

Dear Editor Ma and dear reviewers,

Thank you for your letter and the reviewers' comments concerning our manuscript. Those comments are valuable and very helpful. We have read through comments carefully and have made corrections. Based on the instructions provided in your letter, we uploaded the file of the revised manuscript. Revisions in the text are shown using blue highlight for additions, and strikethrough font for deletions. The responses to the reviewer's comments are presented following.

We would love to thank you for allowing us to resubmit a revised copy of the manuscript and we highly appreciate your time and consideration.

Sincerely,

Zi-Ying Lu.

Q1: In general, if there was a complication such as a local tissue reaction (3 cm×2 cm ulcerated area with a hemorrhagic crust on the left dorsum (Figure 1A) in this case) after a venomous snake bite (Bite injury 10 days prior in this case), we considered antivenom administration initially or in the course of treatment. If it is assumed that the patient's artery occlusion is accelerated or intensified by the pro-coagulatory or hyper-coagulatory effect caused by snake venom, we cannot clearly estimate the treatment effectiveness (whether the antivenom prevented or relieved thrombotic effect in patient), but wasn't the antivenom administration an important factor to consider for the patient condition? I think this is better to be addressed in the discussion.

Response: The patient showed no signs of shock, local or systemic bleeding after snakebite, and he was sent to a local hospital to be injected with antivenom 3 hours later. But he was unable to provide further detailed information, such as blood coagulation function changes before and after antivenin injection, therefore we cannot judge the role of antivenom in the development of a series of the patient's conditions. we guess that the most likely thing is that snake venom caused the patient's hypercoagulable state, but the antivenom partially alleviated this coagulation dysfunction, so the patient's ischemia was limited to the calf. It reminds us that we need to collect more information when we encounter rare cases in future.

Q2: Unlike VICC(Venom-induced consumption coagulopathy) induced hemorrhagic patients, in this case, fibrinogen was higher than normal, and D-dimer was almost normal. It is known that snake venom may increase blood clot formation by consumptive and procoagulant coagulopathy similar to DIC, which may eventually lead to hemorrhagic complications. In relation to hyper-coagulopathy promoted by snake venom in this patient, hematological and coagulopathy profiles such as BT, PTT, aPTT, and PLT count, which are general blood coagulation test items other than fibrinogen and D-dimer, were not described. Are these tests excluded because it is normal range? Explaining this clearly is expected to help readers better understand the difference between this case patient and a patient with VICC hemorrhagic complications.

Response: The patient had normal activated partial thromboplastin time (APTT), prothrombin time (PT), thrombin time (TT), and platelet(PLT) count.

Q3: It is understood that previous hospital has diagnosed artery occlusion through CT angiography. The time frame, such as transfer of patient before CDT treatment, is not clear, but has there been no administration of antithrombotic agents (anticoagulants, antiplatelet agents) since the diagnosis of artery occlusion? It would be nice to have a description of this.

Response:

After CT angiography at another hospital, the patient did not receive any treatment related to vascular occlusion. He received anticoagulant therapy immediately after admission to our hospital. Then he received a 6-day course of catheter-directed thrombolysis (CDT) (a bolus of 300,000U urokinase (UK) was given via the catheter with the pulse spray technique in the first operation, followed by a continuous intra-arterial UK infusion at the rate of 50,000U/h through the infusion catheter.), therapeutic dose of anticoagulant therapy and percutaneous balloon dilatation (percutaneous transluminal balloon angioplasty, PTA) of the right anterior tibial and peroneal arteries.

Q4: A 6-day course CDT treatment for peripheral artery occlusion in this patient is described. As far as I know, standard techniques don't exist. However, if you describe in detail the thrombolytic agent used, the dose, and the delivery method (eg continuous infusion, bolusing, pulse spray, graded infusion, and stepwise infusion? etc.), it will be a great help and reference treatment guide for readers in the treatment of similar case patients in the future.

Response:

A bolus of 300,000U urokinase (UK) was given via the catheter with the pulse spray technique in the first operation, followed by a continuous intra-arterial UK infusion at the rate of 50,000U/h through the infusion catheter.