Autoimmune Hepatitis in Children: One center study

Thesis

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By
Dina Moustafa Hassan
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Under supervision of

Prof. Dr. Amel Abdel Magied El Faramawy
Professor of pediatrics
Faculty of Medicine Ain Shams University

Assist. Prof. Dr. Azza Mohammed Youssef
Assistant Professor of pediatrics
Faculty of Medicine Ain Shams University

Faculty of Medicine
Ain Shams University
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List of Abbreviations

AASLD	American Association For The Study of Liver Disease
AIH	Auto immune hepatitis
ALP	Alkaline phosphatase
ALT	Alanine Transaminase
ANA	Anti nuclear antibody
Anti- SLA…	Anti- soluble- Liver antigen
APCs	Antigen-presenting cells
ASMA	Anti Smooth muscle antibody
AST	Asparate Transaminane
ASGP-R…..	Asialoglycoprotein Receptor
C2	Complement 2
C4	Complement 4
CTL…….	Cytotoxic T Lymphocyte
ELISA	Enzyme Linked immune sorbant assay
EMA	Endomysium antigen
GGT……	Glutamyltranspeptidase
HCC.....	Hepato Cellular Carcinoma
HLA…….	Human Leuckocyte- Antigen
IAIHG…….	International Autoimmune Hepatitis Group
IBD……..	Inflammatory Bowel Disease
IgG	Immunoglobulin G
IIF……	Indirect Immunofluorescent
IL.....	Inter Leukein
LC1	Liver cytosol Type I
LF……	Liver failure
LKM1…….	Liver kidney Microsomal Type I
LP …….	Liver Pancreas antigen

List of Abbreviations (Cont.)

LSP	Liver Specific Lipoprotein
MELD	Model for end stage liver disease
MHC	Major Histo compatibility complex
MMF	Mycophenolate Mofetil
NKC	Natural killer cells
OLT	Orthotopic Liver Transplantation
PANCA	Perinuclear antineutrophil cytoplasmic antibodies
PBC	Primary biliary Cirrhosis
PELD	Pediatric for end stage liver disease
PSC	Primary Sclerosing Cholangitis
SLE	Systemic Lupus Erythroumatousis
TGF.....	Transforming Growth Factor
TH	T- helper
TNF	Tumor Necrosis Factor
TReg……..	T- regulatory
ULN…….	Upper Limit Of The Normal Range

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Abstract

Background and study aims: Auto-immune hepatitis (AIH) in children is a rare chronic progressive liver disorder. It is characterized serologically by high aminotransferase levels, elevated immunoglobulin G (IgG) and the presence of autoantibodies. AIH is divided into two types according to the autoantibody profile. This study aims to assess frequency, clinical manifestations, biochemical features and outcome of AIH in children following up at our Hepatology clinic, Children's Hospital Ain shams University over the last 20 years.

Patients and methods: The medical records of 20 children with AIH, diagnosed on the basis of the International Scoring Criteria of Auto-immune Hepatitis, in the last 20 years were retrospectively analyzed for clinical, biochemical and serological profiles and also treatment outcome.

Results: Among 20 children, 11 were females (55%) and 9 were males (45%). Jaundice represented the most consistent finding in all patients. According to the autoantibody profile, 14 children were classified as type 1, and sex children were seronegative as all their auto antibodies were negative. Complete remission was observed in 70% of patients, incomplete response to therapy in 20% and treatment failure in 10%. There was no significant statistical difference in clinical and biochemical features of AIH in patients regarding the response to treatment. After complete withdrawal of corticosteroids, six patients (65%) developed relapse.

Conclusion: AIH should be kept in mind in the differential diagnosis of both acute and chronic liver diseases in children AIH type 1 was the main form of AIH in the studied cases and treatment with combination of corticosteroids and azathioprine is effective treatment option. Further studies on a larger number of cases and long-term follow-up are recommended.

Introduction

Autoimmune hepatitis (AIH) is an inflammatory liver condition characterized by interface hepatitis, hypergammaglobulinemia, serum autoantibodies, and satisfactory response to immunosuppressive treatment ***(Zhao et al., 2011).***

Immune reactions against host liver antigens are believed to be a major pathogenic mechanism. The histological feature of interface hepatitis, with the infiltration of lymphocytes, plasma cells, and macrophages, suggests an aggressive cellular immune response in the pathogenesis of AIH ***(Vergani and Mieli-Vergani, 2007a).***

According to the pattern of detected antibodies two major forms of autoimmune hepatitis are differentiated. Autoantibodies characterizing type 1 are anti-nuclear antibodies (ANA), anti-smooth muscle antibodies (SMA) and anti-soluble liver protein antibodies (SLA). Type 2 is defined by the detection of liver kidney microsomal autoantibodies (LKM1) and/or liver cytosol 1 antigen (LC1) autoantibodies ***(García Romero et al., 2007).***

Some patients share the clinical and histological features of AIH without the presence of immunological markers (autoantibodies) required for sub classification. These are referred to as unclassified AIH ***(Geylanı Güleç et al., 2011).***

AIH is generally uncommon and is even less common among the pediatric population. The profiles of AIH in the pediatric population are similar to those in adults, the only difference being that the disease tends to be more severe in the former ***(Mieli-Vergani et al., 2009).***

The disease manifests in various ways: asymptomatically, with changes in laboratory parameters, with symptoms similar

to those of acute viral hepatitis, or with the pattern of progressive liver insufficiency culminating in cases of fulminant hepatitis with liver failure. This last clinical form is more common among the young population than it is among adults ***(Prados et al., 2001).***

There are only a very small number of reports on larger series of children reflecting upon the allocation of subtype, sex distribution, clinical features and laboratory characteristics in correlation with age. In terms of these issues in most countries systematic epidemiological data are not available to date. Nevertheless, these information are the basis for synchronization of treatment, determination of prognostic factors and improvement of long term outcome ***(Oettinger et al., 2005).***