Case 43

A 42-year-old male caretaker had abnormal liver function tests when he went to see his family practitioner about back pain and fatigue. He remembered being jaundiced for 2 weeks when he was 18 years of age, but this was never investigated. He drank 2–3 cans of beer each week. He had not been tested for hepatitis C, but he had used intravenous drugs from 17 years of age until he was 24 years. There was no family history of liver disease or autoimmune disease. He was a non-smoker and not on any regular medication. He had been diagnosed with depression in the past and had taken fluoxetine 2 years ago.

On examination, there were multiple spider naevi, but no evidence of hepatosplenomegaly, ascites, or encephalopathy.

Investigations showed:

- Hb 15.2g/dL; WCC 5.6 x 10^9/L; platelets 126 x 10^9/L
- Prothrombin time 13.2 sec
- Bilirubin 30μmol/L; ALT 122 IU; ALP 205 IU; albumin 43g/L
- AFP 5 IU/mL
- HCV antibody positive
- HCV RNA 2,016,074 IU/mL
- HBsAb positive and HBcAb positive
- Ultrasound abdomen revealed a coarse liver texture, and an enlarged spleen (15cm)

Questions

43a) What is the most likely reason for jaundice when the patient was 18 years old?

43b) How severe is the patient's liver disease and what is his prognosis?

43c) Outline the advice that should be given to the patient regarding transmission.

43d) What further investigations are needed and what is the best treatment?

43e) What are the contraindications and possible complications of treatment?

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Answers

43a) **What is the most likely reason for jaundice when the patient was 18 years old?**

Acute presentation of hepatitis C with jaundice is very rare and most individuals present in the chronic phase with abnormal liver function tests. About 20–30% will spontaneously clear hepatitis C infection, which probably occurs within 6 months of acute infection. This cohort will have hepatitis C antibodies, but undetectable HCV RNA in the serum. Such people do not need follow-up and should be considered as uninfected. HCV RNA is therefore an important confirmatory test for hepatitis C infection, since treatment cannot be based on the detection of antibodies alone. In this man, jaundice almost certainly resulted from **acute hepatitis B** infection, which is cleared in 90% of adults who become infected. This is consistent with the detection of hepatitis B core and surface antibodies.

43b) **How severe is the patient's liver disease and what is his prognosis?**

The presence of thrombocytopenia and splenomegaly in a patient with chronic liver disease is highly suggestive of **cirrhosis**, which was subsequently confirmed by liver biopsy. About 10% of people with hepatitis C will progress to cirrhosis within 20 years. Risk factors for progression are coexistent heavy alcohol intake, immunosuppression such as HIV, or organ transplantation, age >40 years at infection, and male gender. Once cirrhosis develops, 25% will develop complications (such as ascites) by 10 years. There is a 1% per year risk of primary liver cell cancer once cirrhosis develops. The degree of elevation of ALT is unrelated to the extent of liver fibrosis although those with persistently normal liver function tests tend to have less fibrosis and progress more slowly. In contrast to HIV, HCV viral load is not a prognostic indicator and is mainly used to evaluate the response to therapy.

43c) **Outline the advice that should be given to the patient regarding transmission.**

Transmission of HCV is either percutaneous (blood transfusion or needle-stick injury) or non-percutaneous (sexual contact, perinatal exposure). After the introduction of anti-HCV screening of blood donors in 1991, the rate of transfusion-related cases of HCV declined significantly in the UK. Intravenous drug use is now the most common risk factor in the UK. Sexual transmission is rare, but has been reported in homosexuals. Hepatitis C is more prevalent in southern Europe and the

Indian subcontinent, where inadequate cleaning of needles used for vaccination has been a prevalent iatrogenic cause in the past. There is no effective vaccine and no effective post-exposure prophylaxis against HCV. Emphasis should be placed on counselling HCV-infected patients and those at risk of infection.

The patient should be advised to avoid sharing razors or toothbrushes and to cover any open wound. Safe sexual practice, such as the use of condoms, should be encouraged in patients with multiple sexual partners, although this is not recommended for people involved in long-term monogamous relationships. HCV-infected patients who are users of intravenous drugs should be vaccinated against HBV if not immune.

43c) **What further investigations are needed and what is the best treatment?**

An **endoscopy** to screen for varices, **hepatic ultrasound**, and measurement of **AFP** every 6 months, to screen for hepatocellular carcinoma (see Case 14), are appropriate. The viral **genotype** and **viral load** should be measured.

The goal of therapy in hepatitis C infection is a **sustained virological response**, defined as undetectable HCV RNA in peripheral blood 24 weeks after antiviral treatment has stopped. **Standard treatment** for hepatitis C consists of pegylated interferon-α given once weekly, together with oral ribavirin. Overall cure rates are 50%, but this depends on the viral genotype. Only 45% with genotype 1 (the most common type in the UK) are cured after a 12-month course of therapy, compared with 60–70% for genotype 3, and 90% with genotype 2. Only 6 months' therapy is needed for genotype 2. Cure rates are lower in cirrhosis or coinfection with HIV.

43d) **What are the contraindications and possible side effects of treatment?**

Ribavirin may cause a 3–4g/dL drop in haemoglobin. A substantial side effect of interferon is psychological depression, fatigue, or irritability. Relative **contraindications** to therapy include a myocardial infarction within 6 months or severe cardiac failure, haemoglobinopathies, renal failure (since ribavirin is excreted by the kidneys), decompensated liver disease, immunosuppression (such as transplant patients), uncontrolled thyroid disease, pregnancy, and male partners of pregnant women.

Potential **side effects** of combined therapy include:

- Flu-like symptoms (to be expected with interferon)
- Diarrhoea

- Fatigue
- Skin rashes
- Increased susceptibility to infection
- Thyroid dysfunction
- Psychiatric disturbance
- Bone marrow suppression
- Local reactions at injection sites.

Side effects frequently necessitate interruption of treatment and dose reduction. Severe or life-threatening side effects are infrequent but do occur. A good **predictor of treatment response** is loss of detectable HCV RNA within 4 weeks of starting therapy.

This patient was treated with pegylated interferon and ribavirin for 12 months. He needed antidepressants during therapy and had to stop work as a consequence. He returned to work a month after stopping therapy. His HCV RNA at 4 weeks dropped to 1540 IU/ml and was undetectable at week 12. Six months after stopping therapy his liver function was normal and HCV PCR remained negative, consistent with cure.

Further reading

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