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Acute autoimmune hepatitis and eosinophilia – a rare case report

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Abstract

BACKGROUND

Autoimmune hepatitis consists of a chronic liver disease whose etiology is unknown. It is comprised of relevant immunological aspects and of immune-mediated liver injury. Eosinophilia may be a considerable feature, particularly happening in male patients.

CASE SUMMARY

We report here a Crohn's disease patient presenting with de novo hypergammaglobulinemia, circulating autoantibodies and elevated transaminase levels. He also had significant peripheral eosinophilia and elevated immunoglobulin E levels at diagnosis. The pathology findings from liver biopsy were compatible with autoimmune hepatitis with eosinophilic infiltration.

CONCLUSION

This is the first report of autoimmune hepatitis with exuberant eosinophilic infiltration in the liver and bone marrow, described in a patient with Crohn's disease.

INTRODUCTION

Peripheral blood eosinophilia is considered either a primary or a secondary phenomenon (1). Primary eosinophilia often takes place within ²hematologic malignancies where

cytogenetic or bone marrow histologic evidence regarding the clonal expansion of these cells can be found. On the other hand, causes of secondary eosinophilia include parasitosis, medications, malignancies and inflammatory or allergic conditions. Idiopathic eosinophilia consists of a diagnosis of exclusion, when no primary or secondary causes are detected.

Peripheral blood eosinophilia may be found in several hepatobiliary and gastrointestinal disorders. Indeed, some gastrointestinal diseases are eosinophil-mediated pathologies, such as eosinophilic gastroenteritis, inflammatory bowel disease, *Helicobacter pylori* infection, gastroesophageal reflux disease, collagenous colitis and celiac disease (2). In addition, hepatic eosinophilia has been presented associated to primary biliary cirrhosis, sclerosing cholangitis, eosinophilic cholangitis and eosinophilic cholecystitis.

Currently, there are very few reported cases of autoimmune hepatitis presenting with peripheral blood eosinophilia, usually associated with other autoimmune conditions (3). Hereafter we explore a case of autoimmune hepatitis associated with peripheral blood and tissue eosinophilia. This report aims at making physicians aware of that association in order to consider this diagnosis in a patient who presents elevated transaminases in concert with a high eosinophil count.

CASE PRESENTATION

Chief complaints

The patient was asymptomatic.

History of current illness

In routine analysis, it was noticed a new-onset cytocholestasis (aspartate aminotransferase 86U/L, alanine aminotransferase 240U/L, gamma-glutamyl transferase 288U/L, alkaline phosphatase 794/L) without hyperbilirubinemia or coagulopathy.

History of past illness

The patient denied any history that can suggest viral prodrome, sick contacts, recent travel, medication ingestion (comprising herbal or over-the-counter), exposure to well water, exposure to recreational drugs, tattoos, alcohol, high-risk sexual behavior or blood transfusions.

Personal and family history

A 36-year-old Caucasian male with asthma and Crohn's disease (Montreal classification A2L2B1), was under azathioprine until 4 years ago when it was discontinued due to clinical and endoscopic remission. His asthma was under control since childhood. He was not on medication and had no known drug allergies.

Physical examination

Normal.

Laboratory examinations

Antinuclear antibody was positive (1:100, speckled pattern) as well as anti-smooth muscle. All other liver-related autoantibodies were negative (anti-mitochondrial, anti-liver-kidney microsomal, anti-soluble liver antigen and antineutrophil cytoplasmic). Immunoglobulin G (IgG) levels were elevated (3650 mg/dL). Serology for human immunodeficiency virus, hepatitis A virus, ¹Epstein-Barr virus, cytomegalovirus, and herpes simplex virus type 1 and 2 were negative. Polymerase chain reaction considering hepatitis B, C and E viruses were negative, too. Alpha-1 antitrypsin, ceruloplasmin and iron tests were all normal. The same could be perceived for thyroid function.

Blood tests presented an absolute white blood cell count of $33.46 \times 10^9/L$. Differential count indicated 89.5% of eosinophilia, as well as an absolute eosinophil count of $30 \times 10^9/L$. In addition, immunoglobulin E (IgE) levels were elevated (8803 kU/L). Blood

cultures and parasitological examination of the stools were negative. FIP1L1-PDGFR α fusion transcript was not detected.

Imaging examinations

The abdominal ultrasound showed a liver with a normal appearance and no intra- or extrahepatic biliary ductal dilation.

Histologic examination

A liver biopsy was then performed, revealing infiltration of the portal tracts and intralobular hepatic parenchyma by numerous eosinophils (Figure 1). Lymphoplasmacytic portal tract inflammatory infiltrate with interface hepatitis was identified as well as small aggregates of plasma cells. The interlobular bile ducts appeared intact and iron and copper stains were negative. Furthermore, bone marrow biopsy showed marked eosinophilia, with normal maturation and absence of blasts (Figure 2).

FINAL DIAGNOSIS

¹ The score regarding simplified diagnostic criteria of the International Autoimmune Hepatitis Group was 7 (likely diagnosis of autoimmune hepatitis) (4). The score considering the revised original pretreatment scoring system of the International Autoimmune Hepatitis Group was 17 (definite diagnosis of autoimmune hepatitis) (5). Due to lack of evidence for parasitic infection, the reactive bone marrow and the absence of other systemic conditions or drugs, the patient was diagnosed with autoimmune hepatitis with peripheral blood eosinophilia.

TREATMENT

He started treatment with prednisone at 40 mg/day. Cytocholestasis (Figure 3) and eosinophilia (Figure 4) progressively improved. The corticosteroid dose was gradually titrated and azathioprine 2mg/Kg was then added.

OUTCOME AND FOLLOW-UP

After a three-month treatment, follow-up tests showed a normal eosinophil count, liver IgG levels and function tests. These data supported the definite diagnosis of autoimmune hepatitis.

DISCUSSION

Autoimmune hepatitis is a chronic liver disease which is responsible for up to 20% of chronic hepatitis in Western countries. It has a mean annual incidence of 1.9 per 100.000 individuals and a prevalence of 16.9 in northern European population (6). It is characterized by hypergammaglobulinemia, circulating autoantibodies and elevated transaminase levels (7). Peripheral blood eosinophilia is present much less frequently. It has been described in a few cases, usually in association with other autoimmune conditions, such as Coombs positive hemolytic anemia, autoimmune thyroid disease, ulcerative colitis and arthritis (8-11). As far as we know, this report is the first one concerning autoimmune hepatitis with peripheral blood eosinophilia described in a patient with Crohn's disease. There are also some cases of blood eosinophilia associated with isolated autoimmune hepatitis, in the absence of other autoimmune conditions (3, 12, 13).

The development of hypereosinophilia when there is also ulcerative colitis and autoimmune hepatitis, which are two autoimmune conditions with a Th2 bias, ³suggests that a Th2-T-cell population is at the crossroads of the pathophysiology underlying these autoimmune diseases (10). Other authors suggest that the concurrent existence of these processes mirrors related abnormal immunological events (8). Another mechanism of eosinophilia can be the result of mast cell activation, which may take place in cholestatic liver disease in which mast cell-derived mediators cause activation and eosinophil chemotaxis (14).

It should be noted that, despite the fact that autoimmune hepatitis is most usually found in women (3:1 ratio), our report presents the case of a male patient (7). Indeed, most cases described in the literature of autoimmune hepatitis with peripheral blood eosinophilia have also occurred in men (Table 1), which makes us ponder whether eosinophilia in autoimmune hepatitis can be considered a characteristic related to males.

Similar to Omata and colleagues, our patient also has a long history of asthma (13). Nevertheless, the eosinophilia and elevated IgE levels were not associated with exacerbation of asthma but rather with elevated liver function tests. In fact, our patient had asthma under control for many years. In addition, other causes of eosinophilia, particularly immediate hypersensitivity to common allergens and parasitic infection, were excluded.

Liver biopsy is considered a prerequisite for the diagnosis of autoimmune hepatitis (15). The classic histologic picture of autoimmune hepatitis includes interface hepatitis with dense plasma cell-rich lymphoplasmacytic infiltrates, emperipolesis, hepatocellular rosette formation, pycnotic necrosis and hepatocyte swelling. The discovery of hepatic eosinophils (even though it is not the predominant inflammatory cell type) enables the diagnosis of autoimmune hepatitis. In a study that describes ² the use of liver biopsy assessment in the discrimination of idiopathic autoimmune hepatitis vs drug-induced liver injury, Suzuki and colleagues discovered that intra-acinar eosinophils could be seen in 32.1% of times and portal tract eosinophils could be found in 60.7% of times regarding autoimmune hepatitis cases. Both of them were more usual than in cases of drug-induced liver injury (16).

In our case, the conjunction of plasma cells with interface hepatitis strongly supported the diagnosis of autoimmune hepatitis. However, the most striking aspect of this patient's disease was the exuberant hepatic eosinophilia. Similarly, the bone marrow aspirate showed a marked increase in normal-appearing cells of the eosinophil series. In this case,

tissue eosinophilia was marked and blood eosinophilia was significant. In contrast, the other authors reported that none or only a few eosinophils were present in the liver biopsy (3).

With regard to treatment, it should be noted that in all cases there was an improvement in liver tests as well as in the eosinophil count. Our patient had a favorable response under treatment with corticosteroids and azathioprine. Other authors also used 6-mercaptopurine and mycophenolate mofetil with an equally favorable response (11, 13). There is a need for long-term cautious management so as to prevent the progression into liver failure or hepatic cirrhosis (17).

CONCLUSION

Pathophysiology of autoimmune disorders is incompletely understood. The coexistence of different diseases could suggest common pathogenic mechanisms. Herein we report a case of autoimmune hepatitis associated with peripheral blood eosinophilia and exuberant liver eosinophilia. Given the absence of other systemic conditions or drugs and its fast resolution with the treatment of the underlying liver disease, it is our goal to emphasize this infrequent presentation of autoimmune hepatitis.

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SIMILARITY INDEX

PRIMARY SOURCES

1	www.ncbi.nlm.nih.gov Internet	60 words — 4%
2	Shoket Chowdry, Erin Rubin, David A. Sass. "Acute autoimmune hepatitis presenting with peripheral blood eosinophilia", Annals of Hepatology, 2012 Crossref	33 words — 2%
3	Benjamin Terrier. "Coexistence and Parallel Evolution of Hypereosinophilic Syndrome, Autoimmune Hepatitis, and Ulcerative Colitis Suggest Common Pathogenic Features", The American Journal of Gastroenterology, 5/2007 Crossref	17 words — 1%