Acute Pancreatitis Secondary to Pembrolizumab-Induced Hypertriglyceridemia: First Clinical Experience

Faisal Inayat, MBBS, Faisal Ibrahim, MBBS, Arslan Afzal, MD, Zaka Ul Haq, MD,
Gul Nawaz, MD, Muhammad Sarfraz, MD, Muhammad Wasif Saif, MD

Introduction

Pembrolizumab is a programmed cell death receptor-1 (PD-1) inhibitor that has revolutionized therapeutics in several advanced cancers. A plethora of immune-related adverse events have also been reported, including pneumonitis, colitis, hepatitis, and autoimmune diabetes. Pembrolizumab-induced hypertriglyceridemia (HTG) has also been reported, but acute pancreatitis secondary to this complication remains an unusual entity. To our knowledge, our patient is the first case of acute pancreatitis with pembrolizumab-related severe HTG as the probable etiological factor.

Case Descriptions/Methods

A 39-year-old woman with stage IVB non-small-cell lung cancer presented with progressive abdominal pain and nausea, 14 days after receiving a pembrolizumab-based chemotherapy cycle. Her lipid profile was normal before pembrolizumab initiation 4 months ago. Clinical examination was remarkable for tenderness and guarding in the epigastrium and right upper quadrant. Laboratory studies revealed serum lipase 12562 IU/L and triglyceride 16901 mg/dL, with significantly elevated HbA1c and deranged liver and renal function test results **(Table 1).** As per the Revised Atlanta Classification, the patient was diagnosed with acute pancreatitis as she fulfilled all three criteria. After careful exclusion of alternative etiologies, pembrolizumab-induced HTG was considered as the probable cause. She was then transferred to the ICU for treatment with lactated Ringer solution, analgesics, and insulin infusion. Gemfibrozil and rosuvastatin were also started as lipid-lowering drugs. However, HTG did not respond to conservative treatment with insulin infusion. Subsequently, she received 2 cycles of therapeutic plasma exchange. The patient recovered well with no complications.

Table 1: Laboratory studies with respective reference limits

Laboratory parameter	Patient value	Reference range
Lipase	12,562	23-300 IU/L
Triglycerides	16,901	10-150 mg/dL
Total cholesterol	1387	<200 mg/dL
Low-density lipoprotein	1016	50-100 mg/dL
Alanine aminotransferase	385	0-34 IU/L
Aspartate aminotransferase	243	15-46 IU/L
Alkaline phosphatase	618	45-140 mg/dL
Total bilirubin	2.8	<1.2 mg/dL
Sodium	118	136-145 mmol/L
Chloride	86	98-107 mmol/L
Bicorbonate	16.8	23-29 mmol/L
Creatinine	1.4	0.6-1.3 mg/dL
Hemoglobin A1c	11.4	≤6.5%

Discussion

The pathogenesis of pembrolizumab-induced HTG remains unclear. However, the deficiency or autoantibodies targeting GP1HBP1 may have a role by halting lipoprotein lipase (LPL) to reach capillary lumen. It causes low LPL levels and deranged intravascular degradation of triglycerides, culminating in HTG. This article has pertinent clinical implications due to the prevalent use of immune checkpoint inhibitors. Community awareness about different presentations of such rare adverse events is imperative for clinical management. HTG can be treated with insulin infusion or therapeutic plasma exchange.

Monitoring of serum triglyceride levels at baseline, during, and after pembrolizumab therapy can be considered, particularly in patients with diabetes and lipid disorders. An updated knowledge of different presentations of rare but important adverse events is of paramount clinical importance. Therefore, clinicians should remain vigilant for acute pancreatitis as it can be a life threatening adverse event of immune-checkpoint inhibitors.

Table 1

Table 1. Laboratory data of the patient at the initial presentation showing remarkably deranged results.