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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 77075

Title: Acute Mesenteric Ischemia Secondary to Oral Contraceptive-induced Portomesenteric and Splenic Vein Thrombosis: a Case Report

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02446526
Position: Associate Editor
Academic degree: FRCP, MBBS, MD, MRCP
Professional title: Academic Editor, Consultant Physician-Scientist, Professor
Reviewer's Country/Territory: United Kingdom
Author's Country/Territory: China

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-05-02 15:04

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Review time: 5 Days and 2 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript was read with interest. There are few pitfalls in the case presentation, some of which are pointed out below: Language and style: - There are several syntax errors throughout the paper that necessitates appropriate corrections with the help of a scientific writer. Introduction: - the statement "Although thrombosis of splanchnic venous system is uncommon, improved CECT has led to an increased incidence of this disease" is wrong. In fact, the disease is increasingly reported from better investigation facilities now. Case presentation: - The reference ranges for normal lab values are not provided (WBC count, CRP, PCT. D-dimer etc.) - international normalized ration (INR) should be international normalized ratio (INR) - It is unusual to have normal lactate level in this patient with acute mesenteric ischemia - Treatment is not clear - What is Cefminox and which LMWH was used (should have mentioned the dose in Units/Kg also). Discussion: - Why there is discrepancy between the reported prevalence of MVT in the introduction and discussion with same reference cited?!.

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Reviewer's code: 05427629
Position: Peer Reviewer
Academic degree: MD

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Reviewer's Country/Territory: Spain

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Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS

In this paper, Zhao and colleagues report an interesting case of acute mesenteric ischemia secondary to portomesenteric and splenic vein thrombosis. Furthermore, they provide a short review of this topic based on their experience. The manuscript is well written. The authors are to be congratulated on the successful outcome in their patient. Nevertheless, I have the following comments: INTRODUCTION: - The authors state: "Although thrombosis of splanchnic venous system is uncommon, improved CECT has led to an increased incidence of this disease". What has really increased? The incidence or the detection of splanchnic vein thrombosis? The real incidence may not have changed, although more patients could being diagnosed nowadays due to the increased accessibility of CT scans and improved sensitivity of diagnostic imaging techniques. Could the authors provide any information, reference or commentary on this point?

CASE PRESENTATION: - Chief complaints: the authors explain that the patient had been hospitalized elsewhere before arriving to their hospital. How long was she hospitalized? How long it took from discharge to readmission? Had the patient ever received thromboprophylaxis during the previous admission? In affirmative case, which thromboprophylaxis? (eg, drug, dose…) Was any diagnostic abdominal imaging test (e.g. ultrasound, CT scan…) performed during the previous hospitalization? What about the determination of D-dimer or any other diagnostic test that could suggest the diagnosis of splanchnic vein thrombosis during the previous hospitalization? - History of present illness: did the symptoms start 11 days ago including the previous admission, or did the symptoms persist or worsen after the previous discharge? The timeline could be clearer.

- History of past illness: who prescribed ethinidyl estradiol/drospirenone and which

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was its indication? (e.g. polycystic ovary syndrome, abnormal uterine bleeding, only contraception…). - Personal and family history: I think that in this case it is important to highlight if there is a personal or family history of venous thromboembolism, thrombophilia, cancer and/or pregnancy losses. How was her weight, height and body mass index? - Laboratory examinations: why was the determination of anticardiolipin antibodies performed in the acute phase? What subclasses of anticardiolipin antibodies were determined? (i.e. IgG or IgM). Why only anticardiolipin antibodies were determined? Why was the determination of anti-beta-2-glycoprotein I antibodies not included? Why were the prothrombin G20210A mutation and the factor V Leiden mutation +/- JAK2V617F mutation not included once you decided to test for anticardiolipin antibodies? - Imaging examinations: the authors explain that abdominal ultrasound was performed before contrast-enhanced CT (CECT). Doppler ultrasonography has a sensitivity of 89-93% and a specificity of 92-99% for the diagnosis of PVT, and has became the first line diagnostic test for PVT. Nevertheless, PVT was not diagnosed in this case by abdominal ultrasound, although thrombosis of the right branch of portal vein (PV) and main vessels of PV was subsequently diagnosed by CECT. Could the authors include any rationale about this missed PVT diagnosis by abdominal ultrasound in the discussion? - Imaging examinations: the patient underwent 4 contrast-enhanced CT scans in a period of 31 days despite her good clinical evolution. What about radiation exposure in this young woman? Are 4 contrast-enhanced CT scans justified in such a reduced time lapse? Could she be managed with fewer CT scans or by using alternative imaging tests, such as an abdominal MRI? Could the authors include any comments on this topic in the discussion section? TREATMET: - The patient received anticoagulation with low molecular weight heparin (LMWH) 5000 U, subcutaneous injection twice daily. Which LMWH was used? How was the patient's weight at that time? - Rivaroxaban 20 mg was then given

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orally for anticoagulation instead of LMWH injection. It is important to include in the discussion the rationale for this decision. DOACs are not recommended for the treatment of splanchnic vein thrombosis in current clinical guidelines (AASLD 2009, AISF 2011, ACCP 2012, Baveno VI 2015 and EASL 2016). Any reference to these guidelines and to any study that might support the use of rivaroxaban in this case is missing. There is little evidence to support this decision, which needs to be discussed. Some of the few studies that could support this decision are: •Hanafy AS, Abd-Elsalam S, Dawoud MM. Randomized controlled trial of rivaroxaban versus warfarin in the management of acute non-neoplastic portal vein thrombosis. Vascul Pharmacol. 2019;113:86–91. doi:10.1016/j.vph.2018.05.002 • Janczak DT, Mimier MK, McBane RD, et al. Rivaroxaban and apixaban for initial treatment of acute venous thromboembolism of atypical location. Mayo Clin Proc. 2018;93(1):40–47. doi:10.1016/j.mayocp.2017.10.007

- When did the patient receive the last dose of LMWH before the scheduled laparotomy? What class of LMWH and dose did she receive? When was LMWH reintroduced after scheduled surgery? (i.e. the same day of the surgery, the first day after the surgery…).

OUTCOME, FOLLOW-UP AND DISCUSSION: - The authors conclude that this is an oral-contraceptive-induced PMSVT, but further investigations for other potential aetiological factors for splanchnic vein thrombosis were not performed during the follow-up, as recommended by de 2016 EASL guidelines (European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu. EASL Clinical Practice Guidelines: Vascular diseases of the liver. J Hepatol. 2016;64(1):179-202). Thus, this young woman should be tested for thrombophilia, including Factor V Leiden, Prothrombin G20210A mutation, antiphospholipid syndrome, protein C and S deficiency, and antithrombin deficiency. In addition, the most prevalent mutations related to mieloproliferative neoplasm and splanchnic vein thrombosis (JAK2V617F +/- CALR) should be considered. Furthermore, the use of rivaroxaban should be avoided when any

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of these conditions are present (e.g. antiphospholipid syndrome). All these important considerations and many bibliographic references regarding splanchnic vein thrombosis management are lacking in the discussion. - What attitude was adopted regarding contraception at splanchnic vein thrombosis diagnosis and during follow-up? Once the diagnosis is clear and the patient starts anticoagulation, do you think that hormonal contraception should be discontinued? What about contraception planning during anticoagulation and after its discontinuation? - What criteria were used to maintain anticoagulation for 4 months? If the authors considered that it was a thrombotic event provoked by transient risk factor (i.e. hormonal contraception), the 2016 EASL guidelines recommend at least 6 months of anticoagulation. Any consideration to this point is absent from the discussion. - The authors state that "Wolters et al demonstrated that D-dimer, as an early serum marker of AMVT, could assist with decision-making and timely treatment of AMVT (12)". First of all, reference 12 is not from Wolters et al (it is from Yang et al). Second, there are some limitations in the use of D-dimer that are not assessed in the discussion. Although some studies showed that mean D-dimer values are increased in patients with SVT, D-dimer can also be elevated in other conditions, such as liver cirrhosis or hepatocellular carcinoma, which reduces its diagnostic predictive value in splanchnic vein thrombosis.

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Reviewer's code: 03252237
Position: Editorial Board
Academic degree: FRCP, MBChB, MD
Professional title: Attending Doctor, Deputy Director, Reader (Associate Professor)
Reviewer's Country/Territory: United Kingdom
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Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This case report highlights the role of OCP as a risk factor for SVT. It is not particularly novel. I am somewhat uncomfortable with the management strategy. It appears that only a prophylactic dose of LMWH was given rather than a full dose. There was also no mention of any attempts to thrombolyse or attempt interventional radiological procedures in view of intestinal ischaemia (see Benmassaoud A. A stepwise thrombolysis regimen in the management of acute portal vein thrombosis in patients with evidence of intestinal ischaemia. Aliment Pharmacol Ther. 2019 Nov;50(9):1049-1058. doi: 10.1111/apt.15479. Epub 2019 Sep 5. PMID: 31489698). These measures could have avoided surgical intervention in a young patient. I also cannot see that a full screen for other provoking factors was done e.g. JAK2, PNH. It is well known that patients can have more than one provoking factor for thrombosis. I also question the 4 month course of DOAC. Most guidelines would recommend indefinite anticoagulation if there has been evidence of intestinal ischaemia. Baveno 7 should be referenced.