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To: Editor, World Journal of Clinical Cases

Re: Manuscript ID: **67735**

“Acute bilateral lower extremity arterial thrombosis after intraocular foreign body removal under general anesthesia: A case report”

Dear Editor,

This letter is intended for the revision of the manuscript according to your request. First of all, we would like to appreciate editorial suggestions and assessors' comments. We corrected the manuscript according to the assessors' comments.

We included a cover letter responding to assessor and detailing all changes and corrections we've done.

Again, we would like to appreciate your suggestions and assessors' comments. I believe that this revised manuscript is highly likely to achieve the priority for publication in World Journal of Clinical Cases. I am looking forward to your early and favorable response.

Sincerely,

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Responses to Assessors' Comments

First of all, thank you very much for your valuable suggestions and recommendations on our study

● Reviewer #1:

The authors present an interesting case of acute arterial thrombosis which occurred shortly in the post-operative period. The following are our recommendations.

1. We recommend that the authors state if they had ruled out the presence of concomitant venous thrombosis in this patient.

A) Postoperative computed tomography (CT) angiography showed no concomitant venous thrombosis. To clarify this point, the manuscript has been revised as follows:

Details are as follows (Page 8, line 8-11):

On computed tomography (CT) angiography, filling defects in the bilateral popliteal arteries, bilateral proximal anterior tibial artery, and bilateral tibioperoneal trunk were visible, thereby confirming the Doppler findings (Figure 2). Concomitant venous thrombosis was not observed.

2. The authors should describe the current local or international guidelines for applying perioperative prophylaxis in patients undergoing prolonged ophthalmic surgery.

A) Thank you for your valuable feedback. Considered as a low-risk procedure, routine thromboprophylaxis is often overlooked, and relevant guidelines for thromboprophylaxis during ophthalmic surgery are scarce. In a previous survey-based study of anesthesiologists involved in the management of ophthalmic surgeries, 45% of respondents reported experiencing thromboembolism after ophthalmic surgery; however, only 40% stated that there were routine assessments for indications or contraindications to thromboprophylaxis in preanaesthetic clinics. In this case, the preoperative thromboembolism risk assessment was also overlooked. Moreover, while it was planned for less than 2 hours, the surgery was unexpectedly prolonged. As prevention is the best policy, this case highlights preoperative thromboembolic risk assessment, intraoperative communication between surgeon and anesthesiologist (particularly in the context of unexpected prolonged surgery), and the need for consensus guidelines for the prevention of thromboembolism during ophthalmic surgery.

Details are as follows (Page 13, line 13-Page 14, line 3):

Considered as a low-risk procedure, routine thromboprophylaxis is often overlooked, and relevant guidelines for thromboprophylaxis during ophthalmic surgery are scarce^[35,36]. In a previous survey-based study of anesthesiologists involved in the management of ophthalmic surgeries, 45% of respondents reported experiencing thromboembolism after ophthalmic surgery; however, only 40% stated that there were routine assessments for indications or contraindications to thromboprophylaxis in preanaesthetic clinics^[36]. In this case, the preoperative thromboembolism risk assessment was also overlooked. Moreover, while it was planned for less than 2 hours, the surgery was unexpectedly prolonged. As prevention is the best policy, this case highlights preoperative thromboembolic risk assessment, intraoperative communication between surgeon and anesthesiologist (particularly in the context of unexpected prolonged surgery), and the need for consensus guidelines for the prevention of thromboembolism during ophthalmic surgery.

Referenced by:

35. **Yang V**, Romeo P. Review: Ophthalmic Surgery as a cause of Pulmonary Emboli. *Journal of Cardiology & Clinical Research* 2020; **8**:1156
36. **Kumar CM**, Macachor J, Seet E. Venous thromboembolism prophylaxis during vitreoretinal surgery – a snapshot survey of international ophthalmic anaesthetists. *Br J Anaesth* 2015;**115**:320-1 [PMID: 26170356 DOI: 10.1093/bja/aev241]

3. The authors should describe if the patient had any pertinent lower extremity physical examination findings of the patient prior to the initiation of surgery.

A) Immediately after admission, the physical examination revealed no abnormal findings, except for the left eye injury. The patient did not complain of any discomfort related to both legs. To clarify this point, we added more detailed descriptions as follows:

Details are as follows (Page 6, line 4-6):

Immediately after admission, the physical examination revealed no abnormal findings, except for the left eye injury. The patient did not complain of any discomfort related to both legs.

4. The authors should detail if a therapeutic aPTT level was achieved during the time the

patient was on heparin therapy.

A) Thank you for your careful and keen feedback. Due to repeated heparin infusion and discontinuation, aPTT monitoring was not performed. Immediately after the diagnosis was confirmed, intravenous unfractionated heparin was administered with a bolus loading dose of 5000 units, followed by a maintenance dose of 800 units/h. After 2 h of heparin therapy, surgical thrombectomy was planned and heparin infusion was stopped for surgery. However, immediately upon arriving on the operating room, 4h after heparin cessation, the arterial pulse of both lower limbs returned, and the surgery was canceled and heparin therapy was reinitiated. After 10 h of heparin reinitiation, the patient had hematochezia with a total volume of approximately 500 mL. Heparin infusion was immediately stopped, and the patient was closely monitored. To clarify this point, the manuscript has been revised as follows:

Details are as follows (Page 9, line 3-16):

Immediately after the diagnosis was confirmed, intravenous unfractionated heparin (UFH) was administered for anticoagulation, with a bolus loading dose of 5000 units, followed by a maintenance dose of 800 units/h. After 2 h of heparin therapy, surgical thrombectomy was planned and heparin infusion was stopped for surgery. However, immediately upon arriving on the operating room, 4h after heparin cessation, the arterial pulse of both lower limbs returned, and the surgery was canceled and heparin therapy was reinitiated. Lipo-prostaglandin E1, a potent vasodilator and platelet aggregation inhibitor, was given as an adjuvant treatment^[10]. After 10 h of heparin reinitiation, the patient had hematochezia with a total volume of approximately 500 mL. Heparin infusion was immediately stopped, and the patient was closely monitored. The patient's vital signs remained stable (HR: 74–92 beats/min; SpO₂: 97–99%; SBP: 120–140 mmHg; DBP: 80–82 mmHg; and RR: 20–21 breaths/min). Due to repeated heparin infusion and discontinuation, aPTT monitoring was not performed.

5. Instances of Protein S deficiency and arterial thromboembolism have been reported (Cho et al. Protein C and/or S deficiency presenting as peripheral arterial insufficiency. Br J Radiol. 2005). The authors should state clearly if the presence of protein S deficiency in this patient could be a risk of developing arterial thrombosis in this patient.

A) Thank you for making this point. Following your recommendation, we added a supplementary explanation for the effect of protein deficiency on the development of arterial thromboembolism.

Details are as follows (Page 12, line 16-23):

Furthermore, Cho et al. suggested that protein S deficiency could be an independent risk factor for peripheral arterial occlusion^[27]. The authors also reported that arterial occlusive patients with protein S deficiency demonstrated characteristic angiographic findings, long segment thrombotic occlusion of a main peripheral artery without atherosclerosis. Also, in this case, protein S deficiency could be considered a possible trigger for arterial thrombosis. Therefore, further well-designed research is needed to investigate the effect of protein S deficiency on the development of arterial thrombosis.

Referenced by:

27. **Cho YP**, Kwon TW, Ahn JH, Kang GH, Han MS, Kim YH, Kwak JH, Lee SG. Protein C and/or S deficiency presenting as peripheral arterial insufficiency. *Br J Radiol* 2005;**78**:601-5 [PMID: 15961841 DOI: 10.1259/bjr/65615343]

● Reviewer #2:

Patient had rhabdomyolysis, authors have not discussed this in the manuscript.

A) Thank you for your valuable feedback. Though myoglobinuria was absent, patient's history, symptoms, and markedly elevated myoglobin and CK levels strongly suggested rhabdomyolysis. Hydration was performed for kidney protection, and serial ECG monitoring and laboratory tests were performed. No specific ECG abnormalities were found in immediately after surgery and POD 1-3. Myoglobin and CK levels were normalized at POD 3 and 11 (37.3 ng/mL and 159 U/L, respectively), the rhabdomyolysis was completely recovered without any sequelae. Our manuscript has been revised as follows:

Details are as follows (Page 9, line 24-Page 10, line 2; Table 1 and Figure 3):

Although myoglobinuria was absent, the patient's history, symptoms, and markedly elevated myoglobin and CK levels strongly suggested rhabdomyolysis. Hydration was performed for kidney protection, and serial ECG monitoring and laboratory tests were performed. No specific ECG

abnormalities were found immediately after surgery and POD 1-3. The serial laboratory results are summarized in Table 1. Myoglobin and CK levels were normalized at POD 3 and 11 (37.3 ng/mL and 159 U/L, respectively), the rhabdomyolysis was completely recovered without any sequelae.

● EDITORIAL OFFICE'S COMMENTS

1. Scientific quality: The manuscript describes a case report of the acute bilateral lower extremity arterial thrombosis after intraocular foreign body removal under general anesthesia. The topic is within the scope of the WJCC.

(1) Classification: Grade B and Grade C;

(2) Summary of the Peer-Review Report: The authors present an interesting case of acute arterial thrombosis which occurred shortly in the post-operative period. **However, the authors have not discussed rhabdomyolysis in the manuscript. The questions raised by the reviewers should be answered;**

A) Thank you for your valuable feedback. Though myoglobinuria was absent, patient's history, symptoms, and markedly elevated myoglobin and CK levels strongly suggested Rhabdomyolysis. Hydration was performed for kidney protection, and serial ECG monitoring and laboratory tests were performed. No specific ECG abnormalities were found in immediately after surgery and POD 1-3. Myoglobin and CK levels were normalized at POD 3 and 11 (37.3 ng/mL and 159 U/L, respectively), the rhabdomyolysis was completely recovered without any sequelae. Our manuscript has been revised as follows:

Details are as follows (Page 9, line 24-Page 10, line 2; Table 1 and Figure 3):

Although myoglobinuria was absent, the patient's history, symptoms, and markedly elevated myoglobin and CK levels strongly suggested rhabdomyolysis. Hydration was performed for kidney protection, and serial ECG monitoring and laboratory tests were performed. No specific ECG abnormalities were found immediately after surgery and POD 1-3. The serial laboratory results are

summarized in Table 1. Myoglobin and CK levels were normalized at POD 3 and 11 (37.3 ng/mL and 159 U/L, respectively), the rhabdomyolysis was completely recovered without any sequelae.

(3) Format: There is 1 table and 3 figures.

(4) References: A total of 33 references are cited, including 1 reference published in the last 3 years;

(5) Self-cited references: There are no self-cited references;

(6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

2. Language evaluation: Classification: Grade B and Grade B. A language editing certificate issued by Editage was provided.

3. Academic norms and rules: The authors provided the CARE Checklist–2016 and Written informed consent. No academic misconduct was found in the Bing search.

4. Supplementary comments: This is an unsolicited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJCC.

5. Issues raised:

(1) The title is too long, and it should be no more than 18 words;

A) Thank you for your valuable feedback. Following your suggestion, we have modified the title of our manuscript (16 words in total).

Details are as follows (Page 1, line 4-5):

Acute lower extremity arterial thrombosis after intraocular foreign body removal under general anesthesia: A case report

(2) The authors did not provide original pictures. 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.

A) Following your suggestion, our original figure files were posted online site.

6. Recommendation: Conditional acceptance.

(2) *Company editor-in-chief:* I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.