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Letter To Editor

Unraveling the Complexity of Drug-Induced Pancreatitis: Mechanisms, Risks, and Management

İlaçlara Bağlı Pankreatitin Karmaşıklığını Çözümlemek: Mekanizmalar, Riskler ve Yönetim

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Abstract

This article explores the complexity of drug-induced pancreatitis, a form of pancreatitis triggered by medications. It emphasizes potential connections between drugs such as azathioprine, valproic acid, and specific antiretroviral agents and pancreatitis. The etiology of drug-induced pancreatitis is shaped by multiple factors, including direct cellular injury, immune response, and genetic predisposition. Challenges in diagnosis and management, as well as future research areas, are also addressed.

Özet

Yazımızda pankreatitin ilaçlarla tetiklenen bir formu olan ilaca bağlı pankreatitin karmaşıklığı inceledik. Azatioprin, valproik asit ve belirli antiretroviral ajanlar gibi ilaçların pankreatite potansiyel bağlantıları vurgulanmıştır. İlaçlara bağlı pankreatitin etiyolojisi, doğrudan hücresel hasar, bağışıklık tepkisi ve genetik yatkınlık gibi çoklu faktörlerle şekillenmiştir. Tanı ve yönetimdeki zorluklar ve gelecekteki araştırma alanları da ele alınmıştır.

Dear Editor

We read with great interest the case report titled "Sitagliptin Kullanımına Bağlı Tekrarlayan Akut Pankreatit: Olgu Sunumu" prepared by Sarı and Sarı and published in the third issue of your journal in 2023[1]. We would like to thank the authors and the editorial board for this interesting case report. However, we would like to point out a few issues regarding drug-induced pancreatitis that may contribute to the discussion of the article.

Pancreatitis, defined as the inflammation of the pancreas, is a complex medical condition with various etiologies. The pancreas, a crucial organ in the digestive system, plays a pivotal role in the regulation of glucose metabolism and the secretion of digestive enzymes. When inflammation occurs, the normal functions of the pancreas are compromised, leading to a spectrum of clinical manifestations[2, 3].

The seriousness of pancreatitis cannot be overstated. This inflammatory process can range from mild and self-limiting to severe and life-threatening. Common symptoms include abdominal pain, nausea, vomiting, and elevated pancreatic enzymes. In severe cases, complications such as pseudocysts, necrosis, and systemic inflammatory response syndrome may ensue, posing a significant challenge in management and often requiring intensive medical intervention[4].

While pancreatitis can be triggered by various factors, this discussion will focus on a specific aspect: drug-induced pancreatitis. Medications, despite their intended therapeutic effects, have been implicated in the development of pancreatitis in some individuals. Understanding the mechanisms and risk factors associated with drug-induced pancreatitis is crucial for clinicians and researchers alike[5, 6].

The association between medications and pancreatitis has been documented across a spectrum of drug classes. Drugs such as azathioprine, valproic acid, and certain antiretroviral agents have been reported to have potential links to pancreatitis. The mechanisms underlying drug-induced pancreatitis are multifaceted and not yet fully elucidated. Some drugs may directly cause pancreatic injury, while others may trigger an immune response leading to inflammation. Genetic predispositions and idiosyncratic reactions further contribute to the complexity of this phenomenon[7].

One of the challenges in recognizing and managing drug-induced pancreatitis lies in the varied presentation and latency period. Symptoms may emerge days to weeks after initiating

the culprit medication, making it challenging to establish a direct causal relationship. Additionally, the absence of specific diagnostic markers for drug-induced pancreatitis complicates the identification of the responsible agent.[8] The severity of drug-induced pancreatitis varies, ranging from mild cases that resolve upon discontinuation of the offending drug to severe forms requiring hospitalization and intensive care. Rechallenge with the same medication can sometimes lead to recurrent pancreatitis, underscoring the importance of prompt recognition and appropriate management[(9)].

The etiology of drug-induced pancreatitis involves intricate and multifaceted pathways that challenge our understanding of this phenomenon. Unlike pancreatitis caused by other factors such as gallstones or alcohol, the mechanisms through which medications induce pancreatic inflammation are not fully elucidated. Several hypotheses have been proposed, highlighting the complexity of the interplay between drugs and the pancreas[(10)].

One proposed mechanism suggests that certain medications may directly injure pancreatic cells, leading to the release of digestive enzymes within the gland itself. This localized damage can trigger an inflammatory response, contributing to the development of pancreatitis. Notably, drugs with inherent cytotoxic properties or those metabolized into toxic compounds may have a more direct impact on pancreatic tissue[(10)]. In addition to direct cellular injury, some medications are believed to incite an immune-mediated response in the pancreas. This inflammatory reaction may be the result of the body's hypersensitivity to the drug, leading to an immune cascade that involves the pancreas. Genetic factors may play a role in predisposing certain individuals to these immune-mediated responses, adding another layer of complexity to the etiology of drug-induced Pancreatitis[(11)].

Furthermore, the idiosyncratic nature of drug-induced pancreatitis poses a significant challenge in understanding its etiology. While some individuals may develop pancreatitis in response to a specific medication, others taking the same drug may remain unaffected. Genetic polymorphisms and individual variations in drug metabolism may contribute to this unpredictability, emphasizing the need for personalized approaches to both diagnosis and management[(12)].

As research in pharmacogenomics and molecular pathways advances, we may gain a clearer understanding of the specific risk factors and mechanisms that underlie drug-induced pancreatitis. This knowledge, in turn, can guide clinicians in identifying individuals at higher risk, facilitating early intervention, and potentially preventing the onset of this adverse drug

reaction[13]. Clinicians must maintain a high index of suspicion when faced with a patient presenting with symptoms suggestive of pancreatitis, especially if they are under medication. Thorough evaluation of the patient's medical history, including a detailed medication history, is paramount. In cases of suspected drug-induced pancreatitis, a careful risk-benefit assessment is necessary to determine whether discontinuation of the medication is warranted and if alternative therapeutic options exist[14].

In conclusion, drug-induced pancreatitis represents a complex and multifactorial phenomenon that requires attention and awareness in the medical community. As our understanding of the mechanisms and risk factors advances, so too can our ability to identify, manage, and prevent this challenging condition. Continued research and collaboration among clinicians and researchers are essential to unravel the complexities of drug-induced pancreatitis and improve patient outcomes.

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