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Case Report

Ethmoiditis during Autoimmune Hepatitis Treatment: A Case Report

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Abstract

Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease, characterized by the elevation of aminotransferases, presence of anti-nuclear antibody or anti-smooth muscle antibody, elevated immunoglobulin G (IgG), and interface hepatitis/plasma-lymphocytic inflammation based on histology. The disease can be serious, and if left untreated, it can lead to cirrhosis of the liver and eventual liver failure. The recommended treatment for AIH includes corticosteroids and azathioprine. Azathioprine (AZA) is indicated in immunosuppressive regimens as an adjunct to immunosuppressive agents that form the mainstay of treatment. AZA is indicated either alone or in combination with corticosteroids and/or other drugs and procedures in several diseases. There are potential dangers in the use of AZA; they should therefore not be prescribed unless the patient can be adequately monitored for toxic effects throughout the duration of therapy.

We present here the case of a 50-year-old female, with autoimmune hepatitis on AZA therapy who developed ethmoiditis.

Keywords: Autoimmune hepatitis; Interface hepatitis Liver disease; Immunosuppressive

1. Introduction

Autoimmune hepatitis (AIH) is chronic inflammation of hepatocytes due to immune cells attacking the patient's own hepatocytes, histologically characterized by interface hepatitis. The disease can be serious, and if left untreated, it can lead to cirrhosis of the liver and eventual liver failure [1-3]. The cornerstone of treatment is steroid induction therapy followed by maintenance therapy with azathioprine, which is effective in most cases. Treatment should be aimed at biochemical remission of the disease, which is defined as normalization of transaminases and

immunoglobulin G [1-3]. Azathioprine is a prodrug of 6-mercaptopurine, first synthesized in 1956 by Gertrude Elion, William Lange, and George Hitchings in an attempt to produce a derivative of 6-mercaptopurine with a better therapeutic index. Azathioprine is used to treat several inflammatory conditions like as an immunosuppressant in the prevention of transplant rejection [4-6]. Patients should be monitored intensively during the first months of treatment in order to monitor side-effects, assess symptoms and individualise treatment.

We present here the case of a 50-year-old female, with autoimmune hepatitis on azathioprine treatment admitted for ethmoiditis.

2. Case Report

A 50-year-old female with heptitis autoimmune on azathioprine treatment (100 mg/day) was admitted with fever, headache, decreased sense of smell and taste, general fatigue or malaise. She began azathioprine treatment 15 days ago. Physical examination revealed facial swelling, hearing disturbance, eyelid afflictions. She had little local manifestation of herpes simplex on the month noscleral icterus, a heart rate of 70 beats/min, respiratory rate of 18 breaths/min, temperature of 38.8°C, blood pressure of 120/80 mm Hg. The lungs were clear with no cardiac abnormalities, abdominal tenderness or hepatosplenomegaly. At neurological examination she had normal pupils, equal in size and shape and situated in center of iris; pupillary size varies with intensity of ambient light, but at average intensity is ≈ 3-4 mm.

Normal level of consciousness, attention, orientation, language was fluency, preserved comprehension and memory. Laboratory results showed leukocytosis (10,860/µL), elevated C-reactive protein (94.03 mg/dL), AST (32 UI/L), ALT (37U/L), bilirubine 1 (mg/dL), normal platelets, LDH 687 (U/L), CK (173 U/L), procalcitonin (0.23 ng/mL), pancreas enzymes were normal. Blood, stool and urine cultures were negative. Neither abdominal ultrasound nor chest Rx showed any abnormality. A Ct scans was performed and revealed thickening of the dura mater and inflammatory granulation around the cerebellar tentorium, periorbital cellulitis.

This is a rare case of presentation of ethomiditis during azathioprine treatment. The patient was started on endovenous ceftriaxone (2 g/day) and Acyclovir (10 mg/kg IV every 8 hours). We Stopped azatioprine. One week later, complete resolution of symptoms was achieved and all laboratory findings returned to normal. During a 2-year follow up, the patient present only one episode of increase of transaminase, we started steroids to induce remission and added slow dosis of azathioprine (50 mg/day) to maintain clinical remission.

3. Discussion

Autoimmune Hepatitis (AIH) is a chronic progressive inflammatory disease of the liver that responds to immunosuppressive therapy. In patients with AIH who have an acute liver failure presentation or those who develop end stage liver disease despite medical therapy, liver transplantation (LT) may become necessary. The presence of

non-organ specific autoantibodies, elevated serum aminotransferases and immunoglobulin G as well as the characteristic histologic features of interface hepatitis (peri-portal plasma cell infiltration) characterize recurrence of disease.

The condition affects all ages, and has a female preponderance. There is no single diagnostic test [1-3]. The International Autoimmune Hepatitis Group (IAIHG) established comprehensive diagnostic criteria in 1993, based on expert opinion, intended to be used for research purposes. After their evaluation in a number of studies, the criteria were updated in 1999. A simplified, clinical practice-friendly version was published in 2008. These criteria are intended to help in guiding diagnosis and decision on therapy initiation in patients presenting with a clinical picture suggesting AIH, and have received extensive external validation since publication.

Sub-classification of AIH in two forms, type 1 and type 2, appears to be of some relevance in the paediatric setting: anti-LKM1-positive children have higher levels of bilirubin and transaminases at onset and present significantly more frequently with fulminant hepatic failure, whereas cirrhosis on initial biopsy and a severely impaired hepatic synthetic function is more common in type 1 AIH; however, in both types of AIH, a more severe disease course and a higher tendency to relapse are associated with the possession of anti-SLA/LP. Type 3 AIH, positive antibodies against soluble liver antigen (anti-SLA, anti-LP).

The notion of type 3 AIH, diagnosed on the sole basis of isolated anti-SLA/LP positivity, has been dismissed when it became clear that ANA/SMA and anti-SLA/LP, often coexisting in the same sera, do not pinpoint patients with different clinical, biochemical, histological and prognostic features, therefore the distinction between type 1 and type 3 AIH remains only serological, and is not clinically helpful. In the population of AIH patients with onset/diagnosis in adulthood, it is as yet unclear if sub-classification is actually justified and clinically useful. According to the guidelines on the management of AIH EASL Prednisone was initial therapy followed by the addition of azathioprine after two weeks is the first line treatment of AIH (I) Initial dose of prednisone should be between 0.5 and 1 mg/kg/day. The initial dosage should be 50 mg/day, and increased depending on toxicity and response up until a maintenance dose of 1-2 mg/kg.

This case report represents the increase of risk during azathioprine treatment, this hypothesis is based on the temporal relationship between exposure to the drug and the onset of symptoms. Azathioprine is an important immunomodulator, it is used alone or in combination with other immunosuppressive therapy to prevent rejection following organ transplantation, and to treat an array of autoimmune diseases, including autoimmune hepatitis. Azathioprine side effects affect 10%-20% of patients and include hepatotoxicity, acute cholestatic hepatitis, pancreatitis, nausea and vomiting, rash, bone marrow suppression, veno-occlusive disease, opportunistic infections, and malignancy. The most common side effect is bone marrow suppression, which is unpredictable, and can be aggravated by concomitant cytopaenia due to liver disease and hypersplenism.

Haematological monitoring is necessary, particularly at the beginning of treatment. Although well tolerated by many patients, there are significant adverse effects which require patient education.

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