Responses to Reviewers

The MS by Tanaka and colleagues describes one adult NAFLD Underlying Myotonic Dystrophy (MD). The MS is well written apart from minor typos needing corrections. This Reviewer has several comments regarding the number of limitations of the report.

Major comments

The Authors should acknowledge that: 1) liver involvement is frequent in MD Achiron A, Barak Y, Magal N, Shohat M, Cohen M, Barar R, Gadoth N (1998) Abnormal liver tests results in myotonic dystrophy. J Clin Gastroenterol 26:292–295 Heatwole C, Miller J, Martens B, Moxley R (2006) Laboratory abnormalities in ambulatory patients with myotonic dystrophy type 1. Arch Neurol 63:1149–1153 Kalafateli M, Triantos C, Tsamandas A, Kounadis G, Labropoulou-Karatza C (2012) Abnormal liver function tests in a patient with myotonic dystrophy type 1. Ann Hepatol 11:130–133 Spaziani M Hormonal and metabolic gender differences in a cohort of myotonic dystrophy type 1 subjects: a retrospective, case-control study J Endocrinol Invest. 2020 May;43(5):663-675

Response

We added the following statements to the Discussion section and cited these references: Indeed, it was reported that liver test abnormalities in MD patients were frequent in MD patients [7-10].

2) NAFLD may be one of the liver histotypes of MD (Finsterer J Myotonic dystrophy 2 manifesting with non-alcoholic and non-hepatitic liver cirrhosis. Acta Clin Belg. 2015 Dec;70(6):432-5 should be mentioned as well).

Response

We added the case of liver cirrhosis in MD type 2 to the Discussion section and cited this reference (#15).

3) Spaziani et al (2020) quote that the pathophysiological mechanism is still unknown and LFTs levels are not associated with clinically significant liver damage. However, regarding NAFLD one should mention that some neurological diseases (e.g. myotonic dystrophy, Parkinson disease, Chagasic enteropathy)

can be complicated by SIBO that is responsible not only for malabsorption/weight loss (Bures et al Small intestinal bacterial overgrowth syndrome World J Gastroenterol. 2010) but also for NAFLD.

Response

SIBO is sometimes detected in MD patients (Reference #19). We described the possible contribution of SIBO to NAFLD pathogenesis in MD in the Discussion section with adding references (#17, 19).

4) In spite of their multiple self-citations #1 to 4, the Authors fail to mention if their patient had tests for at least for GGT, celiac disease, Wilson disease before liver biopsy

Response

We mentioned that immunoglobulins, ferritin, copper, and ceruloplasmin were normal.

5) It is quite unusual nowadays to order a liver biopsy in a patient with abnormal LFTs without excluding first the extrahepatic causes of hypertransaminasemia at all ages (Giannini Liver enzymealteration: a guide for clinicians. CMAJ. 2005; Vajro P, Persistent hypertransaminasemia in asymptomatic children: a stepwise approach. World J Gastroenterol. 2013; Paolella G Fatty liver disease and hypertransaminasemia hiding the association of clinically silent Duchenne muscular dystrophy and hereditary fructose intolerance. Ital J Pediatr. 2012; Veropalumbo C. Aminotransferases and muscular diseases: a disregarded lesson. Case reports and review of the literature. J Paediatr Child Health.)

Response

We would like to emphasize the necessity of CK measurement in patients with abnormal liver function test even in the lack of muscular symptoms. We added these references (#21-24) and revised the Conclusions section to emphasize consideration of myopathy in patients with liver test abnormalities.

6) A mention on the potential value of total serum bile acids for the diagnosis of liver disease vs. muscular disease might be worthy.

Response

Serum/biliary bile acid abnormalities were reported in MD patients. We added the following statements in the Discussion section: Additionally, specific bile acids, such as dihydroxymono-oxocholanic acid and dihydroxycholanic acid, with a steroid-nucleus structure similar to chenodeoxycholic acid, were detected in serum of the MD type 1 patients and biliary ursodeoxycholic acid was reduced [20], indicating bile acid abnormality accompanied by MD. Although the pathogenesis of NAFLD/NASH is multifactorial, these factors might be associated with NAFLD/NASH in MD.

7) Conclusions should be toned down according to the limitations of the study.

Response

We tempered the Conclusions.

Comments from Editor

1. The manuscript is well written apart from minor typos needing corrections. The reviewer suggests the authors to cite some literatures. A mention on the potential value of total serum bile acids for the diagnosis of liver disease vs. muscular disease might be worthy. Conclusions should be toned down according to the limitations of the study. The questions raised by the reviewers should be answered.

Response

We revised them according to the reviewer's comments.

5 Issues raised: (1) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Response

We submitted original PPT.

(2) I found the authors did not add the PMID and DOI in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references.

Response

We added PMID, DOI and the names of all authors to all references.