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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36581
Title: Clinically diagnosed late-onset fulminant Wilson disease without cirrhosis: A case report
Reviewer's code: 00007470
Reviewer's country: Italy
Science editor: Ya-Juan Ma
Date sent for review: 2017-10-16
Date reviewed: 2017-10-22
Review time: 5 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This case report is very interesting because describes a patient with wilsonian hepatic failure in absence of histological evidence of cirrhosis. Unfortunately, there some diagnostic points that are not clear and need to be clarified. The absence of mutations at molecular analysis, the lack of information about copper liver concentration and ultrastructural liver aspects (typical mitochondrial lesions). The absence of this information weakens diagnosis of Wilson disease. On the other hand, the low serum levels of ceruloplasmin and the high levels of cupriuria may be observed in fulminant liver failure of othe causes. Discussion should address this critical points.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36581
Title: Clinically diagnosed late-onset fulminant Wilson disease without cirrhosis: A case report
Reviewer's code: 03699990
Reviewer's country: China
Science editor: Ya-Juan Ma
Date sent for review: 2017-10-24
Date reviewed: 2017-11-01
Review time: 8 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[Y] High priority for publication
[ ] Grade C: Good	[Y] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

There are some Incorrect spelling of words such as "ithas" which should be" it has" and so on. Please check. Some expressions require professional polish. In the first sentence of ITRODUCTION "Wilson Disease (WD) was initially described by Kinnear Wilson in 1912 and…". The year is 1911 in some literature. Please check the literature.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36581
Title: Clinically diagnosed late-onset fulminant Wilson disease without cirrhosis: A case report
Reviewer's code: 00159633
Reviewer's country: Turkey
Science editor: Ya-Juan Ma
Date sent for review: 2017-10-24
Date reviewed: 2017-11-03
Review time: 10 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[Y] Accept
[Y] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[Y] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In some parts English language is very poor and requires a thoroughly edition. Moreover, it is very long and written beyond a case report and seems a novel. Hence, it also should be shortened.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36581
Title: Clinically diagnosed late-onset fulminant Wilson disease without cirrhosis: A case report
Reviewer's code: 00003629
Reviewer's country: Greece
Science editor: Ya-Juan Ma
Date sent for review: 2017-10-24
Date reviewed: 2017-11-04
Review time: 11 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[Y] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The article by T. Amano et al is an interesting case of a patient who, as the authors state, died of fulminant Wilson disease (WD) at age 64, without a previous diagnosis of WD, or a past history of elevated liver enzymes, bouts of jaundice or other signs of chronic liver disease throughout her life. She was admitted with anemia and a 2-day history of jaundice and a family history of an older sister, allegently dead of acute liver disease of undetermined etiology. At admission the patient had marked elevation of total serum bilirubin (TSB 34mg/dL) of obstructive type (direct bilirubin 26mg/dL), moderate elevation of AST, normal ALT, ALP (ALP/TSB ratio 0.77), and biochemical evidence of liver failure. Viral and immunological parameters tested, were all negative. Coombs-negative hemolytic anemia and hemophagocytosis were detected and did not respond to pulse methylprednisolone treatment. Serum and urinary copper were

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markedly elevated, ceruloplasmin borderline low, and Keyser-Fleisher rings absent. The patient died of liver failure and liver was obtained and examined at autopsy. This case presents all the diagnostic problems associated with the confirmation of WD in a patient dying of acute liver failure. Although several parameters indicate that WD was probably present, none of them can be pathognomonic in this setting. The late age of the patent (64 years) and the absence of fibrosis in the liver explant make the diagnosis of WD more improbable and the need of verification more important before this case be published. My comments follow: A. General Comments: 1. The article has major English language problems. In this respect, it needs thorough re-writing. 2. Since the whole liver is available, as stated, authors should consider hepatic copper concentration measurement in an appreciable part of the organ. In the absence of chronic cholestasis, as in this case, finding copper concentration ≥250mg/g of dry liver weight will increase the probability that the reported case had indeed WD (Am J Clin Pathol 1994;102:443, Clin Gastroenterol Hepatol 2005;3:811). B. Major Comments: 1. (Page 1, line 5 from top): What the authors mean by "was declined"? Do they mean that ceruloplasmin was low when first detected or that it was higher at the beginning and became lower latter? 2. (Page 5, line 2 from top): Please give reference. 3. (Table 1): Please give the MCV, MCH, MCHC and the RDW values of the admission RBC's. 4. (Table 1): Please mention the upper normal limits of AST, ALT, ALP and GGT measurements in your laboratory. 5. (Figure 4): Please mention whether the AZAN staining was used to demonstrate absence of fibrous tissue in the preparation. C. Minor Comments: 1. (Page 3, line 2 from top): "Hepatopathy" is a very vague expression. Please be more precise. 2. (Page 3, line 3 & 4 from top): Consider: "she developed hepatic encephalopathy and the diagnosis of fulminant liver failure was made". 3. (Page 5, line 2 from top): Kinnier Wilson. 4. (Page 6, line 5 from bottom): Hemofiltration.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36581
Title: Clinically diagnosed late-onset fulminant Wilson disease without cirrhosis: A case report
Reviewer's code: 02996674
Reviewer's country: Japan
Science editor: Ya-Juan Ma
Date sent for review: 2017-10-24
Date reviewed: 2017-11-05
Review time: 12 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This case report titled 'Clinically diagnosed late-onset fulminant Wilson disease without cirrhosis' is full of useful information. However, there are some issues which should be clarified more clearly. There are three questions. 1. In fulminant Wilson disease, serum copper level may increase. In this case, the authors mentioned that 'serum copper level was greatly elevated up to 105μg/dl'. However, the normal serum copper level is 70～132μg/dl. Therefore, serum copper did not increase in this patient. 2. In this case, rhodanine staining was unclear to examine copper deposition in the scattered residual hepatocytes. Alternatively copper content in the tissue can be relatively easily examined. Did not the authors examine copper content in her liver tissue? 3. Genetic test at ATP7B is mandatory to diagnose WD. DNA sample from the patient could be taken by autopsy. Why did not the authors extract her DNA from autopsy sample? The authors examined

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DNA of her son and DNA analysis was negative for mutation of ATP7B gene. But this information is quite incomplete.