

# A Rare Case of Pembrolizumab-Induced Hepatitis

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## Introduction

- The recent use of immune checkpoint inhibitors (ICI) has contributed to major breakthroughs in cancer therapy.
- Pembrolizumab is a monoclonal antibody used for many solid tumors.
- We report a case of a patient with gastric adenocarcinoma who developed drug-induced liver injury (DILI) from pembrolizumab.

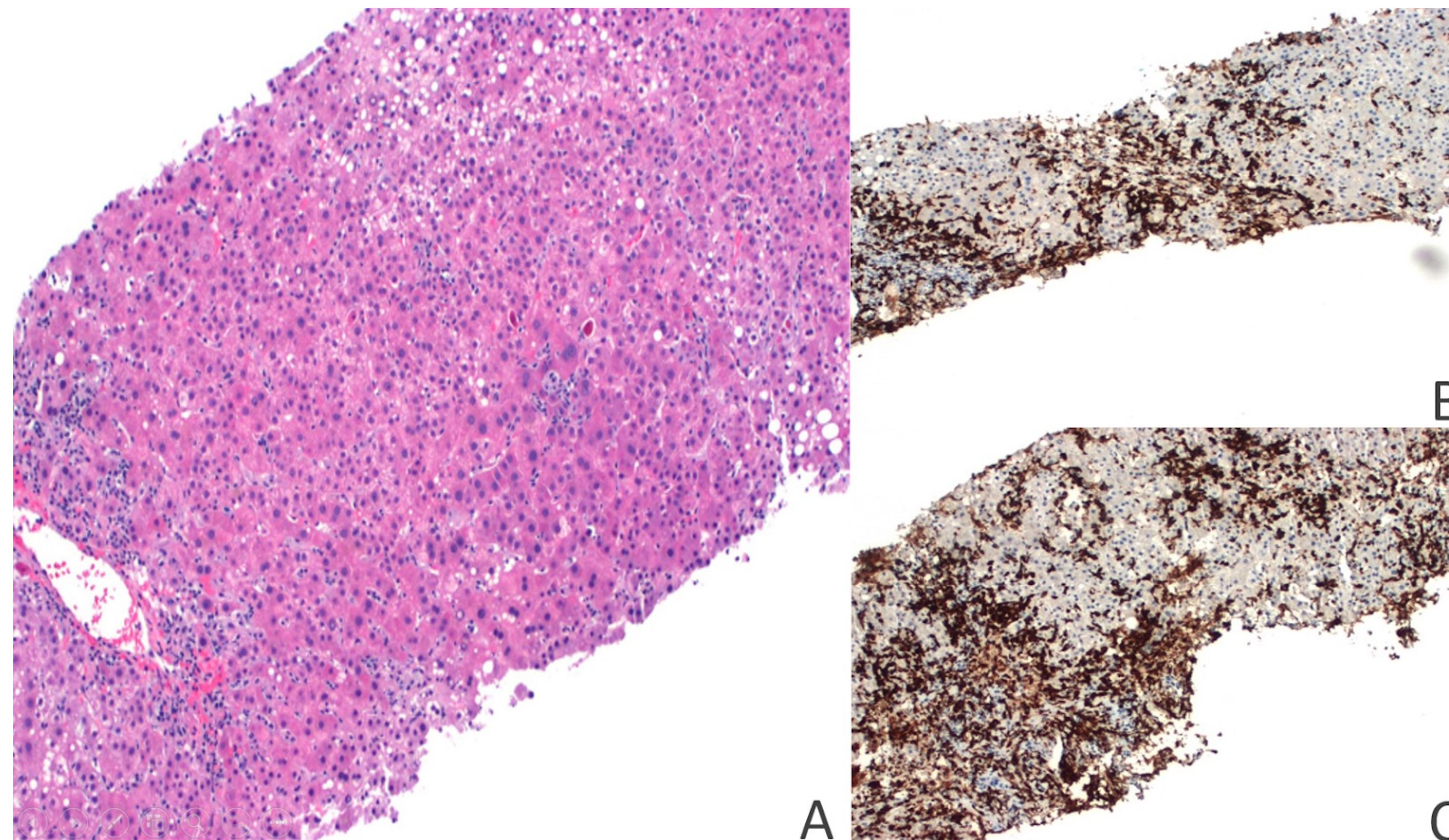
## Case Description

- A 64-year-old woman with a history of latent tuberculosis on isoniazid and gastric adenocarcinoma undergoing pembrolizumab immunotherapy presented for elevated liver enzymes noticed during an outpatient visit.
- The patient was asymptomatic, but laboratory values revealed AST (aspartate transaminase) 227 U/L, ALT (alanine transaminase) 494 U/L, alkaline phosphatase 217 U/L, and total bilirubin 1.4 mg/dL.
- Complete blood count (CBC) was unremarkable.
- She had received seven doses of pembrolizumab, with the last dose being four weeks before admission.
- Computed tomography (CT) of the abdomen and magnetic resonance cholangiopancreatography (MRCP) were unremarkable.

## Case Description (contd.)

- Considering a RUCAM (Roussel Uclaf Causality Assessment Method) score of 5 and a possibility for DILI, liver biopsy was pursued.
- Biopsy results revealed small clusters of plasma cells (CD3+/CD8+) and numerous apoptotic hepatocytes with evidence of confluent centrilobular necrosis (Figure 1).
- Given the immunohistochemical staining pattern, a diagnosis of immune checkpoint inhibitor hepatitis was considered more likely.

## Images



**Figure 1:** A. H&E stain showing apoptotic hepatocytes and centrilobular vein with perivenular inflammation and hepatocellular dropout. B&C. Immunohistochemical staining positive for CD8 and CD3 lymphocytes.

## Case Description (contd.)

- Pembrolizumab was discontinued, methylprednisolone and ursodiol were initiated.
- Patient's liver enzymes improved with discontinuation of pembrolizumab and transition of isoniazid to another anti-tubercular agent.
- Ultimately, pembrolizumab was resumed outpatient with close monitoring.

## Discussion

- Pembrolizumab is a highly selective, humanized monoclonal antibody that inhibits lymphocytes' PD-1 receptors, allowing an immune response against cancer cells.
- The risk of liver injury is higher when combined with other hepatotoxic drugs, as demonstrated in our patient.
- Treatment consists of suspected medication cessation and immunosuppressants. Following cessation of ICI's, liver enzymes usually normalize within weeks, as seen in our patient.
- Although not required for diagnosis, a liver biopsy can help rule out other etiologies.
- As ICIs become more widespread in the fight against malignancies, recognition of their adverse effects can lead to early diagnosis, intervention, and initiation of life-saving treatment.