

1    **13 Nov 2021**

2    Ref: 70605

3    Title: Diagnostic and Surgical Challenges of Progressive Neck and Upper Back Painless Masses in Madelung's Disease: A Case Report

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5    **Journal: World Journal of Clinical Cases**

6    Dear Professor,

7    On behalf of my coauthors, we thank you very much for giving us the opportunity to revise our manuscript. We appreciate the editor and  
8    reviewers very much for their positive and constructive comments and suggestions regarding our manuscript entitled "Diagnostic and Surgical  
9    Challenges of Progressive Neck and Upper Back Painless Masses in Madelung's Disease: A Case Report " ( Manuscript ID: 70605 ).

10    We have carefully addressed the comments from the editorial board and the reviewers. Changes made to the manuscript are highlighted in the  
11    text.

12    Listed below are the revisions we have made according to the editor's and reviewers' comments.

13    We would like to express our great appreciation to you and the reviewers for the comments on our paper. We look forward to hearing from you.

14    Thank you and best regards.

15 Yours sincerely,

16 Ya-Jie Yan

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21 **Responses to comments:**

22 **Reviewer #1:**

23

24 **Question 1:**

25 **1) As we see there is an increasing number of publications about Madelung's disease. Due to its multidisciplinary course, it is valuable to**  
26 **emphasize the aim of the article: dedication for differential diagnosis or treatment. This article explains a developed operation plan to**  
27 **remove the masses. I offer to reflect this in the title. For example, Progressive Neck and Upper Back Painless Mass: Diagnostic and**  
28 **Surgical challenges of Madelung's disease. A case report. Adjustment of keywords (for example, lipectomy) is also recommended.**

29 **Response:** Thank you for highlighting this issue and for your advice. We agree and have revised the title and keywords accordingly (lines 1–3 ,  
30 69-71 in the revised manuscript).

31

32 **Question 2:**

33 **2) It would be great to explain (shortly) the choice of contrast-enhanced computed tomography scan for diagnosis because it is popular**  
34 **among surgeons to prefer MRI firstly, especially when oncology is suspected. Is it enough for planning a surgeon tactic?**

35 **Response:** Thank you for the suggestion. We agree that MRI is more commonly recommended to diagnose masses preoperatively, particularly  
36 when a tumor is suspected. For this patient, we also preferred MRI examination. However, an MRI appointment requires nearly a week, while  
37 contrast-enhanced computed tomography is available in 1–2 days at our hospital. Most importantly, based on the patient's medical history,  
38 clinical symptoms, physical examination and other auxiliary examinations, we deemed that the patient was more likely to have MD. Considering  
39 that both contrast-enhanced computed tomography scans and MRI can show adipose tissue well, we explained the situation to the patient and  
40 obtained his consent. Thus, we finally chose contrast-enhanced computed tomography. We have provided a brief explanation in the revised  
41 version of the manuscript (lines 238-242 in the revised manuscript).

42

43 **Question 3:**

44 **3) The pathogenesis of the disease is a bit confused: in 207-210 lines there is explained that pathogenesis is related to long-term heavy**  
45 **drinking, then there is explained/repeated the same in lines 212-213, I would like to prefer to fix and merge to one base sentence. Also,**  
46 **comorbidities are not part of pathogenesis (line number 211). The place of this sentence has to be changed.**

47 **Response:** Thank you for the suggestion. We agree and have revised the sentence accordingly (lines 213–219 in the revised manuscript).

48

49 **Question 4:**

50 **4) This journal has published 3 reports of Madelung’s disease, please check again (line number 310).**

51 **Response:** Thank you for the reminder. We have checked and corrected the statement in the manuscript (lines 308-315 in the revised  
52 manuscript).

53

54 **Question 5:**

55 **5) Laboratory findings and other tests have to be prepared/submitted in a table form (Word file type) (Figures S1, S2, S3). What is the**  
56 **aim of the heart ultrasound (S4)? Is it for the differential diagnosis to show comorbidity?**

57 **Response:** Thank you for your comments. Laboratory findings and other tests were prepared and submitted in table form (Table 1). This patient  
58 had years of smoking and hypertension and took antihypertensive drugs irregularly. Thus, preoperative cardiopulmonary function assessment

59 was necessary. Heart color Doppler ultrasound examination and pulmonary function tests are routine tests at our hospital before general  
60 anesthesia operations to assess the cardiopulmonary function of patients and determine surgical safety.

61

**Table 1. Main laboratory findings and other tests of the patient**

Main laboratory findings	Value	Normal range
Glucose (mmol/L)	4.61	3.9–6.1
Glycated albumin (%)	14.8	11–16
Alanine aminotransferase (U/L)	12	≤41
Aspartate aminotransferase (U/L)	22	≤40
Alkaline phosphatase (U/L)	78	45–15
γ-glutamyl transferase (U/L)	46	10–60
Creatinine (μmol/L)	90	57–111
Urea (mmol/L)	3.33	3.6–9.5
Uric acid (mmol/L)	445	208–428
Total cholesterol (mmol/L)	4.62	2.6–5.2
Triglyceride (mmol/L)	2.38	0.34–1.70
<i>Treponema pallidum</i> antibody (S/CO)	0.08	<1
Anti-HCV (S/CO)	0.08	<1
Anti-HIV (S/CO)	0.14	<1
HBsAg (IU/mL)	0.00	<0.05
Anti-HBs (mIU/mL)	0.52	<10
HBeAg (S/CO)	0.322	<1
Anti-HBe (S/CO)	1.69	>1
Anti-HBc (S/CO)	0.46	<1

**Pulmonary function test results**

Moderate obstructive pulmonary ventilation dysfunction

The maximum voluntary minute ventilation was slightly decreased

**Heart color Doppler ultrasound examination**

Aortic stiffness  
Enlarged left atrium  
Mitral regurgitation (mild) and tricuspid regurgitation (mild)

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64 **Question 6:**

65 **6) The legends of figures are recommended. The 3rd figure has to be remade: all figures in a one-line and the explanations have to be**  
66 **moved to the legend. The same recommendation for the other two figures. It would be great to mark masses in contrast-enhanced**  
67 **computed tomographic images of the patient's neck and chest (by arrows).**

68 **Response:** Thank you for the suggestion. We agree and have revised the figures accordingly.

69

70 **Question 7:**

71 **7) There are some minor grammatical and spelling errors, please rectify them.**

72 **Response:** Thank you for the suggestion. We have revised the errors accordingly.

73

74 **Reviewer #2:**

75 **The article: "Progressive Neck and Upper Back Painless Mass: A case report of Madelung's disease" is interesting and well written. I**  
76 **congratulate the authors for this report. I suggest only one correction: 1) To add the number of the proevious cases of Madelung**  
77 **published at literature, with some references.**

78 **Response:** Thank you for the suggestion. We will add the cases of Madelung's disease case reports published in the literature in the last five  
79 years ( lines 323–342 in the revised manuscript).

**Table 2. Baseline characteristics of 13 patients with MD treated with different interventions**

Patient	Age, y	Sex	DD	Tumor site	Comorbidities	Treatment	Follow up
1 <sup>[29]</sup>	61	Male	4 y	Mandible, elbows and abdominal area	HD, S, H, D	Alcohol abstinence, Medications to control blood pressure and blood sugar	The patient was in stable condition at follow-up 3 months later.
2 <sup>[8]</sup>	69	Male	15 y	Neck and shoulders	HD, IFH	Surgery on the right groin and Alcohol abstinence	After a 1-year follow-up, no recurrence of the right inguinal femoral hernia was found and no fat accumulation was found in the neck or other areas.
3 <sup>[31]</sup>	87	Male	ND	Tongue	HD, RA	An incisional biopsy, alcohol abstinence observation	On follow-up 6 months, the tongue findings were unchanged and no new growths were observed.
4 <sup>[32]</sup>	45	Male	5 mo	Neck	HD	Alcohol abstinence	After four months, the patient claimed to experience increased cervical mobility. The size of the cervical mass was also reduced with the extended neck

							circumference reduced by 3.8 cm.
5 <sup>[33]</sup>	64	Male	20 y	Posterior pharyngeal wall, neck, torso and upper extremities	HD, H, CRLD	Surgical removal of a mass on the posterior pharyngeal wall, alcohol abstinence	During follow-up examination in one week, two weeks, and six months, further improvement of his swallowing, stertor, and voice were noted.
6 <sup>[34]</sup>	58	Male	ND	Supraclavicular fossa and upper back	HD, AFL	Alcohol abstinence	ND
7 <sup>[35]</sup>	56	Female	ND	Neck, parotid glands, supraclavicular region and larynx	B, HC, HT, Impaired glucose tolerance	ND	ND
8 <sup>[36]</sup>	59	Male	20 y	Face and neck	HD, S	Deoxycholic Acid treatment and alcohol abstinence	Although significant growth of his lipomas was noted, he also showed markedly improved compression symptoms/pain and an increased range of motion of his neck.
9 <sup>[37]</sup>	45	Male	2 y	Anterior cervical region, pre-	HD, D, ACP	Two-step surgical treatment and alcohol abstinence	After 1 year of follow-up, the final esthetic result was satisfactory.

				and postauricular regions bilaterally, and back			
10 <sup>[38]</sup>	38	Male	10 y	Shoulders, arms and upper trunk	A	Avoid alcohol intake	No further progression of the lesions was observed during the 6 months follow-up period.
11 <sup>[39]</sup>	45	Male	2 y	Bilateral breast, upper back, deltoid areas, hips, and thighs	HD	Abstinence, liver protection, and anti-fibrosis agents	This patient was followed up every 6-month and did not undergo surgical treatment. The condition is stable as of this writing.
12 <sup>[40]</sup>	65	Female	ND	Macroglossia	ND	Bilateral partial glossectomy in two times	Improved initial symptoms one year after surgery.
13 <sup>[41]</sup>	72	Male	ND	The breasts, abdomen, and roots of thighs	S, H.	Hypotensive therapy and healthier lifestyle, and diet methods to improve the metabolic syndrome  Plastic surgery for liposuction of inguinal lipoma	ND.

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A, alcoholism, ACP, asymptomatic chronic pancreatitis; HD, heavy drinking; AFL, alcoholic fatty liver; B, bronchiectasis; CRLD, chronic restrictive

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lung disease; D, diabetes mellitus; DD, duration of disease; H, hypertension; HC, hypercalcemia; HT, high triglycerides; IFH, incarcerated femoral hernia; ND, not detected; R, recurrence; RA, rheumatoid arthritis; S, smoking.

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