Author's response to reviews

Title: Can biting of the tongue kill a patient? Acquired hemophilia as cause of life threatening hemorrhage in an elderly patient: A case report

Authors:

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Author's response to reviews: see over
Authors: Theodoros Kelesidis, Sara Osman, Harry Dinerman

Boston, 4/3/2010

Dear Editor,
Thank you very much for your email dated 3/31/10 stating that you found our data to be of interest and that our manuscript may be acceptable for publication in JMCR provided that we revise it further according to your suggestions. We submit herein the manuscript, “Can biting of the tongue kill a patient? Acquired hemophilia as cause of life threatening hemorrhage in an elderly patient: A case report”, by Kelesidis et al, which has been revised according to your comments. Please note that the title of the manuscript was changed according to the suggestions of the reviewer. We would like to thank you for your comments, which prompted us to revise the manuscript extensively. Please see our specific responses to your comments in the following pages.

Please do not hesitate to email or call me if I can be of further assistance.
Sincerely,

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Editorial office:

Please include the ethnicity of the patient in the case presentation section of the manuscript

The following sentence was added in the case presentation section of the manuscript:

“A 94-year-old Caucasian man…:

Reviewer 1:

The clinical case report is well described and represents the main clinical features and the current treatment of Acquired hemophilia.

We would like to thank the reviewer for his/her comments

However, I would add two comments:

1) The bleeding of the tongue is not so surprising when one considers that the disease is mainly characterized by mucosal bleeding.

We would like to clarify that the patient did not have mucosal bleeding. As we mention in the case report “There was no nose bleeding, hematuria, bloody stool, or accompanying hemoptysis”. The patient had soft tissue bleeding (tongue bleeding). The clinical presentation of soft tissue bleeding without concurrent mucosal bleeding is rare and soft tissue bleeding has been described in acquired hemophilia. However, isolated tongue bleeding has not been previously described as a cause of massive bleeding. As we mention in the discussion:

“While bleeding from soft tissues and mucosal surfaces has been described in the setting of this coagulopathy, such profound life threatening bleeding from the tongue has not been described, to our knowledge.”

2) The occurrence of bradycardia is too stressed being more than anything else related to the speed of administration of aminocaproic acid.

As per suggestions of the reviewer we deleted sentences that stress that the bradycardia was related to the speed of administration of aminocaproic acid. Although Naranjo criteria were suggestive that this event may be associated with aminocaproic acid, this cannot be proven. The following sentences were deleted:

“Application of the Naranjo adverse drug reaction probability scale to this case determined that the heart block was possibly the result of the medication.”

“However, recovery of the bradycardia on follow up indicates that the bradycardia was related most likely to the infusion of aminocaproic acid since a conduction abnormality would be irreversible”.
Reviewer 2:

_The manuscript is interesting and well-written._

We would like to thank the reviewer for his/her comments

*A better discussion of the potential role for recombinant factor VII in this setting should be added.*

The following sentences were added in the revised manuscript (discussion part, 4th paragraph) to further elaborate the role of factor VII in treatment of acquired hemophilia:

“Recombinant activated coagulation FVII (rFVIIa) has recently been licensed for use in acquired hemophilia in the United States”

“By directly activating FX on the surface of activated platelets at the site of injury (thereby bypassing FVIII and FIX), rFVIIa can circumvent the actions of inhibitory antibodies present in acquired haemophilia patients”

However, the focus of our manuscript is not to review therapeutic options for acquired hemophilia since this has been done extensively in other manuscripts. Our case adds to the clinical experience of use of FVIII concentrates in this very rare disorder. Thus, our discussion is focused more on use of FVIII rather than factor VII in acquired hemophilia. We would welcome further comments for the Reviewer or the Editorial Office.

*I have some doubts that the complete heart block, although transient, may be causally attributed to treatment with amnocaproic acid.*

As per suggestions of the reviewer we deleted sentences that stress that the bradycardia was related to the speed of administration of aminocaproic acid. Although Naranjo criteria were suggestive that this event may be associated with aminocaproic acid, this cannot be proven. The following sentences were deleted:

“Application of the Naranjo adverse drug reaction probability scale to this case determined that the heart block was possibly the result of the medication.”

“However, recovery of the bradycardia on follow up indicates that the bradycardia was related most likely to the infusion of aminocaproic acid since a conduction abnormality would be irreversible.”