

Acute hepatic failure in pediatric H1N1 infection: a case report from Al-Adan Hospital, Kuwait

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Abstract: Liver involvement in pediatric influenza A (H1N1) infection is rare. Focused clinical evaluation and laboratory tests can rule out or identify hepatic complications early on. Here we report on a 9-year-old boy treated by the Gastroenterology, Hepatology, and Nutrition Unit of Al-Adan Hospital's Pediatric Department. The patient, who was infected with H1N1 during the 2010 pandemic, showed symptoms of associated acute hepatic failure, was managed conservatively, and recovered completely following treatment. The author would like to draw the attention of pediatricians to the hepatic aspect of human H1N1 infection in order for them to recognize it early and treat it in a timely manner.

Keywords: influenza A (H1N1), infection, acute liver failure, children

Introduction

The 2010 human influenza A (H1N1) virus pandemic seriously affected many countries, including Kuwait. In children, respiratory involvement usually occurs with H1N1; extra pulmonary problems are not common.¹ Liver involvement is rare and needs early identification and treatment. A lack of early intervention can lead to worse outcomes.

Case report

A 9-year-old child was admitted with intermittent low-grade fever, cough, vomiting, and abdominal pain lasting for one week. He received oral antibiotics; the fever subsided initially but reappeared after a few days, along with jaundice. There was no history of skin rash, drug ingestion, or recent travel. He was previously healthy, with no past history of liver disease. On examination, he was alert and oriented, his temperature was 39°C, he was icteric, appeared toxic, was sweating, had a respiratory rate of 30 breaths/minute, and had congested tonsils; a respiratory system exam showed prolonged expiration with expiratory rhonchi. He also had right upper quadrant abdominal tenderness. There were no signs of meningeal irritation, and the rest of his physical examination was unremarkable.

Investigations revealed a hemoglobin (Hb) count of 14.5 g/dL, a total leukocyte count of 3.37×10^9 , neutrophils 19%, lymphocytes 68%, a platelet count of 255×10^9 . Random blood glucose and renal function were both within normal limits. Urinalysis showed mild urobilinogen and ketones, but a urine culture was sterile after 48 hours of incubation. His total serum bilirubin was 66 mmol/L, direct fraction was 37 mmol/L, alanine amino-transferase was 1763 U/L, aspartate amino-transferase

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Table 1 The patient's laboratory parameters over time

Parameter	At admission	After 1 week	After 2 months
Hemoglobin count (g/dL)	14.5	13.9	14.1
Total white cell count (10 ⁹)	3.37	5.51	6.45
Neutrophils (%)	19%	26%	29%
Lymphocytes (%)	68%	51%	31%
Total bilirubin (μmol/L)	66	29	6.5
Direct bilirubin (μmol/L)	37	17	4.3
ALT (U/L)	1763	855	34
AST (U/L)	1871	977	31
ALP (U/L)	245	255	234
GGT (U/L)	107	90	56
PT (seconds)	30	14	12
INR (seconds)	2.6	1.3	1.1
Albumin (g/L)	40	42	41
Ammonia (mmol/L)	74	46	50
Lactate (mmol/L)	2.06	1.99	1.8

Abbreviations: ALT, alanine transaminase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, γ-glutamyltransferase; PT, prothrombin time; INR, international normalized ratio; U/L, units per liter.

was 1871 units/L, alkaline phosphatase was 246 units/L, and gamma glutamyl transferase was 107 units/L. Prothrombin time was 30 seconds, international normalized ratio was 2.6, albumin count 40 g/L, serum ammonia count 74 mmol/L, and serum lactate 2.06 mmol/L. The patient had normal serum amylase and lipase levels, a negative cold agglutinin test, a normal ultrasound of the abdomen, and a negative chest X-ray. Nasal and throat swabs for H1N1 were positive by a reverse transcription polymerase chain reaction (PCR) test. A hepatitis A, B, and C serological screen was negative, and his serum acetaminophen level was normal. Furthermore, an additional work-up to rule out other causes of fulminant liver failure was performed, including negative blood tests for herpes simplex virus PCR, adenovirus PCR, Epstein–Barr virus, and cytomegalovirus PCR. He had a normal α-1 antitrypsin level with an MM phenotype. His immunoglobulins (IgG, IgM, and IgA) were within normal limits; he also had a negative antinuclear antibody (ANA) < 1:40 titer and a negative anti-smooth muscle antibody and anti-liver–kidney microsomal antibody (anti-LKM), ruling out the possibility of autoimmune hepatitis. Finally, his serum amino acid and urine organic acids were unremarkable.

He was treated according to Centers for Disease Control and Prevention (CDC) guidelines^{2,3} with TAMIFLU® (oseltamivir; Genentech, San Francisco, CA) for five days and other supportive measures, including fresh frozen plasma, IV-administered vitamin K, lactulose, and prophylactic intravenous antibiotics. Hepatic parameters were monitored closely. He improved through this treatment and recovered

clinically within seven days of admission. His liver enzymes were normalized after two months without any sequel.

Discussion

Influenza is an acute and generally self-limited respiratory illness. Severe infection is characterized by pneumonia, sepsis, septic shock, and multi-organ failure. Extra-pulmonary involvement is rare in uncomplicated human infections.¹ Studies of mouse models suggest multiple organ localization, including the lungs, heart, thymus, liver, and spleen.⁴ Sánchez-Torrent et al reported H1N1 encephalitis in a 3-month-old infant from Spain.⁵ Hepatic involvement is not frequent and accounts for less than 3% of all cases.¹ Carrillo-Esper et al, in 2010, reported two adult H1N1 patients with hepatic involvement.¹ El-Shabrawi et al, in 2011, reported a 10-month-old child with acute myocarditis and fulminant hepatic failure associated with H1N1.⁶ The subject of the current case report had acute hepatic failure that presented as jaundice, elevated liver enzymes, and coagulopathy. Most of the other causes of liver failure had been ruled out by relevant investigations. He responded well to antiviral and other supportive treatment, and showed full clinical and laboratory recovery.

Liver affection in influenza virus infections has been shown in experimental animal models. No viral replication is needed to produce hepatic damage, as there is evidence of hepatic oxidative stress and a decrease in antioxidant defenses even when the virus is isolated only from the lungs. This might be explained by the production of pro-inflammatory cytokines in the respiratory airway that leads to changes in hepatic metabolism and enzymatic activities.^{7,8}

Conclusion

Even though hepatic complications are rare in pediatric H1N1 cases, in reporting this case we would like to draw the attention of pediatric health care professionals to the importance of early recognition, focused investigations, diagnosis, and treatment of complicated human H1N1 infection.

Disclosure

The author reports no conflicts of interest in this work.

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