In this paper, a four-month-old boy with diagnosis of RS was described, who presented with malaise, cyanosis and decreased level of consciousness, but the history of salicylates consumption was negative for him and his mother.

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Keywords: Reye syndrome; Salicylates; Encephalopathy; Coma; Virus diseases

Introduction

Reye's syndrome (RS) was described by Reye *et al*., in 1963 (1,2,3). In 1965, the first association between RS and salicylates was described in the United Kingdom (UK) (4). The incidence of RS decreased dramatically after warnings of UK and US health agencies against using aspirin in children (5,6). Salicylates are found in many natural remedies, such as willow-tree bark herbal tea (7). Other medications, especially antiepileptic's, such as valproate and phenothiazines also have been associated with RS (2,8).

RS is a biphasic illness; in the first phase, the patient presents with a viral prodromal, followed by a 1-5 days long asymptomatic period. In second phase, the symptoms include vomiting, irritability, and possible convulsions, and decreased neurological status (reduction in Glasgow Coma Scale scores). In up to 40% of patients, RS may lead to death (2,9). This syndrome may be associated with raised intracranial pressure, non-inflammatory encephalopathy, elevation of alanine transaminase (ALT), aspartate transaminase (AST), ammonia levels, and pan-lobular microvesicular fatty infiltration on liver biopsy (5). The abdomen may be distended with hepatomegaly, but no signs of rash and jaundice exist (2,3,10).

RS is a rare disease and usually associated with consumption of salicylates during viral illness. In this paper, a 4-month-old boy with diagnosis of RS was described, who presented with malaise, cyanosis and decreased level of consciousness, but the history of salicylates consumption was negative for him and his mother.

Case Report

A 4-month-old boy from Southwest of Iran (Yasuj) presented to the emergency ward with chief complaint of malaise, cyanosis, and decreased level of consciousness.

The patient was well until four days before admission when he was taken to an outpatient clinic for fever evaluation. Acetaminophen and pediatric cold syrup were administered for treatment of common cold. One day after this intervention, the patient was again referred to hospital for malaise and cyanosis. In-hospital course, the patient developed respiratory distress, decreased oxygen saturation, sepsis signs, and symptoms, and decreased level of consciousness. He was intubated and admitted to PICU (pediatric intensive care unit).

He had no history of icterus, failure to thrive, travel history, diarrhea, and rash. In addition, he had no history of any previous disease or metabolic diseases. Administered medications were Acetaminophen and pediatric cold syrup. His parents had no congenital or infectious diseases. His mother had not taken salicylates.

On examination, the body temperature, blood pressure, heart rate, respiratory rate, and oxygen saturation were 37.9° C, 70/50 mm Hg, 148 beats/min, 46

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breaths/min and 87%, respectively.
Physical examination revealed hepatomegaly, mottling of abdomen, and extremities. All other examinations were normal.

The white blood cell count was 11.6 (seg: 35%, lymph: 65%). Hemoglobin and the platelet count were 8.5 (gr/dl) and 827000 (1000×mm3), respectively. The results of other lab tests were: ALT=75 (Iu/L), AST =171 (Iu/L), alkaline phosphatase=542 (Iu/L), albumin=3 (gr/dl) , total bilirubin=2 (mg/dl), conjugated bilirubin=1.25 (mg/dl), lactate dehydrogenase (LDH)=1131 (U/L), sodium=128 (mEq/L)), blood sugar=37 (mg/dl), PH (potential of hydrogen)=7.16, CO2 (Carbon dioxide)=33 (mm Hg), and HCO3 (bicarbonate)=11.5 (mEq/L). Other laboratory tests, such as creatinine, potassium, and calcium were normal. Blood culture was negative. Cerebrospinal fluid (CSF) analysis was normal.

Abdominal ultrasonography revealed mild hepatomegaly with mild increased parenchymal echo pattern of the liver. Chest X-ray (CXR) was normal.

Treatment with dextrose water, normal saline, vancomycin, amikacin, acyclovir, pantoprazole, and phenobarbital was initiated during the hospital course. Unfortunately, the patient died in PICU after 48 hours. The liver was yellowish in gross appearance during autopsy and showed pan-lobular fatty infiltration (Figure 1). Also, brain tissue autopsy showed brain edema (Figure 2, 3).

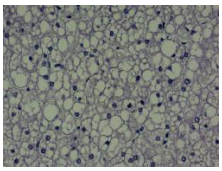

Figure 1. Hepatic tissue autopsy showed pan-lobular fatty infiltration. (Magnification: 400×)

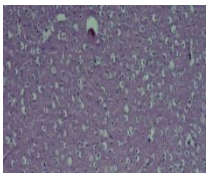

Figure 2. Brain tissue autopsy showed brain edema. (Magnification: 100×)

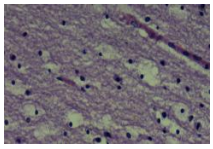

Figure 3. Brain tissue autopsy showed brain edema. (Magnification: 400×)

Discussion

The CDC criteria for definition of RS is: (a) clinically documented acute non-inflammatory encephalopathy (alteration in level of consciousness) and, if available, 8 leukocytes or fewer in cerebrospinal fluid, or cerebral edema that was demonstrated by a histological specimen without meningeal or perivascular inflammation; (b) a liver autopsy or biopsy that is diagnostic of RS, or ≥3 rise in the levels of either serum ammonia, serum glutamic pyruvate kinase or serum glutamate oxaloacetate transaminase; and (c) no other explanation for the liver or brain abnormalities (11,12).

The etiology of RS is unknown. Metabolic disorders that could be confused with RS include 3-hydroxy-3-methyl-glutarate lyase deficiency, primary carnitine deficiency, methylmalonic acidemia, and hereditary fructose intolerance (2,9).

While the use of salicylates was at its peak for management of viral infections in the past, RS occurred at a fairly high incidence rate and patients presented with neurologic compromise, cerebral edema, acute hepatitis, and liver failure especially in children (2,5-8,9).

In this paper, we described a rare case of RS. Although RS usually is associated with salicylates prescription during viral illness, our patient had no history of salicylates consumption.

In children who presented with signs and symptoms of encephalopathy and hepatitis, the RS should be in our differential diagnosis, even though the patient has no history of salicylates consumption.

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