Case Report
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A case of recurrent acute pancreatitis followıng ocrelizumab therapy

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ABSTRACT

Acute pancreatitis is an acute inflammatory process of the pancreas. Drugs are a relatively rare cause of acute pancreatitis with an incidence of 0.1-2%. Ocrelizumab is a monoclonal antibody that causes peripheral B lymphocyte suppression by targeting CD20 receptors on B lymphocytes. In this case report, we aimed to present a case of acute pancreatitis after ocrelizumab use. It is thought that suppression of B lymphocytes by ocrelizumab may induce proinflammatory cytokine release and may also cause pancreatitis by disrupting T lymphocyte regulation. Therefore, ocrelizumab should be considered in the etiology of pancreatitis in patients receiving ocrelizumab treatment.

Keywords: Ocrelizumab, Pancreatitis

Acute pancreatitis is an acute, inflammatory process of the pancreas. Acute pancreatitis presents with typical epigastric pain, high lipase and amylase levels (above 3 times upper limit of normal) and imaging findings. The diagnosis of acute pancreatitis is made by the presence of two of these three findings.[1] Gallstones (40%-70%), alcohol (25%-35%), hyperlipidemia and drugs are the most common etiology of pancreatitis, respectively. With an incidence of 0.1-2%, drugs are a relatively rare cause of acute pancreatitis.[2] The drugs with the highest epidemiological risk are mesalazine, azathioprine and simvastatin. Drug-associated pancreatitis has a good prognosis and low mortality rate.[3]

Ocrelizumab is a monoclonal antibody that causes the suppression of peripheral B lymphocytes by targeting the CD20 receptors on the B lymphocytes.[4] It is used in cases of relapsing refractory multiple sclerosis, or progressive multiple sclerosis. Common side effects include skin infections, decrease in neutrophil and immunoglobulin levels, hypersensitivity reactions and infections. Diarrhea has been reported as a gastrointestinal adverse event with a rate of 6%. With a frequency of 0.2%, pancreatitis following ocrelizumab use is a serious adverse event.

In this case report, we aimed to present a case that we followed up with the diagnosis of pancreatitis attack after ocrelizumab use.

CASE REPORT

A 53-year-old woman with a history of hypothyroidism and relapsing refractory multiple sclerosis (MS) was presented to our clinic for her fourth episode of acute pancreatitis. The patient was diagnosed with MS in 1997 and was on betaferon and azacitidine for 6 years after diagnosis. The patient was then followed up with alternating cyclophosphamide and pulse steroid and baclofen treatment every 2 months. In April 2021,

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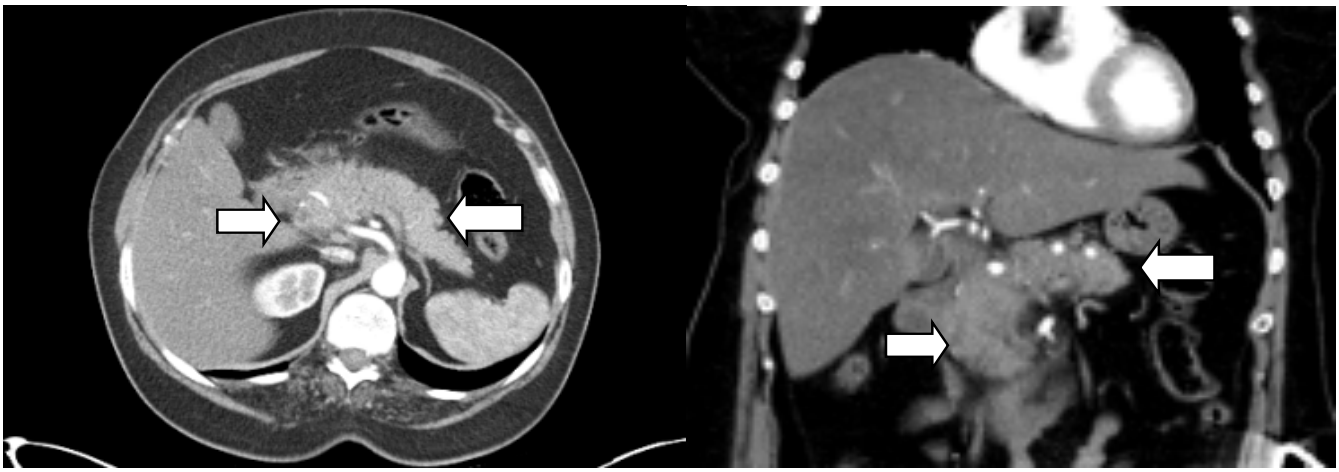

Figure 1. Increased pancreatic volume with impurity in the head and corpus.

the patient was made ready to receive ocrelizumab, and the first full dose of ocrelizumab was administered in June 2021. Four months after the first dose, amylase: 3262 U/L, lipase: 2853 U/L, calcium: 9.2 mg/dl, triglyceride: 90 mg/dl were observed when the patient presented to the emergency department with abdominal pain in November 2021. No additional pathology was found in his hemogram and biochemistry tests. Her abdominal tomography scan was reported to be compatible with edematous pancreatitis (Figure 1). Her extrahepatic bile ducts were assessed as being normal and no dilatation was found. The patient was referred with the diagnosis of acute pancreatitis. When the anamnesis of the patient who received three full doses of ocrelizumab treatment was deepened, it was observed that the pancreatitis attacks occurred approximately one to four months after the ocrelizumab doses had been received. When the retrospective hospital records of the patient with no history of alcohol consumption were examined, hypercalcemia, hyperlipidemia and cholecystopathy were not found in the etiology of the four pancreatitis attacks. In the patient examined for autoimmune pancreatitis, IG-G4 levels were normal and no etiological cause of pancreatitis was found. When the patient's treatment history was analyzed in detail, it was observed that pancreatitis attacks started after ocrelizumab treatment. Considering ocrelizumab in the etiology of pancreatitis, the patient was evaluated in collaboration with the neurology department and the literature was reviewed for the adverse event profile of the drug. As ocrelizumab was considered in the etiology of pancreatitis, ocrelizumab treatment was discontinued and the MS management was reorganized.

DISCUSSION

Possibly due to under-diagnosis, drug-associated pancreatitis is a rare disease entity.[5] Immunological reactions, direct toxic effects, accumulation of toxic metabolites, ischemia, intravascular thrombosis and the increase in viscosity of pancreatic juice are mechanisms of drug-induced pancreatitis.[6] While most drugs cause pancreatitis in the first few weeks of use, this period can last for months or even years.[7] Though the exact mechanism by which ocrelizumab causes pancreatitis is unknown, B-lymphocyte suppression has been shown to induce proinflammatory cytokine release in a model of inflammatory bowel disease.[8] Meanwhile, B lymphocyte suppression disrupts T lymphocyte regulation and may lead to inflammatory changes.

CONCLUSION

By stimulating the inflammatory process, ocrelizumab treatment may be involved in the etiology of pancreatitis. Therefore, ocrelizumab should be considered in the etiology of pancreatitis in patients receiving ocrelizumab treatment.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authors' Contribution

Study Conception: EI, BA, UY, İD; Study Design:

EI, BA, UY, İD; Supervision; EI, BA, UY, İD; Funding: İD, EI; Materials: İD, EI; Data Collection and/or Processing: İD, EI; Analysis and/or Data Interpretation: EI; Literature Review: EI; Critical Review: EI, BA, UY; Manuscript preparing: EI.

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