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SCIENTIFIC LETTERS

Reactivation of pulmonary tuberculosis during treatment with triple therapy for hepatitis C☆

Reactivación de tuberculosis pulmonar durante el tratamiento con triple terapia de la hepatitis C

Treatment of hepatitis C virus (HCV) with peginterferon and ribavirin is associated with a higher risk of infections due to their immunomodulatory action and bone marrow toxicity, which often causes neutropenia. An increase in infections (especially respiratory, sometimes severe) has been described in patients with cirrhosis following the use of triple therapy that includes a protease inhibitor (either boceprevir or telaprevir).[1] Nevertheless, very few cases of tuberculosis reactivation have been reported, even though antiviral treatment of HCV can compromise cellular immunity – essential against tuberculosis infection.

We present the case of a 53-year-old man with a history of smoking and chronic alcoholism of around 100 g/day up to 3 years previously. He had been in prison when 24 years old, had a tattoo and had psoriasis vulgaris involving the face, neck, elbows and knees. He was being followed-up in our clinic for chronic HCV infection–genotype 1a, with a high viral load (4,280,000 IU, 6.63 log)–and for fibrosis grade F3 measured by transition elastography (9.8 kPa). He had not previously received antiviral treatment. Interleukin 28-B was CC genotype. Following the usual preliminary study, treatment was prescribed based on triple therapy with a lead-in strategy for boceprevir. He received 180 μg/week of peginterferon alfa-2a and 1200 mg/day of ribavirin and, since viral RNA had decreased by 2.26 log by the end of week 4, boceprevir was added at the standard dose of 800 mg/8 h. By week 8 of treatment, the viral load was undetectable and continued thus at a further check-up in week 12.

As side effects, the patient presented exacerbation of his psoriasis, treated with topical tacalcitol, and moderate anaemia (Hb 9.8 mg/dL), managed by reducing the ribavirin dose to 800 mg/day. The patient, at this point, began to experience daily episodes of evening fever–not associated with the administration of interferon–but no other infectious symptoms. A urinary or maxillofacial origin was ruled out. A chest X-ray revealed heterogeneous increased density in the upper right apex, with images of nodules, linear opacities and possible cavitation. In view of these findings, tuberculin and quantiFERON-TB tests were requested, both of which were positive. Serology for human immunodeficiency virus (HIV) was repeated and was again negative. Sputum samples were not optimal, as the patient did not have expectoration, and so could not be assessed. Bronchoscopy was performed, resulting in bronchoalveolar aspirate material in which *Mycobacterium tuberculosis* was isolated. The patient was diagnosed with secondary (reactivation) pulmonary tuberculosis and was treated with 4 anti-tuberculosis drugs (rifampicin, isoniazid, ethambutol and pyrazinamide) for 2 months, followed by rifampicin and isoniazid at standard doses for a further 4 months.

With respect to the antiviral treatment, when the pulmonary tuberculosis diagnosis was confirmed, the patient was on week 19 of treatment, with an undetectable viral load, moderate but well-controlled anaemia and a white cell count of 2000 mm^{-3}. Boceprevir was discontinued due to its pharmacological interactions with rifampicin and isoniazid, while dual therapy with peginterferon and ribavirin was maintained. The triple therapy could have been discontinued at week 28, as this was a naive patient without cirrhosis and an extended rapid virologic response. However, in view of the events described, it was considered advisable to continue the dual antiviral therapy concurrently with the anti-tuberculosis treatment until week 48. The patient presented no new adverse events or side effects and, 6 months after completing the antiviral treatment, was found to have a sustained virologic response. Subsequent sputum tests were also negative.

Because tuberculosis is a very rare complication–with only 13 cases described in the literature–no routine clinical practice guidelines recommend screening prior to antiviral treatment.[2–7] Most reported cases were high-risk patients (prisoners, intravenous drug users and HIV-positive individuals) and only 2 were receiving triple therapy (1 boceprevir and 1 telaprevir).[2,3] Accordingly, some authors have proposed tuberculin testing in risk populations prior to antiviral treatment with peginterferon and ribavirin, with or without a protease inhibitor. Since antiviral treatment

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management once anti-tuberculosis treatment has been instigated has not been established, given the patient's excellent initial virologic response we decided to continue the former; however, we discontinued boceprevir as its efficacy is reduced on interaction with rifampicin and isoniazid.

Adverse effects on the immune system are virtually unknown with the new direct-acting antiviral drugs and interferon-free therapies, so an increase in infections is not likely. The new antiviral agents also have fewer pharmacological interactions.[8] Nevertheless, for treatments based on sofosbuvir, ledipasvir, daclatasvir, dasabuvir and ombitasvir, the anti-tuberculosis agent rifampicin is contraindicated due to its P-glycoprotein-inducing effect, which significantly reduces plasma drug concentrations.

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Pseudoachalasia in a patient with a history of non-Hodgkin lymphoma☆

Seudoacalasia en paciente con antecedentes de linfoma no Hodgkin

We present the case of a 48-year-old man with a personal history of non-Hodgkin lymphoma (mucosa-associated lymphoid tissue [MALT]-type) with intestinal involvement, diagnosed in 2004 and treated with chemotherapy. The patient has remained in remission since then.

The patient attended our clinic with a 3-month history of progressive dysphagia, chest pain irradiating to the back and weight loss of 10 kg. Findings for a gastroscopy were normal, while a barium swallow test revealed a 3-cm stenosis at the level of the gastro-oesophageal junction with no mass effect, suggesting incipient achalasia. The oesophageal body was normal in calibre, with no dilation or air-fluid level. Four-channel perfusion oesophageal manometry was performed in decubitus. The upper oesophageal sphincter was located at between 25.3 cm and 20 cm from the nasal ala and had a slightly increased resting pressure and normal function. Good pharyngo-oesophageal coordination was observed. The oesophageal body study with at least 10 swallows of 5 mL of water resulted in negative baseline pressure with respect to the fundal pressure. Waves in the body were low pressure and simultaneous. The lower oesophageal sphincter was located at between 44.5 cm and 40.3 cm, had an increased resting pressure (mean baseline pressure 40.6 mmHg) and showed an absence of complete relaxation during the swallow.

The patient progressed within a few days to aphagia with sialorrhoea. Given the rapid evolution of symptoms, a chest-abdominal computed tomography (CT) scan was performed to rule out pseudoachalasia (Fig. 1) with results pointing to a mass in the posterior–inferior mediastinum, obliterating the distal oesophagus and spreading to invade the mediastinal fat and right lung base and to surround the inferior vena cava. The plane of cleavage was lost with the inferior vena cava (although there was no clear infiltration) and also with the diaphragm. These findings suggested possible oesophageal carcinoma extending to surrounding structures or, less likely, pulmonary neoplasm with mediastinal infiltration. Pathological lymphadenopathies were also identified in the mediastinum, right retrocrural space, retroperitoneum (the largest, in the

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