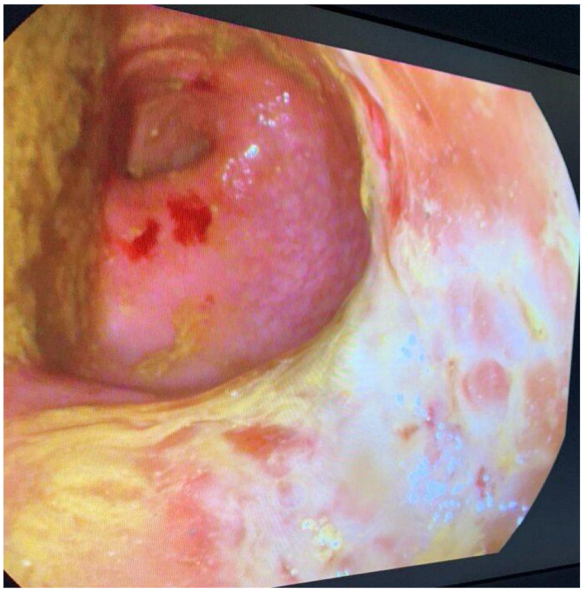

Figure 2 Severe left colitis.

Discussion

The differential diagnosis of enterocolitis in cancer patients includes the classic colitis associated with antibiotics and neutropenic colitis. However, other aetiologies, such drug-induced (in this case, secondary to immunotherapy drugs), are not always taken into account.[1]

Pembrolizumab is an immunotherapy drug approved for the treatment of metastatic melanoma. With the mechanism of action of this monoclonal antibody, it is only logical to expect autoimmune side effects deriving from the production of autoreactive T lymphocytes which act against different body tissues.[1,2]

Pembrolizumab-induced colitis is very rare (<1%), generally affecting the descending colon and becoming apparent with diarrhoea some six to 16 weeks after starting therapy. Less common gastrointestinal adverse effects include: mouth ulcers, oesophagitis, gastritis and perforation.[2]

Flare-ups are treated with corticosteroids. According to clinical experience, if there is no clear improvement in symptoms after three days of treatment with intravenous corticosteroids, it can be considered steroid-refractory colitis. In these cases, combination treatment with infliximab may be beneficial.[3] If symptoms persist after the first dose, a second dose can be given after two weeks. In some cases it is considered maintenance therapy due to the episodes of relapse seen, despite mucosal healing of the colon.[3,4] If symptoms do not improve after infliximab is used or if anti-TNF(is contraindicated, vedolizumab should be considered.[4]

Although there are very few reported cases in the literature, due to the boom in immunotherapy in recent years, an increased frequency of adverse reactions could be seen, and the possibility has to be taken into account. Although an association has been found between immune-mediated effects and a favourable tumour response,[5] in these cases, treatment must be stopped and the toxicity must be treated, as the prognosis and outcome can be fatal.

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Severe intrahepatic cholestasis as the initial manifestation of light chain amyloidosis

Colestasis intrahepática grave como manifestación inicial de la amiloidosis por depósito de cadenas ligeras

Amyloidosis is a rare disease characterized by deposition of insoluble, fibril-forming amyloid proteins in the extracellular space of organs, eventually producing insufficiency and end-organ dysfunction. The most common form of amyloidosis is light-chain (AL) amyloidosis. AL amyloidosis is a clonal plasma cell disorder, being the kidney, heart and peripheral nerves the most commonly organs affected.[1–4] Liver is often involved histologically (60–92%) in patients with AL amyloidosis, but most cases are clinically asymptomatic.[1,4,5]

This research presents the case of a 70-year-old man, without relevant past medical history, admitted to our hospital with progressive jaundice, choluria and abdominal distension for 2 weeks. There was no history of weight loss, encephalopathy or gastrointestinal bleeding. On physical

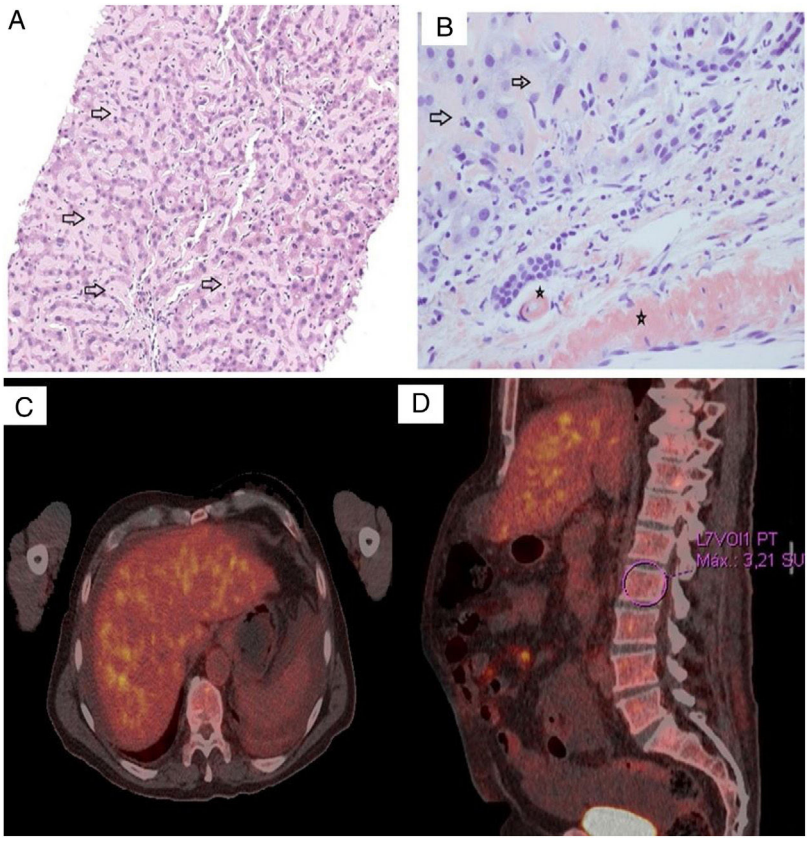

Figure 1 (A) Liver cell trabeculae are compressed by marked amyloid deposition in the sinusoids. Abundant acellular pink material (black arrows) on a H&E stain is seen in this high magnification picture. (B) The presence of amyloid was confirmed by apple green birefringence on Congo Red staining with polarized microscopy. The deposit was observed both in the sinusoids (arrows) as well as in the vessels wall (black star). (C, D) FDG-PET showed signs of hepatic infiltration (SUVmax = 4.3) and axial skeleton bone marrow heterogeneous hypercaptation (SUVmax L2 = 3.2).

examination, the patient presented generalized jaundice, mild peripheral edema and hepatomegaly, with a palpable liver until 3 cm below the right costal margin. Laboratory data showed hyperbilirubinemia (7.5 mg/dl) and cholestasis enzymes elevation (alkaline phosphatase 1273 U/L; gamma-glutamyl transferase 705 U/L). Hemogram, coagulation and renal function were both normal. Ultrasonography and computed tomography (CT) of the abdomen revealed hepatomegaly and portal hypertension signs, such as paraumbilical vein recanalization and mild quantity of ascites. Serologies for hepatitis A, B, C and E viruses, CMV, EBV and HIV were negative. Anti-nuclear, anti-mitochondrial and anti-smooth muscle antibodies were negative. Serum immunoglobulins (IgG, IgA, IgM) were negative. Proteinogram (alpha-1 globulin, alpha-2 globulin, beta globulin), ceruloplasmin and alpha 1-antitrypsin were in normal range.

Due to the existence of an acute cholestatic hepatitis with non-identified etiological agent, we performed a percutaneous liver biopsy. The liver tissue biopsy showed perisinusoidal deposition of an eosinophilic amorphous substance (Fig. 1A). Examination under polarized light of sections stained with Congo red demonstrated apple-green birefringence (Fig. 1B). Immunohistochemistry staining was negative for amyloid A and λ light chain, and positive for κ light chain. The histopathological diagnosis was an AL amyloidosis with κ light chain deposits.

The hematological study showed evidence of a monoclonal plasma cell proliferative disorder, appreciating in the laboratory data the presence of a serum and urine M protein, abnormal serum free light chain and serum protein electrophoresis (SPEP) IgG kappa. Clonal plasma cells could also be identified in the bone marrow. We observed 2.4% plasma cells with aberrant immunophenotype, so multiple myeloma presence was ruled out.

Bence Jones protein was detected in urine, yet kidney involvement was not found. Transthoracic echocardiogram (TTE) and electrocardiogram do not show cardiac involvement. Neurophysiological study was carried out, without appreciating signs of polyneuropathy or myopathy. Positron emission tomography with 18F-fluorodeoxyglucose (FDG-PET) was then performed to complete the study, revealing the presence of signs of hepatic infiltration and

axial skeleton bone marrow heterogeneous hypercaptation (Fig. 1C, D).

While making the assessment, liver function worsened. The patient experienced a deterioration of the liver biochemistry, with bilirubin 24.1 mg/dl and ALP 1065 U/L, and developed moderate ascites, with good response to diuretic treatment. Signs of acute liver failure were not seen during assessment.

Therefore, with the diagnosis of AL amyloidosis with exclusively liver involvement, chemotherapy treatment was initiated with bortezomib (adjusted-dose 0.7 mg/m^2, according to data sheet because of hyperbilirubinemia), cyclophosphamide and dexamethasone. Clinical and laboratory improvement was initially achieved, bringing bilirubin levels down to 10 mg/dl four weeks after initiation of treatment.

However, one month later the patient was readmitted to hospital due to hepatic decompensation with ascites, spontaneous bacterial peritonitis and bilateral pneumonia and finally died due to respiratory failure.

The clinical spectrum of hepatic amyloidosis can range from hepatomegaly (most frequently physical sign observed) and mild abnormal liver function tests, to more severe symptoms rarely observed, such as jaundice, intrahepatic cholestasis, portal hypertension, hepatic failure or spontaneous liver rupture.[1,3–5] Jaundice and intrahepatic cholestasis as the primary manifestation of the disease is very uncommon (<5% cases).[4]

Hyperbilirubinemia and marked elevation of serum alkaline phosphatase may indicate a poor prognosis of hepatic amyloidosis.[1,3–5]

Diagnosis of hepatic amyloidosis is based on a high clinical suspicion, exclusion of other infiltrative disorders of the liver (tuberculosis, sarcoidosis, malignancy and glycogen storage diseases) and tissue biopsy stained with Congo red demonstrating amyloid deposits with apple-green birefringence.[1,2,4,5]

Treatment of AL amyloidosis is based on chemotherapy to eradicate the underlying clone, usually combinations of bortezomib, cyclophosphamide and dexamethasone.[2,4] Patient who meet the criteria will be eligible for autologous hematopoietic cell transplantation.

Liver involvement in patients with amyloidosis is often an indicator of poor prognosis,[3] having been reported as 9 months the median survival of patients with primary hepatic amyloidosis.[1,3–5]

Conflicts of interest

There are no financial or other conflicts of interest regarding this article.

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Dysentery as a rare GI symptom found in COVID-19 patients

La disentería como síntoma digestivo poco frecuente que se encuentra en los pacientes con COVID-19

Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2 first started in Wuhan, China, and soon turned to a pandemic and still continue to spread across the world.[1,2] With an increasing number of COVID-19 cases outside of China, our clinics in Shahid Beheshti Hospital, Qom city, was faced with a large number of patients who were suspected of being infected with the SARS-CoV-2. Following the outbreak of COVID-19, the prevalence of gastrointestinal (GI) tract symptoms significantly goes up. This incidence in COVID-19 patients is well documented in literatures.[3] After February 20, 2020, the day that Iran reported as the start of COVID-19 outbreak, the number of patients referred to our GI clinic was unusually increased. The most important complaint of patients was the incidence of some unusual GI symptoms resistant to medication.[4]