CASE REPORT

Chronic hepatitis C therapy: a rare complication revisited

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SUMMARY

The combined regimen of peg-interferon α 2a plus ribavirin along with protease inhibitors (boceprevir or telaprevir) is considered as a very potent and effective therapy for hepatitis C infections. However, this combined therapy has been associated with a side effect that can make the course of the disease more complicated. In this case, a 50-year-old man developed insulin-dependent diabetes soon after initiating triple hepatitis C therapy. The treatment had to be stopped and the course of his hepatitis C infection has been challenged with this rare side effect.

BACKGROUND

The combined regimen of pegylated interferon α (Peg-IFN α)2a plus ribavirin (RBV) along with protease inhibitors (boceprevir or telaprevir) is considered as a very potent and effective therapy for hepatitis C infections. This regimen has been linked with many side effects that can indicate stopping the therapy. One of the rare complications is the development of insulin-dependent diabetes. The mechanism suggested is the development of pancreatic associated auto antibodies (PAAA) which attack B cell islets and causes diabetes. Routine testing for PAAA before initiating therapy has not been recommended, but checking blood sugars before and during the course of therapy is reasonable.

CASE PRESENTATION

A 54-year-old Caucasian man with a remote history of drug abuse and chronic hepatitis C presented to our emergency department with a 1-week history of non-bloody vomiting and vague abdominal pain associated with polydipsia and polyuria. Initially, he was able to tolerate little oral intake, but the abdominal pain became worse. He denied fever, recent food poisoning, eating outside, recent travel or trauma. He denied personal or family history of diabetes mellitus and recent use of alcohol or drugs. However, on review of medications, he was started on triple therapy of Peg-IFN α 2a (180 μ g subcutaneously every week) plus ribavirin (500 mg twice daily) plus telaprevir (750 mg every 8 h) for genotype 1a hepatitis C virus (HCV) infection and completed 7 weeks of treatment. Physical examination was significant for mild dehydration and epigastric abdominal tenderness with no rebound tenderness or guarding.

INVESTIGATIONS

Blood work showed blood sugar level of 884 mg/dL (normal range 80–120 mg/dL), bicarbonate level of 14 mEq/L (normal range 22–26 mEq/L), anion gap of 20 and positive ketones in the urine. This confirmed the diagnosis of diabetic ketoacidosis; he was managed in the intensive care unit with intravenous insulin infusion and intravenous fluids. Glycated haemoglobin was 9.7% (up from 5.3% 6 months ago; normal range 4% and 5.6%), HCV RNA viral load was undetectable at this point. Antigliutamic acid decarboxylase (anti-GAD) antibodies were markedly elevated at 24 800 U/mL (normal <1.5 U/mL), serum C-peptide level was <0.1 ng/mL and anti-islet cell antibodies were elevated at 30 (normal <5 JDF-U). These results confirmed the link between hepatitis C and diabetes and triple therapy was discontinued.

OUTCOME AND FOLLOW-UP

Few days later, the patient was discharged on subcutaneous insulin with proper diabetic education. Six months after the discharge, he had a relapse in his HCV RNA viral load, but no treatment was initiated due to uncontrolled diabetes.

DISCUSSION

The combined regimen of Peg-IFN α , ribavirin and telaprevir is an effective treatment for 65–75% of patients with genotype 1 chronic HCV infection.¹ This regimen has been linked with many side effects that can indicate stopping the therapy which include influenza-like symptoms, mood disorder, weakness, anaemia, fever, headache and insomnia. Autoimmune hepatitis, haemolytic anaemia, thrombocytopenic purpura, hypothyroidism and systemic lupus erythematosus have been reported as well but less commonly.² Autoimmune diabetes mellitus or diabetes mellitus type I (DMTI) is a rare complication of IFN therapy with less than 30 cases have thus far been reported.³ Although DMTI theoretically can occur after IFN therapy for any disease, an Italian study showed that most cases were seen in patients with chronic HCV infection.⁴ IFN is a well-known immunomodulator; it enhances the expression of major histocompatibility complex (MHC) molecules which ultimately produce cytokines (IFN, interleukin 2). These cytokines enhance the cellular immune responses and stimulate immune system to produce PAAA that mainly include GDA antibodies, islet cell autoantibodies (ICA), insulin autoantibodies and others. PAAA eventually attack β cells and result in DMTI.⁵

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The time elapses from IFN therapy, appearance of PAAA and DMTI development is not very clear, but can be few weeks to few months before the onset of DMTI. Ninety-four per cent of patients had positive ICA at the onset of DMTI.⁶ Positive anti-GAD antibodies and islet cell antibodies in combination have very high specificity and positive predictive value for DMTI (99%) and are sufficient to discriminate it from other types of DM. Because Peg-IFN prolongs its half-life and RBV has similar work mechanisms, cases of DMTI with dual therapy (Peg-IFN plus RBV) are higher in number and faster in occurrence. In most reported cases, investigators suggested to discontinue IFN therapy after the onset of DMTI although doing so does not always halt the evolution of DMTI. Clinical remission of IFN-related DMTI occurred in some cases after IFN therapy discontinuation.⁷ Given the rarity of this complication, we think that checking PAAA routinely before or during IFN therapy is not applicable; however, we suggest that serial measurement of blood glucose levels before and during therapy in order to avoid serious complications (such as ketoacidosis) is still reasonable.

Learning points

- ▶ The combined regimen of pegylated interferon α (Peg-IFN α), ribavirin and telaprevir is an effective treatment for chronic hepatitis C.
- ▶ Once diabetes develops during treatment with IFN α and ribavirin, therapy has to be discontinued.
- ▶ Serial measurement of blood glucose levels before and during therapy for chronic hepatitis C in order to avoid serious complications (such as ketoacidosis) is reasonable.
- ▶ Discontinue IFN therapy after the onset of diabetes mellitus type I does not always halt the evolution of diabetes.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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