

Autoimmune Hepatitis in Children: One center study

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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Contents

List of Abbreviations	i
List of Tables	iii
List of Figures	vii
Abstract	ix
Introduction and Aim of the Work	1
Review of Literature	4
* (Autoimmune Hepatitis).....	4
Patients and Methods.....	59
Results	62
Discussion.....	102
Summary	116
Conclusion.....	120
Recommendations	121
References	122
Arabic Summary	--

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

List of tables

Table No.	Subject	Page
1	Subtypes of Autoimmune Hepatitis	8
2	Criteria for the diagnosis of autoimmune hepatitis in childhood	21
3	International Scoring System for Diagnosis of Autoimmune Hepatitis (2005)	25
4	Simplified Diagnostic Criteria for Autoimmune Hepatitis	27
5	Indications for treatment	31
6	End points of initial treatment and courses of action	38
7	Definition of treatment response according to international Autoimmune Hepatitis Group	60
8	Gender distribution among the patients	63
9	Age, age at presentation, duration from the start of symptoms and duration of the follow up of the patients	64
10	Mode of presentation	65
11	Complaint distribution among patients	66
12	Hepatitis A infection at presentation	67
13	Laboratory studies at presentation of the disease and before treatment	68
14	Auto antibodies testing	69
15	Classification of patients according to auto antibodies	70
16	Comparison between the types of AIH as regards patient's characteristics	70
17	Comparison of the types of AIH as regards sex mode of presentation and complaints	72

List of tables (Cont.)

Table No.	Subject	Page
18	Other auto antibodies	74
19	HLA -DRB1* alleles typing in 10 patients .	75
20	Comparison between types of AIH in the studied cases as regards HLA typing	76
21	Liver biopsy was done for 13 patients	77
22	Histological activity index (HAI) scoring in liver biopsy	87
23	Fibrosis score in liver biopsy	87
24	Histological data in AIH type1 and seronegative patients	79
25	Laboratory findings for other autoimmune diseases	80
26	Treatment modalities	81
27	Laboratory studies after 4-8 weeks of immunosuppressant therapy	82
28	Laboratory studies (Last reported results)	83
29	Occurrence of relapses in our children over the whole disease duration	84
30	Frequency of relapses	84
31	Frequency of complication due to treatment	85
32	Outcome in the studied patients at the end of follow up	86
33	Long term prognosis	87
34	Comparison of different AIH outcomes in the studied cases as regards patient's characteristics	88
35	Comparison of different AIH outcomes in the studied cases as regards patient's sex, mode of presentation and complaints	89
36	Comparison of different AIH outcomes in the studied cases as regards Laboratory studies at presentation before treatment	90

List of tables (Cont.)

Table No.	Subject	Page
37	Comparison of different AIH outcomes in the studied cases as regards presence of hepatitis A infection at presentation	91
38	Comparison of different AIH outcomes in the studied cases as regards auto immune antibodies	92
39	Comparison of different AIH outcomes in the studied cases as regards types of AIH	93
40	Comparison of different AIH outcomes in the studied cases as regards HLA typing	94
41	Comparison of different AIH outcomes in the studied cases as regards laboratory findings of the other autoimmune diseases	94
42	Comparison of different AIH outcomes in the studied cases as regards Liver biopsy	95
43	Comparison of different AIH outcomes in the studied cases as regards Treatment modalities	96
44	Comparison of different AIH outcomes in the studied cases as regards Laboratory studies after 4-8 weeks of immunosuppressant therapy	97
45	Comparison of different AIH outcomes in the studied cases as regards Laboratory studies (last reported results)	98
46	Comparison of different AIH outcomes in the studied cases as regards Complications of treatment	99
47	Comparison of different AIH outcomes in the studied cases as regards frequency of relapses	100

List of tables (Cont.)

Table No.	Subject	Page
48	Comparison of different AIH outcomes in the studied cases as regards long term prognosis	101

List of Figures

Fig. No.	Subject	Page
1	An autoimmune attack can follow different pathways to inflict damage	15
2	Interface hepatitis	22
3	Plasma cell infiltration	23
4	Panacinar (lobular) hepatitis	23
5	Centrilobular (Rappaport zone 3) necrosis	24
6	Overlap syndromes of autoimmune hepatitis	29
7	Nonstandard medications in the treatment of autoimmune hepatitis	46
8	Gender distribution among the patients	63
9	Age, age at presentation, duration from the start of symptoms and duration of the follow up of the patients	64
10	Mode of presentation	65
11	Symptoms and signs at presentation	66
12	Hepatitis A infection at presentation	67
13	laboratory studies at presentation before treatment	68
14	Auto antibodies testing	69
15	HLA typing among patients	75
16	Pathological findings of the liver biopsy	77
17	Thyroid profile	80

List of Figures (Cont.)

Fig. No.	Subject	Page
18	Treatment modalities	81
19	Laboratory studies after 4-8 weeks of immunosuppressant therapy	82
20	Laboratory studies (Last reported results)	83
21	Frequency of relapses distribution among patients	84
22	Frequency of complication due to treatment	85
23	Outcome in the studied patients at the end of follow up	86
24	Long term prognosis of the studied patients at the end of follow up	87
25	Comparison of different AIH outcomes in the studied cases as regards long term prognosis	101

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 six 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: asymptotically, 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**).