CASE REPORT

Profound jaundice in a patient with acute hepatitis C

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SUMMARY

A 52-year-old African-American woman with overall good health and medical history of asthma and depression presented with right lower quadrant abdominal pain, vomiting and icterus for 3 weeks. Her physical examination was remarkable for only sclera icterus and mild tenderness on palpation in the right lower quadrant. Investigations revealed marked hyperbilirubinemia and transaminitis, with other serological and radiological studies unremarkable and a hepatitis A, B and C panel negative 3 weeks before presentation. Repeat hepatitis panel showing hepatitis C antibody positive with viral load 20 739 524 IU/mL. Liver biopsy supported the diagnosis of acute hepatitis C infection.

BACKGROUND

It is estimated that about 2.7–3.5 million people in the USA have hepatitis C infection¹ and about 17 000 were newly infected in 2010 alone.² Studies have indicated that most people with hepatitis C virus (HCV) infection are unaware of the diagnosis and thereby do not receive proper care.^{3–6} In 2011, chronic liver disease and cirrhosis was listed among the top 15 leading causes of death in the USA.⁷ There is an estimated 17-fold increased risk of developing hepatocellular carcinoma in people with chronic HCV infection and these cases account for approximately 48% of liver cancers occurring in the USA.^{8–9} Many recent advances in medical therapy and treatment regimens offer higher cure rates and shorter treatment duration for HCV infection. Among the 130–170 million people worldwide with chronic HCV infection, current treatment options are promising and offer a greater than 60% likelihood of sustained virological response, regardless of viral genotype.^{10–13} Research is underway to develop a HCV vaccine, but development is difficult due to existence of multiple HCV genotypes, the limited availability of animal models and complex immunological responses to HCV infection.¹⁴

CASE PRESENTATION

A 52-year-old African-American woman with overall good health and medical history of asthma and depression presented with right lower quadrant abdominal pain, vomiting and icterus for 3 weeks. The pain was constant and cramping, fluctuating in intensity from 5 to 9 of 10, located mostly in the right lower quadrant and umbilical areas, and was associated with bilious vomiting. There were no changes in her mental status and no signs of any encephalopathy. No history of any recent blood transfusions. Her other history was unremarkable except for the occasional alcohol intake of 1–2

beers once a week and actively snorting cocaine. She was a commercial sex worker and had multiple sexual partners. Her home medications included albuterol and methadone.

On presentation, she was haemodynamically stable (body mass index 29), afebrile and oriented. Physical examination was remarkable for only sclera icterus and mild tenderness on palpation in the right lower quadrant with no guarding or rigidity. She had no palpable hepatomegaly.

INVESTIGATIONS

Her labs revealed hyperbilirubinemia and transaminitis with total bilirubin 15.8, direct bilirubin 12, alanine transaminase 1316, aspartate aminotransferase 2749, prothrombin time/international normalised ratio 15.9/1.49, ferritin 5351, iron saturation 88% and iron 211. Her acetaminophen levels were negative and drug screen positive cocaine and methadone. Hepatitis A, B and C panel 3 weeks ago was negative and an HIV test negative. On subsequent follow-up's her HIV 1/2 enzyme immunoassay remains non-reactive. An abdominal ultrasound showed cholelithiasis with no signs of cholecystitis. Autoimmune panel—antinuclear antibody, antimitochondrial antibody, antismooth muscle antibody and antiliver kidney microsomal 1 antibody were negative. Repeat hepatitis A and B showed hepatitis C antibody positive with viral load 20 739 524 IU/mL and genotype 1. A liver biopsy (figures 1 and 2) showed severe active-chronic hepatitis and hepatocytes showing ballooning degeneration and hyaline degeneration within the hepatocytes. Prominent Kupffer cell and councilman bodies were seen with no increased iron stores. On trichrome stain (figure 3) areas of prominent collagen was seen with no regenerative nodule. Fibrosis which was pan-zonal may be due to parenchymal collapse.

OUTCOME AND FOLLOW-UP

During her admission, nausea and vomiting resolved, she tolerated a clear fluid diet and remained haemodynamically stable, with no change in her mental status. Her transaminases and bilirubin trended down and she was discharged with outpatient follow-up for hepatitis C management.

DISCUSSION

Acute HCV mono-infection rarely presents clinically and most patients are asymptomatic.¹⁵ As per a report of the CDC published in 2009, 849 confirmed cases of acute hepatitis C were reported in 2007 of which 2/420 died, 242/494 were hospitalised, 340/478 had jaundice.¹⁶ Since most patients do not exhibit any symptoms, a majority of acute

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Figure 1 Biopsy slide showing hepatocyte ballooning and degeneration. Also seen are acute and chronic inflammatory cells.

HCV infection cases are unrecognised. Typically within 7–21 days after exposure, hepatitis C viral RNA becomes detectable in serum.¹⁷ Specific antibodies usually appear within 20–150 days of exposure (mean 50 days) and jaundice occurs in 1/5th of the total cases and correlates with a viral titre of 10^5 – 10^7 IU.^{15 18 19} Clinical illness is usually preceded by a prodrome of fatigue, lethargy, myalgias, low-grade fevers, nausea and vomiting, and right upper quadrant pain or discomfort.

A majority of HCV infections are transmitted by percutaneous exposure, and include intravenous drug use, needle-stick injuries, blood or blood product transfusions before availability of a standard screening test (1992) and inadequate infection control in healthcare settings.²⁰ In high-income countries intravenous drug use has been recognised as a major route of HCV infection²¹ and in medium–low income countries iatrogenic transmission accounts for majority of cases.²² Sexual route as a mode of transmission of hepatitis C has been less defined. Numerous studies have looked at sexual route as transmission for HCV and majority conclude the risk between 0% and 18%. The risk for transmission is lower for heterozygous monogamous couples and increases with presence of other risk factors including multiple sexual partners and sexual orientation. Thereby, sexual transmission presents a minimal or negligible risk for transmission of HCV infection.^{21 23–29} In the last few years there have been an increased incidence of HCV infection cases in HIV positive men, who have sex with men and several cases have been reported across Europe, Australia and USA.^{30–32}

As seen in our patient, she presented with classical clinical picture of prodrome of symptoms of nausea, vomiting, myalgias

Figure 2 Biopsy slide showing hyaline degeneration within the hepatocytes and councilman bodies are identified.

Figure 3 Trichrome stain on biopsy demonstrating areas of prominent collagen and fibrosis which is pan-zonal.

and abdominal pain associated with icterus. Her labs were remarkable for hyperbilirubinemia and transaminitis and derangement in the synthetic liver function. She had several risk factors identified in the case and includes substance misuse and at high risk secondary to being a commercial sex worker. In her case before her presentation she had earlier had a negative hepatitis A, B and C test 3 weeks before her presentation, however, this does not rule out acute infection ongoing before her presentation as she might have been in the window period. Standard second and third generation ELISA tests have positive predictive value of close to 95%, but the window period between HCV infection and seroconversion is at least 6–8 weeks.^{33 34}

She was also taking methadone; however, methadone has shown little evidence of hepatic injury in humans.³⁵ Cocaine can lead to hepatic necrosis as well as microvesicular steatosis.³⁶ In cocaine-mediated toxicity, site of necrosis can vary, some have zone 1 and 2 involvement, some have zone 2 and 3 involvement and in some can be non-zonal.³⁷ In our patient on the trichrome stain she had areas of prominent collagen and fibrosis which was pan-zonal, maybe due to parenchymal collapse. Also seen were active inflammatory cells, ballooning degeneration, councilman bodies and Kupffer cells. Similar findings can be noted in autoimmune hepatitis, however, her autoimmune panel was negative and her history is only remarkable for active cocaine use. Thereby it can be postulated that she had chronic inflammation secondary to cocaine use and as a second inciting factor developed severe acute hepatitis C infection which is substantiated by liver biopsy findings. However as yet there is no confirmatory histological marker for hepatitis C on biopsy, unlike hepatitis B.

Learning points

- ▶ Recognise acute hepatitis C as a differential diagnosis of acute liver injury and transmission routes.
- ▶ Recognise clinical features in a patient presenting with acute hepatitis C infection.
- ▶ Highlight spectrum of hepatitis C infection with acute presentation.

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