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Case Report

Acute Liver Failure by Autoimmune Hepatitis (AIH) and Liver Cirrhosis in Adolescent Patient: Case Report

Zamarripa VL[1], Valdez PRA[1], Ramirez LDH[1], Barrios OC[1] and Ochoa MC[2]*

[1]Department of Family Medicine, Family Medicine Unit #1 (IMSS), Mexico

[2]Department of Pediatrics, Regional General Hospital #1 (IMSS), Mexico

***Corresponding author:** Ochoa Maria Citlaly, Department of Pediatrics, Regional General Hospital #1 (IMSS), Sonora Delegation, Sonora, México, Colonia centro, Cd. Obregon, Sonora, Mexico

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Abstract

Autoimmune hepatitis (AIH) is defined as chronic liver parenchyma inflammation of unknown etiology. In pathogenesis are involved environmental triggers and immunological tolerance in genetically predisposed patients resulting in liver parenchymal attack by T lymphocytes. For diagnosis, histologic features and specific analytic are required (hypergammaglobulinemia and specific autoantibody), disease is classified as type 1 (ANA and/or SMA and/or SLA positive) and type 2 (LKM-1 and/or LC1 positive).In few cases AIH remission is acquired, main goal of treatment is to modify natural history, relieve symptoms, improve biochemical parameters and decrease liver tissue inflammation and fibrosis. We report a 19 years old female with acute liver failure secondary to relapse autoimmune hepatitis and liver cirrhosis with a clinical course of 16 years in maintenance treatment with prednisone who presented multiple complications.

Keywords: Autoimmune hepatitis; Acute liver failure; Adolescence

Introduction

First autoimmune hepatitis reference was in 1942 known as lupus hepatitis [1]. In Atlanta, Georgia (1999) was named as autoimmune hepatitis (AIH) and criteria for diagnosis were determined [2]. Currently, AIH is considered a progressive necro-inflammatory and chronic liver disease which is characterized by presence of immunological abnormalities (hypergammaglobulinemia and autoantibodies), with a good response to immunosuppressive therapy and higher prevalence in women (3.6:1) [3]. Pathogenesis is result of alterations in immune tolerance, genetic predisposition and environmental factors. There are potential "triggers" as infectious agents (measles virus, hepatitis virus, cytomegalovirus, and Epstein-Barr virus) and drugs (antibiotics, statins, and anti-TNF) [4].

AIH as a world wide incidence of 1-2 cases per 100,000/year, a prevalence of 10-20 cases per 100,000/year and is observed in all ethnic groups. Highest incidence occurs in adolescence and between 35-40 years [5]. AIH diagnosis is based on a scoring system developed by International Autoimmune Hepatitis Group (IAIHG) in 1999 and updated in 2010 [6]. In USA, AIH is leading cause of chronic liver disease in 11-23% cases [7]. Specifically in Latin America and Mexico it is not exactly known AIH prevalence.

Case Presentation

Female 19 years old, native and resident of Cd. Obregon, Sonora, Mexico, with weight and height according to age. Started her condition in October 2000 at age of three with episodic epistaxis and two months later with jaundice, acholia, and choluria. Initial laboratory tests revealed elevation of aminotransferases; liver ultrasonography was normal. With clinical data, diagnosis of acute viral hepatitis was considered. Was treated with unspecified symptomatic management.

Eight months later continued with episodic epistaxis and jaundice; a new liver ultrasound showed multiple regenerative nodules, steatosis and portal hypertension. She was hospitalized and laboratory tests reported (Table 1): cholesterol 100 mg; total protein 7.6 g; albumin 3.2 g; globulin 5.5 g; direct bilirubin 1.8 mg; indirect bilirubin 1.6 mg; alanine aminotransferase (ALT) 880 IU; aspartate aminotransferase (AST) 452 IU; alkaline phosphatase (AF) 678 IU; lactate dehydrogenase (LDH) 302 IU; gamma glutamyl transferase (GGT) 425 IU; prothrombin time (PT) 22 sec, partial thromboplastin time (PTT) 31 sec. Serology panel for hepatitis B, C and HIV was negative. Due to persistence of symptoms for more than 6 months a liver biopsy was performed. Histopathological result: presence of necrosis bridges to portal space with regenerative nodules, inflammatory infiltrate composed by lymphocytes and plasma cells in liver parenchyma. Right lobule with multifocal hepatocellular necrosis and some rosettes. Histological diagnosis was chronic hepatitis probably autoimmune and moderate fibrosis.

After biopsy, immune studies showed (Table 1): IgG 5050 mg/dl (reference value: 690-1620), IgA 400 mg/dL (reference value: 70-380); T/B lymphocytes and subclasses showed no abnormalities; antinuclear antibodies (ANA) negative, anti-smooth muscle negative (SMA), anti-microsomal against liver and kidney (LKM-1) positive, anti-soluble liver antigen (SLA) negative; diagnosis of type 2 AIH (AIH-2) was established. Prednisone at dose of 2 mg/kg/day and azathioprine (AZA) 0.5 mg/kg/day was started like initial treatment with improvement at four weeks, jaundice and epistaxis disappear; however she had 5.5 kg weight gain and hair loss as steroid complication, dose of prednisone was decreased at 1 mg/kg/day and subsequently to 5 mg/day with maintenance of AZA (0.5 mg/kg/day). AIH remission was achieved by normalizing levels of transaminases and bilirubin. Five years after diagnosis, patient was admitted to emergency room for abdominal pain, jaundice, dark urine and acholia. Blood test showed (Table 1): direct bilirubin 2.3 mg; indirect bilirubin 1.2 mg; ALT 540 IU; AST 436 IU; LDH 350 IU; GGT 479 IU; PT 23 sec; PTT 32 sec; IgG 5220 mg/dL (reference value: 690-1620),

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Table 1: Laboratory test results.

Laboratory test	Oct 2000	May 2005	Mar 2016	Apr 2016	Jul 2016
Hemoglobin	14.5 g/dl	13.2 g/dl	15.7 g/dl	---	10.2 g/dl
hematocrit	43.5 %	41.5 %	40 %	---	38 %
leucocytes	9.2 10^3/µl	7.6 10^3/µl	9.2 10^3/µl	---	10.2 10^3/µl
platelets	256 10^3/µl	232 10^3/µl	256 10^3/µl	---	148 10^3/µl
Glucose	80 mg/dL	84 mg/dL	72 mg/dL	---	89 mg/dL
BUN	10 mg/dL	13 mg/dL	20 mg/dL	---	31 mg/dL
Urea	19.4 mg/dL	22 mg/dL	21 mg/dL	---	50 mg/dL
creatinine	0.3 mg/dL	0.45 mg/dL	0.5 mg/dL	---	0.8 mg/dL
Total protein	7.6 g/dl	6.9 g/dl	7.0 g/dl	---	4.9 g/dl
Albumin	3.2 g/dl	2.9 g/dl	4.3 g/dl	---	1.3 g/dl
Globulin	5.5 g/dl	4.5 g/dl	4.5 g/dl	---	2.2 g/dl
Total bilirubin	3.4 mg/dl	3.5 mg/dl	3.0 mg/dl	---	15.6 mg/dl
Direct bilirubin	1.8 mg/dl	2.3 mg/dl	2.0 mg/dl	---	10.2 mg/dl
Indirect bilirubin	1.6 mg/dl	1.2 mg/dl	1.0 mg/dl	---	5.4 mg/dl
AST	452 UI/dl	436 UI/dl	105 UI/dl	---	2290 UI/dl
ALT	880 UI/dl	540 UI/dl	130 UI/dl	---	3190 UI/dl
GGT	425 UI/dl	479 UI/dl	220 UI/dl	---	670 UI/dl
DHL	302 UI/dl	350 UI/dl	220 UI/dl	---	600 UI/dl
AF	678 UI/dl	714 UI/dl	213 UI/dl	---	890 UI/dl
Cholesterol	100 mg/dl	130 mg/dl	120 mg/dl	---	100 mg/dl
triglycerides	88 mg/dl	95 mg/dl	90 mg/dl	---	70 mg/dl
Calcium	9.2mg/dL	10.0 mg/dL	9.8 mg/dL	9.9 mg/dL	8.5 mg/dL
Potassium	4.3 mmol/l	5.0 mmol/l	6.0 mmol/l	5.5 mmol/l	4.3 mmol/l
Sodium	139 mmol/l	145 mmol/l	100 mmol/l	137 mmol/l	138 mmol/l
Chlorine	109 mmol/l	102 mmol/l	103 mmol/l	99 mmol/l	105 mmol/l
PT	22.0 seg	23.0 seg	15.0 seg	---	35.0 seg
PTT	31.4 seg	32.0 seg	25.0 seg	---	45.0 seg
INR	1.8	1.9	1.13	---	2.3
IgG	5050 mg/dl	5220 mg/dl	---	---	---
IgA	400 mg/dl	450 mg/dl	---	---	---
ANA	Negative	---	---	---	---
SMA	Negative	---	---	---	---
LKM-1	1:40 Positive	---	---	---	---
SLA	Negative	---	---	---	---

AIH relapse was diagnosed and prednisone dose was increased to 2 mg/kg/day and AZA 2 mg/kg/day, with improvement after two weeks of treatment. A new liver biopsy reported: autoimmune hepatitis with moderate inflammatory activity, portal fibrous and irregular nodular liver parenchyma.

At age 19, 16 years after diagnosis and medical management, was admitted into emergency room for diarrhea, vomiting, disorientation, dyspnea moderate, orthopnea and edema since a month ago; laboratories reported (Table 1): Hb 15.7 g/dl; WBC 9.2 10^3/L; platelets 256,000/L; glucose 72 mg/dl; urea 21 mg/dl; creatinine 0.5 mg/dL; albumin 4.3 g/dl; AST 105 IU; ALT 130 IU; LDH 220 IU; Sodium 100 mmol; Potassium 6.0 mmol; chlorine 98 mmol; PT 15 sec; PTT 25 sec; INR 1.13. Severe hyponatremia was detected in blood test. Initially severe hyponatremia was confirmed and use of hypertonic saline was considered, subsequently continued with isotonic saline, intravenous diuretic, achieving a negative balance of water and a positive sodium balance during next days; required intravenous potassium replacement. Patient was discharged 10 days later with normal serum sodium (137 mmol) without neurological disorders; AIH treatment with prednisone 10 mg/day.

Three months later she was admitted to emergency room with jaundice, nausea, vomiting and disorientation, laboratories showed (Table 1): Hb 10.2 g/dl; WBC 10.2 10^3/L; platelets 148000; glucose 89 mg/dl; urea 50 mg/dl; creatinine 0.8 mg/dl; albumin 1.3 g/dl; bilirubin

Table 2: Simplified diagnostic criteria for AIH [6].

Immunoglobulin G (IgG)	
IgG Higher than normal	1 point
IgG Higher than 1.10 times normal	2 points
Autoantibodies	
ANA o SMA ≥1:40	1 point
ANA o SMA ≥1:80	1 point
LMK ≥1:40	2 points
SLA positive	2 points
Chronic hepatitis histology	
AIH compatible	1 point
AIH typical	2 points
Absence of viral hepatitis	2 points
Score	
AIH probable ≥6 points	
AIH diagnosis ≥7 points	

AIH: autoimmune hepatitis, ANA: antinuclear antibodies, SMA: anti-smooth muscle, LKM-1: anti-microsomal against liver and kidney, SLA: anti-soluble liver antigen

direct 10.2 mg; indirect bilirubin 5.4 mg; AST 2290 IU; ALT 3190 IU; LDH 600 IU; sodium 138 mmol; potassium 4.3 mmol; chlorine 105 mmol; PT 35 sec, PTT 45 sec; INR 2.3. Once stabilized, acute liver failure secondary to AIH was diagnosed, a third liver biopsy reported: autoimmune chronic hepatitis, liver necrosis, severe inflammatory activity and cirrhosis. Aggressive treatment was started with steroids and immunosuppressant (cyclosporine). Six hours later development a severe hepatic encephalopathy; despite support measures implemented, patient presented cardiorespiratory arrest without response to advanced support and died five days after admission.

Discussion

In this clinical case, disease started with clinical and biochemical manifestations of liver failure, initially was considered secondary to acute viral hepatitis as differential diagnosis but serological markers were negative. Due to persistence of symptoms for more than six months a liver biopsy was done. Chronic hepatitis is defined as a necro-inflammatory liver syndrome, which persists for at least 6 months without remission of symptoms and biochemical alterations [8]. In our case, viral etiology was discarded by negativity of viral markers. Autoimmune etiology is supported by clinical and biochemical features, histologic findings, hypergammaglobulinemia and disease evolution.

Definitive diagnosis of AIH in our patient was established on basis of clinical, laboratory and histopathological criteria defined by IAIHG. Some of these criteria are directly related to diagnosis and others have been associated with worse prognosis [9]. In diagnostic criteria (Table 2), ANA/SMA/LKM-1 has been set up as positive 1:40 for adults, but for children, 1:20 is enough for ANA/SMA, and 1:10 for LKM-1 [10]. SLA positivity is related to severe course and higher tendency to relapse [11].

Treatment goals are: improve symptoms, induce biochemical remission, abate liver inflammation and prolong survival [12]. Clinical and biochemical remission does not necessarily reflect histological resolution because histopathologic changes are late [13]. After at least4 years of treatment, there is improvement in fibrosis and portal inflammation in more than 95% cases. Patient in our case was always treated, discontinuation of treatment is not recommended because in AIH-2 relapses are more frequent and remission failure is almost certain [14].

Standard therapy with prednisone-AZA is effective in 85% cases [15], there are another alternatives treatments that must be considered. Infusion of antigen-specific T cells to restore immune regulation and peripheral tolerance has been suggested for AIH-2 [16]. It is important to remember that 55% of patients in complete biochemical remission still have histological activity. In case of therapeutic failure, is possible to change prednisone for budesonide and azathioprine for mycophenolate mofetil or cyclosporine, with different results [17].

Conclusion

It is important to identify both clinical and laboratory AIH abnormalities, such as hepatomegaly, increased bilirubin and transaminases alterations and begin quickly differential study of liver disease [18]. Relapses are common in course of treatment (45-60% cases) and are most frequently seen in AIH-2. Prednisone-AZA is initial treatment. Another thing to consider is psychological support for treatment compliance because AIH is a chronic disease.

Optimal treatment duration is not defined. It has been reported that 25% of pediatric patients with AIH type 1 could remove medication after a year of normal liver function, something impossible in AIH-2 [19]. In adults, long-term remission is possible increasing dose of azathioprine without corticosteroids [20]; unfortunately, there are no controlled studies in children, decision in treatment should be carefully evaluated in each case, monitoring liver function for long time periods. Liver transplantation can be a therapeutic resource to consider for selected patients. More genetic, immunological markers, prognostic factors and treatment studies are required.

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