


Case Report

A rare case of Reye's syndrome induced by influenza A virus with use of ibuprofen in an adult

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Background: Reye's syndrome (RS) is a rare but severe acute life-threatening disease characterized by encephalopathy and fatty liver damage. Reye's syndrome is most common in children and rarely occurs in adults.

Case presentation: A 56-year-old woman was admitted to the emergency department with disturbance of consciousness and respiratory failure. She had taken ibuprofen for headache. Her Glasgow Coma Scale score was E3V3M5 on admission. The laboratory findings revealed acute liver failure with prothrombin time – international normalized ratio of 3.16, aspartate aminotransferase 12,548 IU/L, alanine aminotransferase 5,725 IU/L, and blood ammonia 102 µg/dL. Head magnetic resonance imaging showed hyperintense signals on diffusion-weighted images of globus pallidus.

We diagnosed the patient with RS induced by influenza A and use of ibuprofen. The patient received supportive care in the intensive care unit and her clinical outcome was favorable.

Conclusion: Ibuprofen might be a risk factor for RS.

Key words: Acute liver failure, encephalopathy, ER, influenza A, Reye's syndrome

INTRODUCTION

REYE's syndrome (RS) is a rare but severe acute life-threatening disease characterized by encephalopathy and fatty degeneration of liver.¹ The etiology, epidemiology of RS remains largely unknown.¹ Reye's syndrome occurs almost exclusively in children.¹ There are few reports of RS in adult patients.² Epidemiologic evidence indicates that aspirin is the major preventable risk factor for RS.³ The mechanism by which aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) trigger RS is not completely understood.^{3,4} A "Reye's-like" illness can occur in children with genetic metabolic disorders and other toxic disorders.⁵ After warnings were issued against treating children with aspirin and other NSAIDs, the number of cases of RS has dramatically declined.¹ There are many over-the-counter drugs that contain aspirin or NSAIDs, so the risk of RS

persists. Here, we report the case of a 56-year-old woman with RS induced by influenza A and ibuprofen.

CASE PRESENTATION

A 56-year-old woman was admitted to our emergency department (ED) with disturbance of consciousness and respiratory failure. She had influenza-like symptoms including cough and fatigue without fever 2 days prior to presentation. She did not have a medical history but took an over-the-counter drug that contains ibuprofen for headache.

The patient's height was 139 cm and weight was 29.0 kg. Her vital signs were: blood pressure, 131/78 mm Hg; heart rate, 78 b.p.m. and regular; axillary temperature, 35.1°C; respiratory rate, 30 breaths/min; SpO₂, 85% with oxygen delivered through a face mask (3 L/min); and a Glasgow Coma Scale score of E3V3M5 on admission.

Rapid viral testing was positive for influenza A virus. Significant laboratory results included hypoglycemia (serum glucose, 48 mg/dL), transaminitis (aspartate aminotransferase [AST] 12,548 IU/L and alanine aminotransferase [ALT] 5,725 IU/L), hyperbilirubinemia (total bilirubin 3.5 mg/dL and direct bilirubin 1.6 mg/dL), elevated

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international normalized ratio (INR; 3.16), hyperammonemia (ammonia 102 $\mu\text{g/dL}$), lactic acidosis (7.0 mmol/L), azotemia (blood urea nitrogen 55 mg/dL), hypercreatinemia (serum creatinine 2.32 mg/dL), hyponatremia (134 mmol/L), hyperkalemia (6.7 mmol/L), hypolipidemia (total cholesterol 114 mg/dL and triglyceride 29 mg/dL). Carnitine was normal (223 $\mu\text{mol/L}$). Her liver function was normal 5 days before presentation.

The head computed tomography (CT) revealed no specific findings, although the head magnetic resonance imaging showed hyperintense signals at the bilateral globus pallidus in diffusion-weighted images and fluid attenuation inversion recovery (FLAIR)-weighted images and a hyperintense signal at the left front parietal lobe in FLAIR-weighted images (Fig. 1). Abdominal CT revealed fatty and enlarged liver. Chest CT showed diffuse alveolar type infiltrates in the patient's right middle lobe with air bronchograms and respiratory muscle loss. Based on these findings, we diagnosed the patient with RS induced by influenza A virus and pneumonia. The clinical course of the patient is shown in Figure 2. She

was intubated and placed on mechanical ventilation in the ED then transferred to the intensive care unit for supportive care. She was treated with prednisolone (500 mg/day for 3 days) and peramivir (100 mg/day for 5 days) for influenza encephalopathy. The patient's liver function gradually improved with supportive care, fresh frozen plasma, and vitamin K. Her transaminase trended down from AST 7,546 IU/L and ALT 4,127 IU/L on day 2, to AST 85 IU/L and ALT 704 IU/L on day 7, and to AST 23 IU/L and ALT 169 IU/L on day 14 of hospitalization. Her INR trended down from 3.16 on day 1, to 1.28 on day 7, and to 1.07 on day 14. A tracheostomy was carried out on day 12 because of respiratory insufficiency type II due to muscle atrophy with chronic malnutrition.

On 14 day, the patient's condition had dramatically improved, with no abnormal neurological findings. Her appetite returned to normal and anorexia resolved. Her total duration of hospital stay was 71 days, and she was transferred to a rehabilitation hospital without neurological deficits.

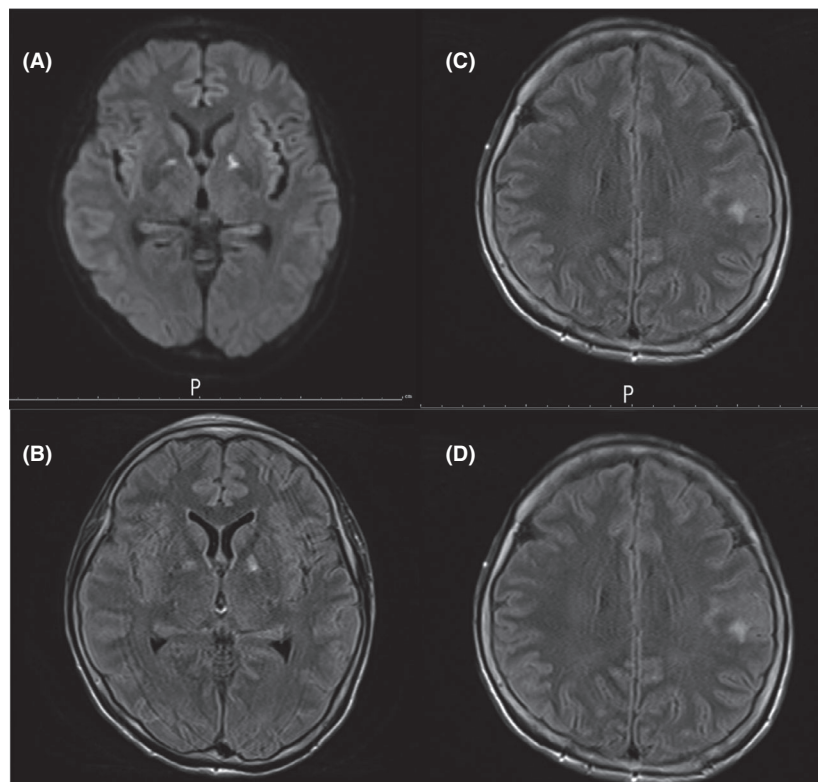


Fig. 1. Imaging findings of a 56-year-old woman with Reye's syndrome induced by influenza A and use of ibuprofen. Head magnetic resonance imaging shows hyperintense signals at the bilateral globus pallidus in diffusion-weighted images (A) and fluid attenuation inversion recovery (FLAIR)-weighted images (B), no signal at the left front parietal lobe in diffusion-weighted images (C), and a hyperintense signal at the left front parietal lobe in FLAIR-weighted images (D).

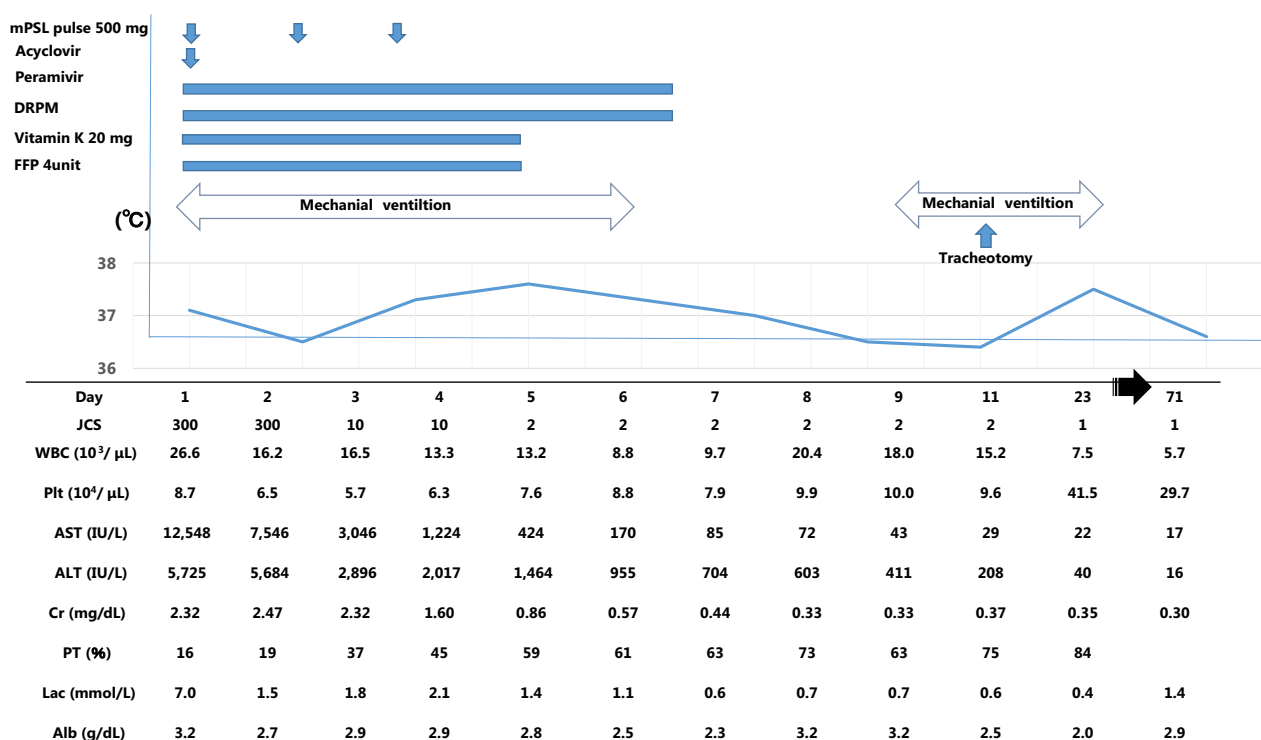


Fig. 2. Clinical course of a 56-year-old woman with Reye's syndrome induced by influenza A and use of ibuprofen. Data regarding the patient's body temperature, Japanese coma scale (JCS) score, white blood cell count (WBC), platelet count (Plt), aspartate transaminase (AST), alanine transaminase (ALT), creatinine (Cr), prothrombin time (PT), lactate (Lac), and albumin (Alb) are shown. DRPM, dori-penem; FFP, fresh frozen plasma; mPSL, methyl prednisolone.

DISCUSSION

REYE's syndrome is a rare illness defined as acute non-inflammatory encephalopathy with fatty liver failure.^{1,2} Reye's syndrome was described as a distinct clinicopathological entity in 1963, characterized by disturbed consciousness, fever, convulsions, vomiting, disturbed respiratory rhythm, altered muscle tone, and altered reflexes.¹ The US Centers for Disease Control and Prevention has published the clinical criteria.⁶ Our patient had disturbance of consciousness on admission to the ED, even though she had been living independently and her liver function was found to be normal by a local doctor 5 days before presentation. She also had transaminitis. We did not undertake a lumbar puncture because of coagulation disorder induced by liver failure. Although the patient was an adult, based on the findings, she was diagnosed with RS.

Few published reports have described RS in adults. However, RS in adults might be more common than previously thought. There should be a high index of suspicion for RS in adult patients who present with vomiting and deterioration

in mentation following influenza virus infection.⁷ Our patient had symptoms other than vomiting.

Reye's syndrome needs supportive care (mechanical ventilation, transfusion, thiamine, vitamin K, lactulose, and neomycin) and monitoring of multiple organ parameters in an intensive care unit setting in both adults and children.^{4,7} The use of corticosteroids is controversial. However, we treated our patient with corticosteroids to prevent brain edema. In published reports, multi-organ function might recover completely within a few days in cases in which encephalopathy resolves.⁴ However, the severity and duration of both metabolic and hydrostatic effects on the nervous system will determine prognosis.⁸ The prognosis in adults with RS is extremely poor in case of serum ammonia over 300 μg/dL. However, the prognosis of RS in adults is favorable compared with RS in children.⁷

Although the precise cause of RS is unknown, a previous study reported a strong epidemiological association between aspirin ingestion during antecedent viral infection and subsequent RS development.³ Ibuprofen is a widely used NSAID

and over-the-counter medication. There are no published reports of an association between RS and ibuprofen. Complications of ibuprofen include gastrointestinal hematoma, acute renal failure, anaphylaxis, and metabolic acidosis. However, ibuprofen was found to have a very low rate of liver toxicity.⁹ Central nervous disorders, such as coma and seizures, occur in less than 10% of ibuprofen overdose cases.¹⁰ Pires *et al.*¹¹ described ibuprofen-induced aseptic meningitis. Aseptic meningitis induced by NSAIDs, including ibuprofen, can occur in patients that previously tolerated the offending drug. Prior exposure to the drug has been noted in 35% of patients with ibuprofen-induced meningitis.¹¹ The mechanism of aseptic meningitis and RS induced by ibuprofen are unknown. However, RS might be related to NSAIDs because they include aspirin and ibuprofen.

CONCLUSION

WE REPORT A rare case of RS induced by influenza A virus in an adult. More reports of such rare cases are needed to confirm our findings. We should keep in mind the risk of RS with use of ibuprofen.

DISCLOSURE

Approval of the research protocol: None.

Informed consent: Informed consent was obtained from the patient.

Registry and registration no. of the study/trial: None.

Animal studies: None.

Conflict of interest: None declared.

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