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Case Report

The Potential of Liver Fibrosis Indexes/Scores for the Screening of Cryptic Liver Fibrosis in Patients with NASH Risk Factors: A Case Report

Abstract

The unintentional discovery of cirrhosis in a patient with prostate cancer lead us to enquire if some of the indexes/scored designed for the evaluation of liver fibrosis/cirrhosis, in Chronic Hepatitis C patients, could have helped us in the detection of incipient liver fibrosis, and its follow up, in this patient.

We applied seven indexes/scores using the analytical results obtained throughout eighteen years before the diagnosis of cirrhosis. The analysis of the results leads us to hypothesize that AP index, Forns Index, FIB4, and modified Phol Score, could alert of initial fibrosis stages and its progression to cirrhosis in NASH patients.

Introduction

Non-alcoholic Fatty Liver Disease (NAFLD) has a worldwide distribution. It is present in a high percentage of citizens, at least in many countries where obesity is considered as epidemic (i.e.: nowadays it is present in a range of 17 to 33 per cent of USA citizens). Non-alcoholic steatohepatitis (NASH) might be present in one third of NAFLD cases. Different factors predispose to cirrhosis and many cases of cryptogenic cirrhosis are usually the end of NASH stage [1]. Being able to diagnose NASH patients with liver fibrosis is the key to give a specific treatment at an early stage, and trying to modify environmental factors, which predispose to cirrhosis. Consequently, the fibrosis progression could be halted.

A retrospective analysis of a hidden cirrhosis case, evaluating liver fibrosis indexes/scores designed for the evaluation of liver fibrosis or cirrhosis in Chronic Hepatitis C patients [2], leads us to select some of them as useful to detect incipient fibrosis and its evolution to cirrhosis.

Currently, we are addressing two studies: the first one in a swine model of NAFLD/NASH, the second one screening liver fibrosis in NAFLD/NASH risk patients.

Methods

Seven indexes/scores used for the evaluation of liver fibrosis/cirrhosis in Chronic Hepatitis C patients [2] have been calculated from precedent analytical determinations scheduled by general practitioner throughout eighteen years before the diagnosis of cirrhosis. The calculated indexes/scores are: AAR [3,4], APRI[5], Forns Index [6], FIB4 [7], HGM-1 [8], Phol Score Modified [9], AP Index [10], Table 1.

Case Report

The unpredicted discover of hidden cirrhosis in a patient (68 years old), diagnosed of prostate cancer, lead us to hypothesize about the possibility of unmask cryptic liver fibrosis in NASH patients applying liver fibrosis indexes/scores designed for chronic hepatitis C (CHC) patients. We calculated the possible indexes/scores according to clinical biochemistry and hematological previous analysis during the eighteen years before the diagnosis of cirrhosis. Regarding to the patient's risk factors, he presented obesity since his young age; diffuse hepatopathy and ecography suggestive of steatosis both since 43 years old. Diabetes mellitus type II, since 51 years old, was treated initially by diet and suboptimal dosis

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of metformine due to digestive intolerance, posteriorly it was supplemented with gliclacide with very bad metabolic control; finally, it was controlled when gliclacide was substituted by roxiglitazone and repaglidine. Nevertheless obesity increased getting 42.7 IMC. Nowadays it is controlled by insulin. Two years ago a prostatic cancer was diagnosed and, during the clinical evaluation process, cirrhosis was discovered by computer assisted tomography (CAT); portal hypertension and esophageal varicose veins were present. In the retrospective analysis we could obtain data of the eighteen precedent years, and only seven indexes/scores could be determined according to analytical data reported in the clinical history. Data obtained are presented in Table 2 and are marked in green, yellow, orange or red according to our previous selected cut-off point for CHC patients [2].

Discussion

Taking for granted that some of the mechanisms involved in hepatic fibrogenesis may be common in different liver diseases, we hypothesized that some of the indices/scores for the diagnosis of fibrosis stage in patients with CHC could help to unmask cryptic liver fibrosis in NASH patients.

Assuming a progressive evolution towards fibrosis for the last eighteen years, we conclude that some evaluated indicators might be useful for the detection of this process. Besides, some others show that the liver is not working properly but they do not diagnose a progression from initial stages of fibrosis to cirrhosis. Finally, some others are not able to show that something wrong is happening in the liver, neither that fibrosis is occurring. In fact, AP index, Forns Index, FIB4, and modified Phol Score, used for the diagnosis of fibrosis/cirrhosis in CHC patients, when applied retrospectively to an obese patient belatedly diagnosed with cirrhosis, are capable to detect early fibrosis leading to cirrhosis. Others like APRI and HGM-1, are unable to detect any liver abnormality even when cirrhosis is clearly established. AST/ALT ratio (AAR) could be indicating that something in the liver is wrong but it is unspecific regarding liver fibrosis. Indeed, AAR did not show progression according to the expected evolution of fibrosis.

In conclusion, some easy and low-cost indexes/scores used for the diagnosis of fibrosis/cirrhosis in CHC patients could be highly useful for fibrosis screening of patients diagnosed or suspected of NAFLD or NASH (i.e.: morbidly obsesses, patients with metabolic syndrome, etc). Nowadays we are not able to diagnose accurately liver fibrosis stage by clinical chemistry methodology, but this methodological approach could be useful to detect hidden cases of fibrosis in risk patients in general practice, and, consequently to monitor its progression/regression. However, further research is needed in large cohorts of risk population (i.e: obese and metabolic syndrome patients).

Table 1: Indexes/scores calculated. ● Phol score have been modified in order to obtain intermediate classification between 0 and 1

Indexes/Scores	Refs
AST/ALT ratio = AST [IU/L] / ALT [IU/L]	[3,4]
APRI = 100* (AST[IU/L] / ULN) / PTL[10^9/L]; ULN Male 40 [IU/L]	[5]
Forns Index = 7.811 − 3.131 x ln(PTL[10^9/L]) + 0.781 x ln(GGT [IU/L]) + 3.467 x ln age − 0.014 x CHOL[mg/dl]	[6]
FIB4 = age x AST [UI/L]/ (PTL [10^9/L] x (ALT [UI/L]) $^{1/2}$)	[7]
HGM-1 = 1/(1+ e (1.97 + 0.012 x PTL [10^9/L]-0.026 x AST [IU/L] − 0.033 x GLU [mg/dL]))	[8]
Pohl Score modified• **=0** if AAR<1 and PTL > 150 x10^9/L; **=0,5** if only one agree AAR>1 or PTL < 150 x10^9/L; **=1** if AAR>1 and PTL < 150 x10^9/L	[9]
AP index (0-10) = Age (value) + PTL (value) Age: <30 = 0, 30-39 = 1; 40-49 = 2; 50-59 = 3; 60-69 = 4; ≥70 = 5; PTL: ≥225 = 0, 200-224 = 1; 175-199 = 2; 150-174 = 3; 125-149 = 4; <125 = 5	[10]

Table 2: Some Indexes/scores designed for the diagnosis of fibrosis/cirrhosis in CHC patients, when applied retrospectively to an obese patient belatedly diagnosed with cirrhosis, are capable to detect early fibrosis leading to cirrhosis; others do not.

	6/1995	6/1996	6/2003	6/2005	6/2006	6/2008	6/2009	6/2010	6/2011	6/2012	02/2013	10/2013	06/2014	12/2014	6/2015
AAR	0,61	0,62		0,76	0,61	1,29		1	1,10	1,07	1,07				1,80
APRI	0,34	0,21		0,55	0,51	0,48		0,39			0,54				0,44
Forns Index	4,97	4,50		6,79	6,89	6,43		6,73			7,19				6,79
FIB4	1,00	0,75		1,8	1,6	2,4		1,9			2,6				3,1
HGM-1	0,40	0,58		0,84	0,99	0,66		0,45			0,67				0,50
Pohl Score •	0	0		0	0	0,5		0,5			1				1
AP index	4	3	4	5	6	7	7	7			8	7	8	8,5	7,5

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