Case Report

Alopecia in autoimmune hepatitis: Association with zinc deficiency

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SUMMARY

The aim this report is to describe three cases of alopecia in patients with autoimmune hepatitis and correlate this with possible etiologies. The three patients presented alopecia associated with autoimmune hepatitis and zinc deficiency. In two cases the alopecia was not a side effect of the treatment with azathioprine. Although alopecia may be an autoimmune disease in its own right, the need for zinc supplementation in patients with autoimmune hepatitis or other chronic hepatic diseases must be evaluated.

INTRODUCTION

In the absence of any other etiology, autoimmune hepatitis (AIH) is considered an inflammatory liver disease that is characterized by a dense lymphomonocytic infiltration in the portal tract and liver-specific autoantibodies. The outcome of AIH is favorable when treated with immunosuppressors.[1] The International Autoimmune Hepatitis Group has defined guidelines for the diagnosis of autoimmune hepatitis based on clinical and biochemical criteria.[2]

Three types of AIH are currently recognized: type 1 AIH is characterized by the presence of smooth muscle antibodies (SMA) and/or antinuclear antibodies (ANA), type 2 AIH is characterized by the presence of anti-liver/kidney microsome type 1 antibodies (LKM-1) or antibodies to liver cytosol and type 3 AIH is characterized by the presence of soluble liver and pancreas antigen autoantibodies (SLA/LP).[3-5] Other autoantibody markers such as have been also proposed for the diagnosis of AIH. However, autoantibodies are absent in ~10-20% of cases.[6]

Jaundice and choluria are usually present, although some patients have only subtle, nonspecific symptoms because of an increase in aminotransferase levels. Gregorio et al. reported that acute symptoms, similar to viral hepatitis, occurred in over 50% of patients.[7]

Only one case of AIH-related alopecia has been reported in the literature and involved a 14-year-old girl with anti-liver-kidney microsome autoimmune hepatitis preceded by alopecia three years earlier.[8] The alopecia in this case may be attributed to the autoimmune disease itself, the patient´s nutritional status or the side effects of azathioprine (AZA), although the latter have been observed only in animals.[9]

In this report, we describe three cases of alopecia in AIH patients and correlate this with possible etiologies.

ETHICAL ASPECTS

The study was approved by the institutional Ethics Committee (protocol no. 676/2005). The patients and their relatives were aware of the intent to publish, agreed to this and gave written informed consent prior to participation in this investigation. The patients´ identities were kept confidential.

CASE REPORTS

Case 1

A 13-year-old boy presented with hepatosplenomegaly, ascites and jaundice. After investigation, he was diagnosed with type 1 AIH and was positive for anti-SMA. Treatment

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Figure 1: Patient 1 with alopecia before Zn supplementation.

included prednisone (60 mg/day), ranitidine (300 mg/day) and vitamins A, C, D, E and complex B. After two months of treatment, the patient presented with alopecia (Figure 1) and was diagnosed with a Zn deficiency (plasma zinc: 42 μg/dL; reference value = 70-120 μg/dL).

Supplementation with Zn sulfate (1 mg/kg/day of elementary Zn; total: 50 mg/day) and treatment with AZA were initiated. The first signs of improvement in alopecia, with the appearance of new wire hair, were noticed after 20 days of Zn supplementation. An adequate plasma Zn concentration (at least 70 μg/dL) was reached only after two months of supplementation with the alopecia reverted (Figure 2), but plasma Zn was markedly lower in subsequent analyses without impairment of alopecia. After 13 months of supplementation, the Zn supplementation was doubled to 50 mg twice a day. After five months of double supplementation, the plasma Zn concentration (101 μg/dL) was within the reference range.

Figure 2: Patient 1 with reverted alopecia after Zn supplementation.

Difficulties with schooling were reported throughout the 18 months of treatment with Zn. The weight/age (W/A) and height/age (H/A) indexes decreased from the 50th percentile to the 25th percentile during the period of Zn supplementation.

Case 2

A 6-year-old girl presented with jaundice, coluria, acholia, anorexia and abdominal distension. The child was diagnosed with type 2 AIH and was positive for antibody to liver cytosol. Shortly after the beginning of treatment (4th day) with prednisone and AZA, the patient developed acute, intense alopecia. The use of AZA was interrupted and Zn supplementation was initiated (1 mg/kg/day of elementary Zn; total: 25 mg/day). When the child returned to the service after two months of Zn supplementation, the alopecia had reverted although the plasma Zn concentration was still only 64 μg/dL (reference value = 70-120 μg/dL). Azathioprine was prescribed again, without side effects. After three months of zinc supplementation, the plasma Zn concentration was 118 μg/dL. Throughout the period of treatment, the W/A and H/A indexes were within the 50th–75th and 25th–50th percentiles, respectively.

Case 3

A 16-year-old girl presented with jaundice, choluria, an elevation in aminotransferase levels, alopecia and a plasma Zn concentration of 52 μg/dL (reference value = 70-120 μg/dL). Autoimmune hepatitis was diagnosed by the International Score, although the patient was negative for autoantibodies. Zinc supplementation (50 mg/day of elementary Zn) was initiated, concomitant with the administration of prednisone and AZA. After two months of Zn supplementation, the alopecia had reverted. The W/A index was within the 75th–90th percentiles and the H/A index was within the 97th percentile. After two months of Zn supplementation, the plasma Zn concentration was 95 μg/dL.

DISCUSSION

Only one case of type 2 AIH-related alopecia had been reported in the literature and involved a 14-year-old girl who developed anti-liver-kidney microsome autoimmune hepatitis preceded by alopecia three years earlier.[8] Chronic hepatic diseases such as AIH in infancy may result in nutritional deficiencies in vitamins and minerals.[10-12] Hepatic diseases may reduce the availability of Zn through low intestinal absorption, high urinary elimination because of drug use, and changes in nitrogen metabolism. In addition, these patients probably have a poor intake of Zn because

of dysgeusia, precocious satiety, nausea and vomiting.[13] A short-term deficiency in Zn results in reduced immune function, appetite loss, delayed wound healing, alopecia, skin injuries and night blindness. In contrast, a chronic deficiency in this metal leads to an altered nutritional status, a low weight gain, a decrease in height growth, and delayed sexual maturation and cognitive development.[14] Hepatic function is impaired in chronic liver disease, as is also tissue mineral distribution. Valberg et al[15] studied low zinc absorption in patients with alcoholic cirrhosis and Goode, Kelleher and Walker[16] reported a Zn deficiency in patients with alcohol-induced and non-alcohol-induced liver disease.

There is no report in the literature on Zn deficiency in patients with AIH, although alopecia caused by Zn deficiency has been described for patients submitted to intestinal surgery.[17] Zinc supplementation prevents alopecia in apparently healthy children with low serum Zn levels (hair loss ceased after three weeks of Zn supplementation.[18] As shown here, patient 1 was of low weight and stature, and had frequent episodes of influenza and cognitive difficulties. These signs and symptoms have also been reported in cases of Zn deficiency, and may result in a decrease in the concentration of circulating growth hormone (IGF-I), damage to the immune system and alterations in the function of enzymes that depend on Zn as a cofactor.[19- 21]

In cases 1 and 3, alopecia was not a side effect of the treatment with AZA since in these patients hair loss began before administration of the drug. Additionally, the patients´ nutritional status was not a determining factor in the etiology of alopecia.

Although alopecia may be an autoimmune disease in its own right, the need for Zn supplementation in patients with AIH or other chronic hepatic diseases must be evaluated because of the deleterious effects of a Zn deficiency and possible worsening of the clinical picture.

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