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Autoimmune Hepatitis at the Moulay Ismail Military Hospital in Meknes: Epidemiological, Clinical and Immunological Aspects

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Abstract **Original Research Article**

Introduction: Autoimmune hepatitis (AIH) is a chronic inflammatory disease of the liver linked to an immunological response directed against hepatocytes. Their etiopathogenic mechanism involves several factors: viruses, bacteria and drugs as agents triggering autoimmunization [1, 2]. It is relatively rare and of unknown etiology. There are two types (I, II) associated with the presence of certain auto-antibodies. These diseases are characterized by an anatomo- clinical and immunobiological polymorphism, which can lead to diagnostic and therapeutic difficulties, and therefore medical management [3]. The presence of auto-antibodies (auto-Ab), associated with different categories of AIH, would be of great help at the diagnostic and sometimes prognostic level, justifying their interest in clinical practice. ***Materials and Methods:*** The objective of our work is to analyze the epidemiological, clinical, para-clinical and immunological profile of this affection through a retrospective study including the cases of AIH followed at the Department of Internal Medicine within the Military Hospital Moulay Ismaïl of Meknes (HMMI) over a period of 05 years from January 2013 to December 2017. ***Results:*** The age of our patients varies between 30 and 48 years old with an average of 39 years old. There is a clear female predominance (4 women and one Man). The clinical signs are dominated by jaundice, found in 4 patients, i.e. 80% of cases, it was accompanied by: pruritus in 2 patients; asthenia, anorexia and arthralgia in one patient; of ascites in a patient. Biologically, hepatic cytolysis was found in all our patients. A marked biological cholestasis was observed in 2 patients, hypergammaglobulinemia was found in all cases with predominance on IgG. Immunologically, AIH was type 1 (ANA, SMA) in 80% of cases and type 2 (anti-LKM1) in 20% of cases. On the histological panel, a morphological aspect of active hepatitis in favor of AIH is found in 3 cases, an alteration of the bile canaliculi associated with the signs of AIH is found in one case.

Keywords: Autoimmune hepatitis, auto-antibodies, antinuclear antibodies, Anti-smooth muscle antibodies.

INTRODUCTION

Autoimmune hepatitis (AIH) is a chronic inflammatory disease of the liver linked to an immunological response directed against hepatocytes. Their etiopathogenic mechanism involves several factors: viruses, bacteria and drugs as triggering agents of autoimmunization [1, 2]. It is relatively rare and of unknown etiology. There are two types (I, II) associated with the presence of certain auto-antibodies.

These diseases are characterized by an anatomo-clinical and immunobiological polymorphism, which can lead to diagnostic and therapeutic difficulties, and therefore medical management [3]. The presence of auto-antibodies (auto- Ab), associated with different categories of AIH, would be of precious help at the diagnostic and sometimes prognostic level, justifying their interest in clinical practice (fig. 1).

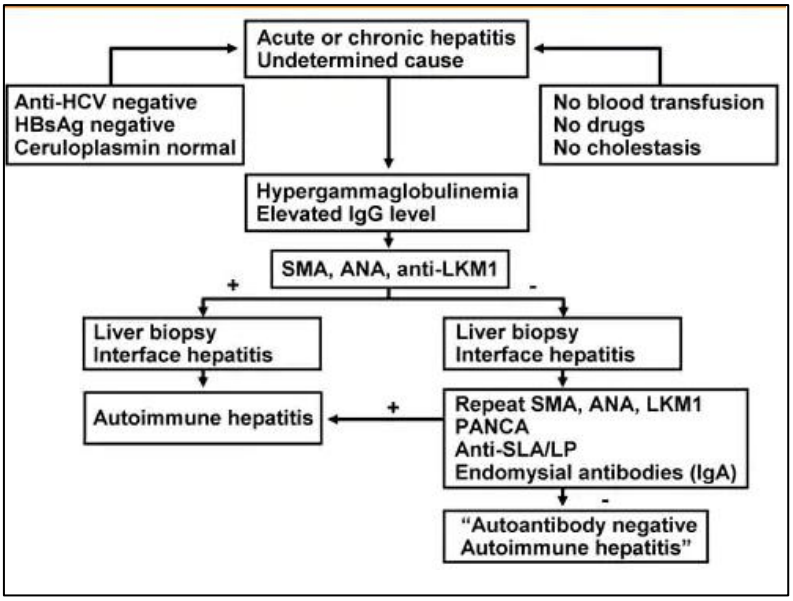

Figure 1: Approach to the immunobiological diagnosis of AIH [4]

The International Autoimmune Hepatitis Group (IAHG) established a diagnostic score in 1993, revised in 1999 then simplified in 2008 for a better diagnostic approach (Tab 1).

Table 1: 2008 "simplified" score of the IAIHG [5]

Variable	Threshold	Points
ANA ouSMA	≥1/40	1
ANA ouSMA	≥1/80	2*
OR anti-LKM	≥1/40	
OR anti-SLA	Positive	
IgG	>N	1
	> 1,1N	2
Liver histology	Compatible with an AIH	1
(need for the presence	Typical of AIH	
hepatitis)		2
Absence of viral hepatitis	YES	2
		≥6: probable AIH, ≥7: AIH certain

*addition of points for all auto-antibodies: maximum 2 points

Its spontaneous evolution in the absence of treatment is towards cirrhosis and hepatocellular insufficiency. Immunosuppressive therapy usually controls the progression of the disease.

The objective of our work is to analyze the epidemiological, clinical, paraclinical and immunological profile of this condition through a retrospective study including patients with autoimmune hepatitis (AIH) followed within the Internal Medicine Department within the Moulay Ismaïl Military Hospital in Meknes (HMMI).

MATERIALS AND METHODS

This is a retrospective study of 5 cases of AIH followed up at the Internal Medicine Service within the Moulay Ismaïl Military Hospital in Meknes (HMMI) over a period of 5 years from January 2013 to December 2017. Included all patients meeting the diagnostic criteria for autoimmune hepatitis according to the diagnostic criteria of the AIH. The different variables were carried out using the Excel table and the epi info 3.5 software.

RESULTS

The age of our patients varies between 30 and 48 years old with an average of 39 years old. Our series consists of 4 women and one man. There is a very clear female predominance with a female/male sex ratio of 4/1. The notion of taking hepatotoxic drugs (anti-tuberculosis drugs) was observed in a patient for meningo-encephalic tuberculosis. A patient is followed for hypertension and dry syndrome. In addition, we noted the absence of the notion of blood transfusion, viral hepatitis and alcohol consumption in our patients.

The clinical manifestations are dominated by jaundice, found in 80% of cases. It is cholestatic type.

Jaundice was accompanied by pruritus in 40% of cases; asthenia, anorexia and arthralgia in 20% of cases and ascites in 20% of cases.

Biologically, hepatic cytolysis was found in 100% of our patients. Intense cytolysis (over 10xN) was observed in one patient. Total bilirubin and direct bilirubin were elevated in 80% of patients. As for alkaline phosphatase, it was increased (over 105 IU/L) in 4 patients, i.e. 80% of cases. Gamma Glutamyl Transferase was elevated in 100% of patients, the level of which varied between 1.5 and 13 times the normal value. Protein electrophoresis performed in all our patients revealed polyclonal hypergammaglobulinemia in 100% of cases with a rate varying between 19.5 g/l and 46.2 g/l (NV 8-13.5).

Regarding hematological manifestations, the presence of pancytopenia was noted in 1 patient, isolated thrombocytopenia at 55000/mm3 in a single patient. Bicytopenia in 1 case (anemia and thrombocytopenia). Viral hepatitis serologywere negative (HAV, HBV, HCV) in 100% of cases.

An immunological assessment by search for autoantibodies was carried out in all patients. 80% of cases (n=4) had positive antinuclear antibodies (ANA) with a speckled appearance on immunofluorescence IFI. Anti-smooth muscle antibodies (SMA) were found in 4 patients, i.e. 80% of cases. Anti-liver and kidney microsome antibodies (LKM1) were found in one patient, i.e. 20% of cases. Anti-mitochondria are positive in 2 patients, i.e. 40% of cases. Through this identification, we were able to classify the AIHs of our patients, 80% of the cases presented with AIH of type 1 (ANA, SMA) and 20% of cases with AIH of type 2 (SMA). An ultrasound examination was carried out in all our patients; it objectified liver cirrhosis with signs of portal hypertension in 50% of cases and chronic liver disease in 20% of cases. The liver biopsy puncture performed in 4 patients showed a morphological appearance of active hepatitis with inflammatory lymphoplsmocytic infiltrate in the portal spaces in the 4 cases associated with an alteration of the bile canaliculi in one case.

DISCUSSION

AIH is a condition that can be seen at any age but particularly in young adults [6]. From 16 to 75 years [7] and in another study the average age was 47 years (33 - 61 years) [8]. In our series, the age of diagnosis varies between 30 and 48 years with an average of 39 years. AIH is described as a disease of young women. A female predominance has been confirmed in almost all studies with a sex ratio that varies between 32/18 (64%) and 27/5 (84%) [7-9]. In our study, 80% of patients were women, with a sex ratio of 4F/1M.

In our series, the average delay between the onset of symptoms and the consultation was 1 to 2 months. This delay was very variable, from 1 to 2 months to over 20 months [10, 11], this variability may be due to the character insidious, fluctuating and non-specific manifestations.

Clinically, jaundice was the most frequent manifestation in more than 50% of cases [12, 13]. The frequencies of manifestations during AIH are variously appreciated in the literature (tab 2).

Table 2: Clinical manifestations according to the literature

Clinical manifestations	Jaundice	Asthenia	Pruritus	Arthralgia	Anorexia	Hepatomegaly
Our série	80%	20%	40%	20%	20%	0%
Debbeche [12]	65%	68%	32%	33%	41%	17%
Chaouali [14]	80%	66%	43%	13%	23%	33%

Biologically, as in all hepatitis, an increase in transaminases of very variable intensity has been observed; the values are between 1.5 and 30 times. In the majority of studies, cytolysis was found in all cases, it is the case in our series, intense cytolysis (greater than 10xVN) was observed in 20% of cases. Hakem *et al.*, [9] noted intense cytolysis in 68% of cases.

AIH is characterized by the presence of hypergammaglobulinemia, in the majority of cases it is a polyclonal gammopathyoften of the Immunoglobulin G (IgG) type [9, 10, 15]. This elevation is significant during periods of activity of the disease and can then return to normal spontaneously. In our series, it was present in all cases, it is of the polyclonal type and predominates over IgG and is greater than 30 g/l in 40% of cases.

On the immunological level, the search for autoantibodies is a crucial step in the diagnosis of AIH. On the one hand it makes it possible to confirm the diagnosis and on the other hand to classify the AIH. It is essentially anti-nucleus antibodies (ANA), anti-smooth muscle antibodies (SMA) (ANA and SMA: auto-Ab defining the 'AIHI type 1) and type 1 anti-microsomes (anti-LKM1) and anti-cytosol (anti-LC) anti-LKM1 and anti-LC: auto-Ac defining AIH type 2) and SMA were positive in 80% of patients and 20% of cases had positive anti-LKM1. AIH type 1 (ANA, SMA) is more frequent compared to AIH type 2 (anti-LKM1). These results are consistent with those found in the literature (Tab 3).

Table 3: Main auto-Abs associated with AIH according to the studies

Auto-Ab	OUR SERIES	Dehghani SM [16]	Rodrigues [17]	Garcia [18]
ANA	80%	22,6%	66,7%	
SMA	80%	41,5%	52,8%	71,42%
Anti-KLM1	20%	15%	3%	28,57%
AIH seronegative		29,9%	7,6%	

Histologically, liver biopsy puncture is a key examination for the diagnosis of AIH. He also appreciates the importance of fibrosis and helps eliminate other causes or associated liver disease (PBC, PSC).

In our study, 60% of patients showed signs of chronic active hepatitis, an alteration of the bile canaliculi and marked cholestasis associated with signs of AIH were found in 20% of cases. These results agree with those described in the literature [8, 9, 13].

CONCLUSION

Autoimmune hepatitis is a relatively rare disease whose etiology remains unclear. The diagnosis must be considered in the face of any acute or chronic hepatitis without obvious etiologies, particularly in women. The diagnosis of AIH should be established in the presence of clinical symptoms, biological abnormalities (transaminases, serum IgG), immunological results (ANA, anti-ML, anti-LKM-1, anti-LC1) ethistological (internal hepatitis) - face). Its spontaneous evolution in the absence of treatment is towards cirrhosis and hepatocellular insufficiency. Immunosuppressive therapy usually controls the progression of the disease.

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