Rare Presentation of NASH with Haematemesis in An Obese Young Man

Dr. P. Anandan[1], Dr. P. Benish Pius[2]*, Dr. Yalamanchi Sriram Srujan[3], Dr. Devang J. Barad[4]

[1]Associate Professor, Department of General Medicine, Sree Balaji Medical College and Hospital, Chromepet, Chennai-600044, Tamil Nadu, India.

[2]Junior Resident, Department of General Medicine, Sree Balaji Medical College and Hospital, Chromepet, Chennai-600044, Tamil Nadu, India.

[3]Senior Resident, Department of General Medicine, Sree Balaji Medical College and Hospital, Chromepet, Chennai-600044, Tamil Nadu, India.

[4]Junior Resident, Department of General Medicine, Sree Balaji Medical College and Hospital, Chromepet, Chennai-600044, Tamil Nadu, India.

*Corresponding Author

Dr. Benish Pius P

Junior Resident, Department of General Medicine,
Sree Balaji Medical College and Hospital, Chromepet, Chennai-600044.
Tel: 9500519250
Email: drbenishpius@gmail.com

Abstract

Obesity increases a person's risk of development of insulin resistance and an increased predilection for non alcoholic induced fatty liver disease, both of which are key contributors to chronic liver disease. Non alcoholic Steatohepatitis (NASH) can potentially show a progression to end stage liver disease, necessitating a liver transplant, by causing the development of liver cirrhosis on its own. Some patients may already have severe liver fibrosis when they first show This case study describes a 36-year-old man who was hospitalised in our hospital with haematemesis brought on by the rupture of gastric varices. He was identified as having severe liver fibrosis and NASH. This example serves as a reminder of the need to be on the lookout for liver fibrosis caused by NASH, especially in individuals who are severely obese.

Keywords: Non-alcoholic Steatohepatitis, NASH, Obesity, Obese, Insulin resistance, Haematemesis, Young adult, Liver Fibrosis.

1. Introduction

As the prevalence of obesity and metabolic syndrome increases daily, non alcoholic fatty liver disease (NAFLD) is swiftly rising as one of the major aetiologies of chronic liver disease that eventually results in liver cell failure. The umbrella term NAFLD refers to both non alcoholic steatohepatitis and non alcoholic fatty liver (NAFL). By developing through multiple phases of liver fibrosis to cirrhosis, NAFLD promotes liver cell failure. Hepatocellular carcinoma (HCC) risk is also increased by it [1].

Non alcoholic fatty liver disease (NAFLD), which is regarded as the manifestation of metabolic syndrome in the liver, is characterised by hepatomegaly and a buildup of liver fat. Non Alcoholic Steatohepatitis (NASH) is identified through a histological examination of a liver sample. NASH is characterised by Mallory-Denk bodies (MDB), excessive lipid buildup (steatosis), enlargement of the liver cells, and liver fibrosis [2]. The primary idea utilised to explain the pathophysiology of NASH is the "multiple hit" hypothesis, which clarifies the pathogenesis and development of NAFLD[3]. The processes of cell damage in NASH include oxidative damage, changes in mitochondrial permeability brought on by free fatty acids, activation of apoptosis pathways that cause caspase-induced cell damage, visible as Mallory-Denk bodies (MDB), and cell death by necroapoptosis.

The development of NASH is now thought to be significantly influenced by insulin resistance, that is primarily induced by sedentary lifestyle, diet heavy in calories, fat, and carbs, as well as hereditary and epigenetic vulnerability. Patients are more likely to develop liver steatosis if they have type 2 diabetes and are obese (T2DM). Additionally, it has been reported that the degree of insulin resistance is correlated with the severity of NASH's clinical characteristics, specifically lobular inflammation and fibrosis [4]. Due to the rising prevalence of obesity in children and younger individuals, NAFLD incidence is rising among the younger population [5].

Cirrhotic NASH consequences can occasionally result in bleeding stomach varices, failing liver cells, and potentially lethal hepatocellular cancer. To stop NAFLD from progressing into liver fibrosis, it is crucial to distinguish NASH from it. Despite being an intrusive procedure with a higher risk of complications, liver biopsy and histological

Doi.org/10.31838/hiv22.02.792 Received: 14.07.22, Revised: 28.08.22, Accepted: 02.09.22

examination remain the gold standard for diagnosing NASH and evaluating hepatic fibrosis. As a result, it may be difficult to make a rapid diagnosis of cirrhotic NASH, especially in younger people without a main illness or a long medical history. We are talking about a case of a 36-year-old man, who was obviously obese, who had stomach varices that had ruptured, causing haematemesis to manifest as the first sign of NASH.

2. Case Report

History

A 36-year-old male patient was hospitalised to our hospital with complaints of haemorrhage from gastric varices that had ruptured. The patient's medical history was normal prior to this. The patient had no known relatives who had liver illness. He didn't admit to drinking excessively or using drugs for recreational purposes. He was hospitalised with a BMI of 42.5, a height of 174 cm, and a weight of 128.6 kg.

Examination

Patient had hepatosplenomegaly and a mild pallor upon examination. A neurological examination revealed no abnormalities. The haemoglobin level was 9.4 g/dL, the WBC counts were higher (15,400/L), and the platelet counts were within normal range (18.4 104/L). A biochemical test revealed levels of serum total bilirubin of 0.8 mg/dL, serum albumin of 2.9 g/dL, as well as gamma glutamyl transferase of 75 U/L, AST (SGOT) of 20 U/L, ALT (SGPT) of 21 U/L, and alkaline phosphatase (ALP) of 143 U/L. There was a little increase in C-reactive protein (1.45 mg/dL). Type-4 collagen (251 ng/mL), Mac-2 binding protein (2.76 COI), and hyaluronic acid (196 ng/mL) were all determined to be enhanced. Fibrosis 4 (FIB4) index [7] and the AST to platelet ratio index (APRI) [6] were not elevated (APRI = 0.344 and FIB4 index = 1.06). Serum ferritin and ceruloplasmin levels were found to be within normal limits. Hepatitis B core antibody, hepatitis B surface antigen, and hepatitis C viral antibody tests all yielded negative results. Despite having significant anti-nuclear antibody (ANA) titres, both anti-glutamic acid decarboxylase and anti-mitochondrial antibodies were negative. IgG, IgM, and IgA concentrations were appropriate. It was found that the prothrombin time was shorter. Other results included 276 mg/dL fasting plasma glucose (FPG), 8.6% glycated haemoglobin (HbA1c), 16.2% glycoalbumin, 14.5 U/mL immunoreactive insulin (IRI), and 10.7 HOMA-IR scores. The quantitative insulin sensitivity check index (QUICKI), a novel and accurate method of determining insulin resistance, was found to be 0.28. [8]

Course

Mild hepato-renal contrast echoes that were bright, uneven in surface, dull along the borders of the liver, and splenomegaly were visible on an abdominal USG. The left lobe of the liver and the spleen were enlarged on contrast-enhanced computed tomography (CECT), which is a sign of liver cirrhosis. Additionally, active contrast material extravasation was observed, which is a sign that the gastroesophageal varices are actively bleeding. The gastroesophageal endoscopy revealed varices. Endoscopic variceal ligation and injectable sclerotherapy were used to treat the varices. Histological examination of the liver biopsy material produced the following findings: mild steatosis, a modest chronic inflammatory cell infiltrate, severe fibrosis in expanded portal areas, bridging fibrosis, and patchy or isolated necrosis. Mallory-Denk bodies (MDBs) and the nucleus's vacuolation were also seen. MDBs were identified by immunostaining as cytoplasmic inclusions with atypical shapes that are frequently seen close to the nucleus. These findings allowed for the identification of the patient's NASH-induced liver cirrhosis and portal hypertension. Additionally, he received a Type 2 DM diagnosis for the first time. When hyperglycaemia was discovered upon admission, insulin therapy was initiated. Glycemic control was attained following the start of the insulin treatment. Dapagliflozin, a SGLT2 inhibitor, was then given to the patient.

3. Discussion

The hepatic symptom of metabolic syndrome, NAFLD is characterised by liver fat accumulation. Metabolic syndrome is characterised by obesity, insulin resistance, type 2 diabetes, hypertension, and dyslipidemia. Non alcoholic steatohepatitis and non alcoholic fatty liver are the two kinds of NAFLD that progress from liver fibrosis to cirrhosis, liver failure, and hepatocellular carcinoma (HCC) [1]. The pathogenesis of NASH is known to be influenced by metabolic syndrome, insulin resistance, oxidative stress, mitochondrial stress, adipocytokines, and endotoxins [4]. Hepatocytes produce more reactive oxygen species and lipid per-oxidation as a result of enhanced peroxisomal oxidation brought on by insulin resistance. TNF-alpha and other pro-inflammatory and fibrinogenic cytokines are produced as a result of this process' activation of the Kupffer cells and stellate cells of the liver [9].

NASH is typically diagnosed after ruling out other chronic liver disease causes. The gold standard for determining a NASH diagnosis is still a liver biopsy. Our case had extensive fibrosis, portal inflammation, and MDBs as its pathological findings. The score for NAFLD activity was 5. (steatosis 1, lobular inflammation 2 and ballooning 2). MDBs were the subject of an immunohistochemical analysis employing an anti-p62/SQSTM1 antibody. Despite the presence of an antinuclear antibody, little IgG was identified in the serum. This led to the diagnosis of liver cirrhosis brought on by NASH. However, the liver biopsy sample only had little steatosis. We noticed that the mild steatosis correlated with "burned-out NASH" on histological examination, which is the advanced stage of NASH.

According to a recent study, a high BMI (28) strongly impacted the development of septal fibrosis in the liver [10]. Class I obesity is defined by the World

Health Organization (WHO) as having a BMI of 25 to 29.9, class II obesity is defined as having a BMI of 35.0 to 39.9, and class III obesity is defined as having a BMI of >40.0. Asian adults exhibited a higher risk of Type 2 DM and cardiovascular disease even at a BMI below the recognised WHO cut-off for being overweight (BMI 25.0) [11]. The WHO classifies this patient's long-term overt obesity as class II-III, and it has existed for at least two years. At the time of admission, our patient had high values for the HOMA-IR, QUICKI, and serum IRI, as well as significant levels of C-peptide excretion in the urine. These results point to severe insulin resistance-related hyperinsulinemia. The discovery that hyperinsulinemia stimulates the expression of tissue growth factor [12] indicates that the extreme obesity and insulin resistance that our patient had contributed to the development of liver fibrosis. The patient was started on SGLT2 inhibitor therapy for T2DM, which enhances glycemic control by encouraging urine glucose excretion independent of insulin secretion and action.

The annual incidence of liver cirrhosis in NASH cases varies between 0.7 and 3.6%, per reports [13]. Hyaluronic acid levels, Mac-2 binding proteins, and type-IV collagen levels are accurate indicators of liver fibrosis in NASH. Additionally, this patient had elevated levels of liver fibrosis markers. The evolution of liver fibrosis in NASH cases should be carefully monitored, especially when aminotransferase levels and/or platelet counts were within normal ranges. Gastric varices bleeding can commonly and fatally accompany end-stage liver disease. NASH, which initially manifests as gastric variceal haemorrhage, can be fatal, particularly when there is underlying long-term obesity and inadequate glycemic management, as in our case.

4. Conclusion

As a result, we should carefully watch out for the possibility of NASH with liver fibrosis in those with chronic severe obesity and thoroughly monitor all of its effects. Subsequent timely follow up for markers of fibrosis, ultrasonogram, and/or upper GI endoscopy should also be done in these circumstances. It is crucial to closely monitor the onset of liver fibrosis and portal hypertension in people with excessive obesity and NAFLD, especially when platelet counts and aminotransferase levels are within the normal range. Additionally, it has been demonstrated that NAFLD affects the likelihood of acquiring T2DM and complications connected to the metabolic syndrome, such as cardiovascular diseases.

References

1. Angulo P. Nonalcoholic fatty liver disease. N Engl J Med. 2002 Apr;346((16)):1221–31.
2. Matteoni CA, Younossi ZM, Gramlich T, Boparai N, Liu YC, McCullough AJ. Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. Gastroenterology. 1999 Jun;116((6)):1413–9.
3. Tilg H, Moschen AR. Evolution of inflammation in nonalcoholic fatty liver disease: the multiple parallel hits hypothesis. Hepatology. 2010 Nov;52((5)):1836–46.
4. Dixon JB, Bhathal PS, O'Brien PE. Nonalcoholic fatty liver disease: predictors of nonalcoholic steatohepatitis and liver fibrosis in the severely obese. Gastroenterology. 2001 Jul;121((1)):91–100.
5. Doycheva I, Watt KD, Alkhouri N. Nonalcoholic fatty liver disease in adolescents and young adults: the next frontier in the epidemic. Hepatology. 2017 Jun;65((6)):2100–9.
6. Wai CT, Greenson JK, Fontana RJ, Kalbfleisch JD, Marrero JA, Conjeevaram HS, et al. A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. Hepatology. 2003 Aug;38((2)):518–26.
7. Sterling RK, Lissen E, Clumeck N, Sola R, Correa MC, Montaner J, et al. APRICOT Clinical Investigators Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. Hepatology. 2006 Jun;43((6)):1317–25.
8. Katz A, Nambi SS, Mather K, Baron AD, Follmann DA, Sullivan G, et al. Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. J Clin Endocrinol Metab. 2000 Jul;85((7)):2402–10.
9. Leclercq IA, Da Silva Morais A, Schroyen B, Van Hul N, Geerts A. Insulin resistance in hepatocytes and sinusoidal liver cells: mechanisms and consequences. J Hepatol. 2007 Jul;47((1)):142–56.
10. Ratziu V, Giral P, Charlotte F, Bruckert E, Thibault V, Theodorou I, et al. Liver fibrosis in overweight patients. Gastroenterology. 2000 Jun;118((6)):1117–23.
11. Expert Consultation WH, WHO Expert Consultation Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004 Jan;363((9403)):157–63.
12. Paradis V, Perlemuter G, Bonvoust F, Dargere D, Parfait B, Vidaud M, et al. High glucose and hyperinsulinemia stimulate connective tissue growth factor expression: a potential mechanism involved in progression to fibrosis in nonalcoholic steatohepatitis. Hepatology. 2001 Oct;34((4 Pt 1)):738–44.
13. Hashimoto E, Tokushige K. Prevalence, gender, ethnic variations, and prognosis of NASH. J Gastroenterol. 2011 Jan;46((S1 Suppl 1)):63–9.