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Clinical characteristics and outcomes of autoimmune pancreatitis based on serum immunoglobulin G4 Levels: A single-center, retrospective cohort study

Autoimmune pancreatitis based on serum immunoglobulin G4 Level

Abstract

Autoimmune pancreatitis (AIP) is a complex, poorly understood disease gaining increasing attention. Zhou *et al*'s study, "Clinical Characteristics and Outcome of Autoimmune Pancreatitis Based on Serum IgG4 Levels," investigated AIP with a focus on serum immunoglobulin (Ig) G4 Levels. The 213 patients with AIP were classified according to serum IgG4 Levels: abnormal (elevated) and normal. Patients with higher IgG4 Levels exhibited a more active immune system and increased relapse rates. Beyond IgG4, the IgA levels and age independently contributed to relapse risk, guiding risk assessment and tailored treatments for better outcomes. However, limitations persist, such as no IgA correlation with IgG4 Levels, absent data on autoantibody-positive AIP cases critical for Asian diagnostic criteria, and unexplored relapse rates in high serum IgG AIP by subtype. Genetic factors and family histories were not addressed. As the understanding and referral of seronegative AIPs increase, there's a growing need for commercially available, highly sensitive, and specific autoantibodies to aid in diagnosing individuals with low or absent serum IgG4 Levels.

Key Words: Autoimmune pancreatitis; Relapse; Immunoglobulin G; Immune System, Immunoglobulin A; Outcomes

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Core Tip: The study by Zhou *et al* on autoimmune pancreatitis (AIP) based on serum IgG4 Levels offers valuable insights into this complex condition. Elevated IgG4 and IgA levels in patients with AIP were associated with more active immune system and higher relapse rates, highlighting the potential of IgG4 as a biomarker. However, limitations include the lack of analysis on IgA levels in relation to IgG4 Levels, the absence of data on autoantibodies, and the lack of reporting on family history and genetic factors. As awareness of AIP grows, there is a need for highly sensitive and specific autoantibodies to aid in diagnosis, especially for IgG4-negative AIP patients.

TO THE EDITOR

We read with great interest a recent article published in your esteemed journal, titled "Clinical Characteristics and Outcome of Autoimmune Pancreatitis Based on Serum IgG4 Levels" by Zhou *et al* [1]. Autoimmune pancreatitis (AIP) is a complex and poorly understood condition that has garnered considerable attention in recent years. This study by Zhou *et al* offers valuable insights into the characteristics and outcomes of AIP, focusing on the role of serum immunoglobulin (Ig) G4 Levels [1]. We believe that the findings presented in this research hold significant clinical implications and merit further discussion and dissemination.

The authors meticulously investigated a cohort of 213 patients with AIP, and their decision to categorize them into two groups based on serum IgG4 Levels, the abnormal group with high IgG4 Levels and the normal group, is particularly noteworthy [1]. By comparing these groups, the study reveals several compelling findings that deserve

attention from the medical community.

Firstly, in line with other studies [2-4], this study highlights that patients with AIP and elevated IgG4 Levels have distinct clinical features, such as a higher relapse rate [1]. This observation contributes to our understanding of the heterogeneity within the population of patients with AIP and highlights the potential importance of serum IgG4 Levels as a biomarker of disease activity.

Furthermore, identifying factors associated with AIP relapse is of utmost importance for clinical management. The multivariate analyses performed in this study suggest that not only serum IgG4 Levels but also IgA levels and patient age play independent roles in predicting relapse [1]. This information could help physicians stratify risks and adjust treatment strategies for patients, ultimately improving their long-term outcomes.

However, a few limitations are worth mentioning. While the study found an association between IgA levels and higher relapse rates [1], no further analysis of IgA levels relative to serum IgG4 Levels was performed. One study mentioned that serum IgA and IgM levels were lower in patients with high-level serum IgG4 AIP than in patients with normal serum level IgG4 AIP [5], while another study reported an inverse correlation between serum IgG4 and IgM or IgA in 20 cases of AIP [6]. Further stratification based on IgA levels could expand our knowledge of the association between IgG4 and IgA in AIP.

Furthermore, the proportion of patients with AIP with positive autoantibodies was not discussed in this study [1]. While serum IgG levels and anti-nuclear antibody positivity were previously part of the classical criteria for AIP [7], neither the current international consensus diagnostic criteria for AIP [8] nor the Japanese revised clinical diagnostic criteria for AIP [9] included these two elements. Nonetheless, some studies have reported lower IgG4 Levels in patients with positive serum autoantibodies compared to

patients without autoantibodies. This finding may contribute to demonstrating the presence of AIP with an association of autoantibodies alone in a subset of patients. Furthermore, in one study, higher serum IgM and IgA levels were observed in serum autoantibody-positive (+) patients with AIP compared to serum autoantibody-negative (-) patients with AIP, suggesting that examining the properties of high serum IgG4 AIP and serum autoantibodies could provide valuable insights [5]. With increasing understanding and prevalence of seronegative AIP among general clinicians, there is a growing demand for commercially available autoantibodies with superior sensitivity and specificity to aid in the identification and diagnosis of AIP in individuals with low or absent serum IgG4 Levels.

Another limitation to consider is that the study did not examine relapse rates in patients with high serum IgG levels based on the type of AIP [1]. Previous research has suggested different relapse rates, with type 1 AIP in patients with high serum IgG4 having higher rates (20-40%) compared to type 2 AIP [5, 10, 11]. The lack of this information limits our understanding of how serum IgG levels may impact relapse risk in different AIP subtypes.

Finally, Zhou *et al* reported neither family history nor genetic factors [1]. It is important to note that HLA-DRB1 haplotypes are associated with AIP susceptibility [12] as well as other diseases, such as rheumatoid arthritis [13]. This genetic aspect requires further study to better understand the complex interplay between genetics and AIP.

In conclusion, the research conducted by Zhou *et al* [1] sheds light on the clinical aspects of AIP and highlights the importance of serum IgG4 Levels as a prognostic indicator. It also provides valuable insights into risk factors for relapse, which can serve as a basis for more targeted therapeutic interventions. As AIP continues to be a challenge for physicians worldwide, studies such as these contribute significantly to our knowledge and have the potential to improve patient care.

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