Rapid Development of Autoimmune Hepatitis Secondary to Minocycline

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Abstract

Autoimmune hepatitis (AIH) is a condition that affects the liver which, potentially, may render it fibrotic and eventually cirrhotic. This condition has many etiologies ranging from genetic predispositions and immunological defects to medication and environmental side effects. Essentially, we will explore the risks, presentation, diagnosis, and treatment of this condition as it relates to a medication-induced etiology. Here we report a case where a patient developed this condition from taking the antibiotic minocycline. The patient was treated with prednisone therapy and went into complete remission with no reoccurrence of AIH. The purpose of this case report is to highlight the fact that these cases have the potential to occur fairly sooner than expected, in a matter of weeks or months, after the induction of minocycline. Hence, carefully monitoring liver functions more frequently may aide in the prevention of minocycline-induced AIH.

Categories: Gastroenterology
Keywords: hepatitis workup, steroid therapy, gastroenterology, minocycline, autoimmune hepatitis

Introduction

There are two main types of autoimmune hepatitis (AIH). Type 1 accounts for the majority of cases, representing 96% of the total AIH cases in North America [1]. Antinuclear antibodies (ANAs) and anti-smooth muscle antibodies (ASMs) are the markers for this type. The latter is the more specific marker as the former occurs in many other conditions. Type 2 AIH is more severe and less common accounting for 4% cases in North America [1]. The markers for this type are anti-liver kidney microsomal antibody type 1 (anti-LKM1) and anti-liver cytosol type 1 (anti-LC1). The prognosis for type 2 is poor compared to type 1. Young females are the primary target of this condition with a female-to-male ratio of about 4:1 [2]. The United States has a marginally higher prevalence of about 31.2 per 100,000 people compared to Europe’s 11–25 per 100,000 per year [2,3].

Tetracyclines are a major class of antibiotics used for a variety of clinical conditions such as rosacea, infections, and many other conditions. However, since their initial description in 1951, the hepatitis cases in patients taking this medication have been on the rise [4]. Standing out from the rest, minocycline is the most common cause of AIH in this class. The duration of usage is a key factor in further understanding the link between AIH and minocycline. As it pertains to our case, we will focus on its use in acne vulgaris. The question, “For how long are most patients on minocycline before AIH develops?”, is where the gray area starts in our knowledge of this link. Most cases have been reported in the first two years of taking minocycline [5]. However, it is also possible for AIH to develop after just a few months of minocycline therapy. In our case, for example, AIH transpired in a matter of three months. Thus, it is safe to say that the duration of minocycline therapy is only one of the many variables that predisposes one to AIH.

Furthermore, although we know tetracyclines can cause AIH, it is important to understand the other etiologies as well to better understand why duration varies from case to case. Genetic conditions certainly can play a role. Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy syndrome (APCEDS) is an inheritable condition involving AIH [1]. In addition to APCEDS, many patients with AIH present with co-existing autoimmune conditions such as diabetes mellitus type 1, Graves disease, and celiac disease, possibly due to the similar autoimmune dysfunction mechanism involved in both cases. Moreover, there are other genetic factors such as human leukocyte antigen (HLA) subtypes that lead to a greater predisposition in developing AIH. Although HLA DRB1*03 and HLA DRB1*04 can lead to AIH type 1, the former leads to a worse prognosis [1]. Such variables can certainly have an impact on when AIH will occur during minocycline therapy.

Case Presentation

A 16-year-old male presented to the emergency department with flu-like symptoms, one week of progressively severe abdominal pain and darker than usual urine. The pain was described as constant and deep. The patient reported taking tylenol for the pain and it helped reduce the pain from 9/10 to 2/10 on the pain scale. He denied any pain changes with positional movement. The pain radiated slightly to the flank
One last point to be made about this case, in light of his negative HLA tests, is that it is unlikely that remission to begin weaning the patient off of steroid therapy. Months, including both induction and maintenance. A repeat biopsy of the liver should be taken that shows multiacinar necrosis on histology normal limit coupled with an IgG level twice the normal limit, or a liver biopsy representing bridging or necrosis.

Treatment should be individualized on a case-per-case basis and should last for a total of 24 therapy. Prednisone, budesonide, and azathioprine are common medications used to treat AIH secondary to hepatitis panel was ordered that ruled out common viral etiologies. An ultrasound of the abdomen showed heterogeneous features on the liver with some nodularity throughout. A high-resolution CT scan revealed diffuse heterogeneous material on the liver. Magnetic resonance cholangiopancreatography (MRCP) revealed clear irregular-nodular patterns over the entire liver surface. Consequently, a biopsy was performed that demonstrated interface hepatitis along with bridging necrosis between portal tracts. The diagnosis of autoimmune hepatitis was made.

Deciding when to treat is crucial as better prognosis is often correlated with treatment being started at the right stage. Immunosuppressive therapy is the choice of treatment for AIH. However, this mode of treatment carries a vast array of side effects, including but not limited to the risk of opportunistic infections. Hence, treatment is advised when there are signs of disease progression to a serious stage by at least one of these characteristics: AST/ALT levels exceed 10 times the normal limit, AST/ALT level exceeds five times the normal limit coupled with an IgG level twice the normal limit, or a liver biopsy representing bridging or multincinar necrosis on histology [1]. By virtue of the last characteristic, our patient qualified for immediate therapy. Prednisone, budesonide, and azathioprine are common medications used to treat AIH secondary to medications. Treatment should be individualized on a case-per-case basis and should last for a total of 24 months, including both induction and maintenance. A repeat biopsy of the liver should be taken that shows remission to begin weaning the patient off of steroid therapy.

One last point to be made about this case, in light of his negative HLA tests, is that it is unlikely that the...
rapid onset of AIH was brought about by genetic predisposition. The fact that he denied a family history of autoimmune diseases led us to one other likely predisposition category: environmental factors. These range from diet to chemical exposures. In the absence of common etiologies in this patient, it is logical to postulate that environmental factors likely played a role in the relative quick AIH development secondary to minocycline therapy.

**Conclusions**

AIH is a complex condition with many environmental triggers as well as genetic predispositions. Our minocycline-induced AIH case was fortunate enough to respond to therapy because he was treated at the right stage when bridging necrosis had just started. Repeat liver biopsy after maintenance prednisone therapy showed total remission. A later follow-up after a decade showed no recurrence of AIH nor any residual liver dysfunction after the triggering agent was removed from his diet. Contrary to the two-year average that majority of cases present with, this article serves to shed light on the possibility of AIH occurring fairly quick in some patients taking minocycline. Although a rare complication, minocycline-induced AIH is still a potentially fatal complication that necessitates more frequent monitoring of liver functions of patients taking this medication.

**Additional Information**

**Disclosures**

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