

Decision Letter (JCQ-2026-0029)

From:

To:

CC:

BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2026-0029

Body: 23-Sep-2026

Dear Mr. Uy:

Manuscript ID JCQ-2026-0029 entitled "Focal Neurologic Deficits after Yttrium-90 Transarterial Radioembolization for Hepatocellular Carcinoma" which you submitted to the Journal of Clinical Question, has been reviewed. The comments of the reviewer(s) are included at the bottom of this letter.

The reviewer(s) have recommended publication, but also suggest some revisions to your manuscript. Therefore, I invite you to respond to the reviewer(s)' comments and revise your manuscript.

To submit your revised manuscript, follow the below steps.

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 2. Click "Author" at the top left of the screen at "Home" page.
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You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript using a word processing program and save it on your computer. Please also highlight the changes to your manuscript within the document by using the track changes mode in MS Word or by using bold or colored text.

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When submitting your revised manuscript, you will be able to respond to the comments made by the reviewer(s) in the space provided. You can use this space to document any changes you make to the original manuscript. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s).

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Because we are trying to facilitate timely publication of manuscripts submitted to the Journal of Clinical Question, your revised manuscript should be uploaded as soon as possible. If it is not possible for you to submit your revision in a reasonable amount of time, we may have to consider your paper as a new submission.

Once again, thank you for submitting your manuscript to the Journal of Clinical Question and I look forward to receiving your revision.

Sincerely,
Richard S. Isaacs
Editor in Chief
Journal of Clinical Question

[Editor's Comments]
Associate Editor
Comments to the Author:
(There are no comments.)

[Reviewer(s)' Comments]
Reviewer: 1

Comments to the Author

This is an interesting and clinically important case describing acute right lower-extremity weakness following Y-90 transarterial radioembolization (TARE), with imaging evidence suggestive of thoracic spinal cord ischemia. The temporal association with embolization of the right intercostal and inferior phrenic arteries makes the case relevant to interventional radiologists because spinal cord ischemia is a rare but potentially devastating complication of embolization of extrahepatic tumor-supplying vessels. However, several aspects of the manuscript require clarification before publication.

Causality needs to be established more carefully. The manuscript attributes the spinal cord infarction predominantly to embolization of the intercostal arteries, particularly the artery of Adamkiewicz (AKA). However, the procedural angiographic findings demonstrating the spinal arterial supply are not described. It would be important to clarify whether spinal angiography was performed before embolization and whether an identifiable radiculomedullary artery or AKA arose from the embolized intercostal arteries. Without such documentation, the causal relationship remains presumptive.

The embolic material and technique require greater detail. The manuscript states that particle and liquid embolic agents were used but does not clearly specify the embolic agent, particle size, liquid embolic concentration, injection technique, and level of distal embolization. These details are critical because the mechanism of spinal cord ischemia may differ substantially between proximal vessel occlusion and distal penetration of embolic material.

The role of the inferior phrenic artery should be discussed. The authors appropriately emphasize the intercostal arteries, but the possibility of spinal or diaphragmatic arterial anastomoses from the inferior phrenic artery should also be addressed. A detailed review of the pre- and post-embolization angiograms could help identify potentially relevant collateral pathways.

MRI findings require more precise characterization. The manuscript describes T2/STIR hyperintensity at T9-T10 and T11-T12 as early ischemic changes. It would be useful to provide diffusion-weighted imaging/ADC findings, if available, and clarify whether the distribution was consistent with an anterior spinal artery, posterior spinal artery, or central cord vascular territory.

The neurological examination should be correlated with the imaging. The unilateral predominant motor and sensory deficits, hyperreflexia, clonus, and bilateral Babinski responses suggest an upper motor neuron process. The authors should explain how this clinical pattern corresponds to the level and vascular territory of the presumed infarction.

The discussion of TARE safety could be better focused. The extensive description of general TARE complications is somewhat lengthy relative to the central message. The discussion would be stronger if it emphasized the specific mechanism of spinal ischemia following embolization of extrahepatic collaterals and highlighted preventive strategies, including careful angiographic assessment for spinal arterial supply before embolization.

Any comparative evaluation between glass and resin microspheres for TARE should be looked upon Overall, this is a potentially valuable case, but the manuscript would benefit from stronger angiographic evidence establishing the relationship between the embolized intercostal arteries and spinal cord vascular supply, as well as greater technical detail regarding the embolization procedure.

Reviewer: 2

Comments to the Author

This is a case report in which the authors present a patient who developed neurological complication which was assumed to have occurred because of Y-90 microsphere therapy. Since this is not a known complication of Y-90 microsphere therapy, the authors present that as a rare complication to be cautious about.

It is apparent that the complication they reported does not necessarily seem to be occurred as a result of Y-90 microsphere administration, but rather because of using large sized embolic liquid and gel materials which have had nothing to do with Y-90 microspheres themselves and used as an adjunct to avoid possible extrahepatic shunting of Y-90 microspheres, though those issues are not clearly stated and needs much more clarification by the authors. There are also some not-easy-to-understand parts, as "Head Imaging" (what do the authors mean with that? CT? MRI of Head?). Although the manuscript may be of impact for the professionals in the field dealing with Y-90 microsphere treatment, the authors should make further clarifications in order to provide more information about the procedure details (glass/resin microspheres? the intent of therapy as curative (ablative) or palliative? dose assessment methodology? whether they used cone-beam CT during the therapy? whether they performed a planning angiography along with Tc99m-MAA hepatic artery perfusion scintigraphy?).

The case report is not very easy to follow unless such issues will be further clarified and answered by the authors appropriately.

Thank you.

Date Sent: 23-Sep-2026

Author's Response to Decision Letter for (JCQ-2026-0029)

Focal Neurologic Deficits after Yttrium-90 Transarterial Radioembolization for Hepatocellular Carcinoma

Dear Editor and Reviewers,

We sincerely thank the Editor and Reviewers for their careful evaluation of our manuscript entitled "Focal Neurologic Deficits after Yttrium-90 Transarterial Radioembolization for Hepatocellular Carcinoma" and for their constructive comments and suggestions. We have carefully revised the manuscript to address the concerns raised and to improve its clarity, accuracy, and clinical relevance. Our detailed point-by-point responses are provided below, with corresponding revisions indicated by page and line numbers in the revised manuscript.

Reviewer 1

Comment 1 : Causality needs to be established more carefully. The manuscript attributes the spinal cord infarction predominantly to embolization of the intercostal arteries, particularly the artery of Adamkiewicz (AKA). However, the procedural angiographic findings demonstrating the spinal arterial supply are not described. It would be important to clarify whether spinal angiography was performed before embolization and whether an identifiable radiculomedullary artery or AKA arose from the embolized intercostal arteries. Without such documentation, the causal relationship remains presumptive.

Response: We thank the Reviewer for this important comment. We agree that the temporal association and anatomical plausibility do not establish a definitive causal relationship between the embolization procedure and injury to the artery of Adamkiewicz (AKA). During the procedure, we performed selective angiography of the right intercostal arteries and right inferior phrenic artery, supplemented by C-arm CT. However, dedicated spinal angiography was not performed, and neither the AKA nor other radiculomedullary arteries were identified. We have revised the Discussion to clarify two plausible mechanisms of spinal cord ischemia: interruption of segmental arterial inflow and inadvertent nontarget embolization. Nevertheless, the precise vascular pathway remains uncertain without direct angiographic confirmation. We have therefore avoided definitively attributing the neurological complication to AKA injury. (p. 5, lines 62–70; pp. 7–8, lines 118–141.)

Comment 2: The embolic material and technique require greater detail. The manuscript states that particle and liquid embolic agents were used but does not clearly specify the embolic agent, particle size, liquid embolic concentration, injection technique, and level of distal embolization. These details are critical because the mechanism of spinal cord ischemia may differ substantially between proximal vessel occlusion and distal penetration of embolic material.

Response: We thank the Reviewer for this important comment. We performed adjunctive particulate and liquid embolization of the right ninth through eleventh intercostal arteries and right inferior phrenic artery. The original case description identifies Embozene particles measuring 100, 250, and 500 μm , while the procedural report records particle sizes of 100, 250, and 500 for the right inferior phrenic artery. We have discussed how these technical factors may influence the mechanism of spinal cord ischemia, particularly the distinction between proximal interruption of segmental arterial inflow and inadvertent distal penetration or reflux of embolic material into spinal arterial branches. The precise mechanism remains uncertain without further procedural evidence. (p. 5, lines 65–70; p. 8, lines 131–141.)

Comment 3: The role of the inferior phrenic artery should be discussed. The authors appropriately emphasize the intercostal arteries, but the possibility of spinal or diaphragmatic arterial anastomoses from the inferior phrenic artery should also be addressed. A detailed review of the pre- and post-embolization angiograms could help identify potentially relevant collateral pathways.

Response: We have incorporated the right inferior phrenic artery into both the procedural description and the mechanistic discussion. The Case Presentation documents its substantial supply to the posterior tumor and its subsequent embolization, with the angiographic finding represented in Figure 1B. The Discussion addresses lower intercostal and phrenic–intercostal anastomoses as plausible routes by which spinal perfusion could be compromised. Neither the AKA nor a patient-specific collateral connection to the spinal circulation is described as directly visualized. (p. 5, lines 67–69; pp. 7–8, lines 125–130; p. 14, lines 230–234.)

Comment 4: MRI findings require more precise characterization. The manuscript describes T2/STIR hyperintensity at T9–T10 and T11–T12 as early ischemic changes. It would be useful to provide diffusion-weighted imaging/ADC findings, if available, and clarify whether the distribution was consistent with an anterior spinal artery, posterior spinal artery, or central cord vascular territory.

Response: We thank the Reviewer for this important comment. We have clarified the MRI findings and their correlation with the neurological examination. Although the initial thoracic spine MRI was interpreted as normal, a subsequent neuroradiology addendum identified faint T2-weighted and STIR hyperintensities

at T9–T10 and T11–T12. Axial T2-weighted images showed corresponding intramedullary signal abnormalities, although detailed assessment was limited by motion artifact. Diffusion-weighted imaging (DWI) was not performed, and apparent diffusion coefficient (ADC) data were therefore unavailable. We have also clarified the MRI sequences in Figure 2. Given the asymmetric neurological findings and imaging limitations, we could not reliably distinguish involvement of the anterior spinal artery, posterior spinal artery, or central cord vascular territory. We have acknowledged these limitations in the Discussion without assigning a definitive vascular territory. (p. 3, lines 30–35; p. 6, lines 92–99; p. 7, lines 104–117; p. 14, lines 235–240.)

Comment 5: The neurological examination should be correlated with the imaging. The unilateral predominant motor and sensory deficits, hyperreflexia, clonus, and bilateral Babinski responses suggest an upper motor neuron process. The authors should explain how this clinical pattern corresponds to the level and vascular territory of the presumed infarction.

Response: We thank the Reviewer for this important comment. We have further clarified the correlation between the neurological examination and MRI findings. The patient exhibited severe right lower-extremity weakness with preserved left-sided strength, a right T10 sensory level, impaired vibratory sensation, asymmetric hyperreflexia, ankle clonus, and bilateral extensor plantar responses. These findings indicate an upper motor neuron lesion consistent with lower thoracic myelopathy, corresponding to the T2-weighted and STIR hyperintensities observed at T9–T10 and T11–T12. However, the asymmetric neurological deficits, involvement of multiple sensory modalities, and limited axial MRI findings without DWI preclude definitive localization to a specific spinal arterial territory. We have addressed this clinical–radiological correlation and its limitations in the Discussion. (pp. 5–6, lines 73–99; p. 7, lines 104–117.)

Comment 6: The discussion of TARE safety could be better focused. The extensive description of general TARE complications is somewhat lengthy relative to the central message. The discussion would be stronger if it emphasized the specific mechanism of spinal ischemia following embolization of extrahepatic collaterals and highlighted preventive strategies, including careful angiographic assessment for spinal arterial supply before embolization.

Response: We thank the Reviewer for this constructive suggestion. We have refocused the Discussion to emphasize the mechanisms and prevention of spinal cord ischemia associated with adjunctive extrahepatic arterial embolization. Specifically, we have expanded the discussion of the anatomical relationships between the lower intercostal arteries, right inferior phrenic artery, and spinal circulation. We have also addressed two potential mechanisms of ischemia: interruption of segmental arterial inflow and inadvertent nontarget embolization. To highlight preventive strategies, we emphasize careful evaluation of selective angiography and C-arm CT for potential spinal arterial branches, along with appropriate embolization techniques to minimize reflux and nontarget ischemia. We have shortened the discussion of general Y-90-related complications and summarized their reported frequencies in Table 1, while distinguishing these adverse events from the risks associated with adjunctive extrahepatic embolization. (pp. 7–9, lines 118–152; p. 13, lines 223–225.)

Comment 7: Any comparative evaluation between glass and resin microspheres for TARE should be looked upon

Response: We thank the Reviewer for this valuable suggestion. We have expanded the Discussion to compare glass and resin Y-90 microspheres, particularly their differences in specific activity and embolic particle burden. We have also clarified the distinction between radioactive Y-90 microspheres administered through the hepatic arterial branches and the particulate and liquid embolic agents used for adjunctive extrahepatic arterial embolization. Although the specific Y-90 microsphere type and dosimetry details were unavailable, the anatomical distribution and temporal relationship suggest that the neurological complication was more closely associated with the adjunctive extrahepatic embolization rather than the radioactive microspheres themselves. However, the precise mechanism remains unconfirmed. (p. 8, lines 142–149.)

Comment 8: Overall, this is a potentially valuable case, but the manuscript would benefit from stronger angiographic evidence establishing the relationship between the embolized intercostal arteries and spinal cord vascular supply, as well as greater technical detail regarding the embolization procedure.

Response: We thank the Reviewer for this important observation. We agree that direct angiographic evidence would strengthen the causal relationship between extrahepatic arterial embolization and spinal cord ischemia. We performed selective angiography of the right ninth through eleventh intercostal arteries and right inferior phrenic artery, supplemented by pre- and post-embolization C-arm CT. However, dedicated spinal angiography was not performed, and neither the artery of Adamkiewicz nor other radiculomedullary branches were identified. We have clarified the procedural details and expanded the Discussion to address two plausible mechanisms: interruption of segmental arterial inflow and inadvertent nontarget embolization. Although the temporal association and anatomical distribution support procedure-associated spinal cord ischemia, we acknowledge that the precise vascular pathway remains unconfirmed. (p. 5, lines 62–72; pp. 7–8, lines 118–141.)

Reviewer 2

Comment: It is apparent that the complication they reported does not necessarily seem to be occurred as a result of Y-90 microsphere administration, but rather because of using large sized embolic liquid and gel materials which have had nothing to do with Y-90 microspheres themselves and used as an adjunct to avoid possible extrahepatic shunting of Y-90 microspheres, though those issues are not clearly stated and needs much more clarification by the authors.

Response: We thank the Reviewer for this important comment. We agree that the neurological complication should not be attributed directly to Y-90 microsphere administration without supporting

evidence. During the procedure, we first performed adjunctive embolization of the right ninth through eleventh intercostal arteries and right inferior phrenic artery using particulate and liquid embolic agents, followed by administration of three vials of Y-90 microspheres through two right hepatic arterial branches. We have clarified the distinction between these two procedural steps in the Case Presentation and Discussion. Given the anatomical proximity of the embolized extrahepatic arteries to potential spinal arterial connections, the neurological complication was more plausibly associated with the adjunctive embolization rather than the intrahepatic Y-90 administration. However, the precise mechanism of spinal cord ischemia remains unconfirmed in the absence of direct angiographic evidence. We have revised the Discussion to emphasize this distinction and avoid unsupported causal attribution. (p. 5, lines 58–72; p. 8, lines 131–149.)

Comment 2: There are also some not-easy-to-understand parts, as "Head Imaging" (what do the authors mean with that? CT? MRI of Head?).

Response: We thank the Reviewer for pointing out this ambiguity. We have replaced the nonspecific term "head imaging" with the precise imaging modalities used, namely noncontrast head CT and brain MRI, which were performed to exclude acute intracranial causes of the neurological deficits. We have also clarified the subsequent diagnostic workup, including CT angiography of the abdomen, pelvis, and bilateral lower extremities to assess vascular and access-site complications, and thoracic spine MRI to evaluate potential spinal cord pathology. These revisions provide a clearer and more comprehensive description of the diagnostic evaluation. (p. 3, lines 29–35; p. 6, lines 86–99.)

Comment 3: Although the manuscript may be of impact for the professionals in the field dealing with Y-90 microsphere treatment, the authors should make further clarifications in order to provide more information about the procedure details (glass/resin microspheres?)

Response: We thank the Reviewer for this valuable comment. We used glass Y-90 microspheres, administering three vials through two right hepatic arterial branches supplying the majority of the tumor. We have clarified the microsphere type in the Case Presentation and expanded the Discussion to compare glass and resin Y-90 microspheres in terms of specific activity and embolic particle burden. We have also distinguished the intrahepatic administration of glass Y-90 microspheres from the preceding adjunctive embolization of extrahepatic tumor-feeding arteries using particulate and liquid embolic agents. Given the anatomical distribution of the treated vessels, the neurological complication was more plausibly associated with the adjunctive extrahepatic embolization, although the precise mechanism remains unconfirmed. (p. 5, lines 69–72; p. 8, lines 142–149.)

Comment 4: the intent of therapy as curative (ablative) or palliative?

Response: We thank the Reviewer for this important question. The treatment was undertaken with curative intent as part of a tumor-downstaging strategy before planned hepatic lobectomy, rather than as definitive ablative or palliative therapy. We have clarified this treatment objective in the Case Presentation to distinguish the role of Y-90 TARE in facilitating subsequent surgical resection. (p. 5, lines 58–60.)

Comment 5: dose assessment methodology?

Response: We thank the Reviewer for this important question. We administered three vials of glass Y-90 microspheres through two right hepatic arterial branches supplying the majority of the tumor. The lung shunt fraction was assumed to be approximately 15% based on preprocedural mapping findings. However, the available procedural records did not specify the total administered activity (GBq), absorbed radiation doses, or dosimetry calculation methodology. We have clarified the available procedural information and acknowledged these limitations in the Discussion. As the detailed dosimetry records were unavailable, we could not retrospectively verify the dose assessment methodology. (p. 5, lines 69–72; p. 8, lines 146–149.)

Comment 6: whether they used cone-beam CT during the therapy?

Response: We thank the Reviewer for this question. Yes, we performed intraoperative C-arm CT (cone-beam CT) with and without contrast before and after embolization, in addition to selective digital subtraction angiography. The acquired images were transferred to a workstation for three-dimensional vascular reconstruction and assessment. We have clarified the use and timing of C-arm CT in the Case Presentation. (p. 5, lines 61–65.)

Comment 7: whether they performed a planning angiography along with Tc99m-MAA hepatic artery perfusion scintigraphy?).

Response: We thank the Reviewer for this important question. We performed selective angiography of the celiac axis, right hepatic arterial branches, right intercostal arteries, and right inferior phrenic artery during the procedure. The procedural record refers to preprocedural mapping and an assumed lung shunt fraction of approximately 15%. However, a separate planning angiography report and completed technetium-99m macroaggregated albumin (99mTc-MAA) hepatic perfusion scintigraphy results were unavailable for verification. Therefore, we could not confirm whether 99mTc-MAA scintigraphy was performed or provide a scintigraphy-derived lung shunt fraction. We have limited the procedural description to the documented findings. (p. 5, lines 61–72.)

Comment 8: The case report is not very easy to follow unless such issues will be further clarified and answered by the authors appropriately.

Response: We thank the Reviewer for this comment. We have reorganized the Case Presentation to clarify the procedural sequence, neurological findings, and diagnostic workup. The Discussion now focuses on the relationship between the clinical and MRI findings, relevant spinal vascular anatomy, potential mechanisms of ischemia, and preventive strategies. We have also revised the figure legends to clarify the angiographic and MRI findings while acknowledging the limitations of the available procedural evidence. (pp. 5–6, lines

58–102; pp. 7–9, lines 104–152; p. 14, lines 230–240.)

We sincerely appreciate the Reviewers' constructive feedback and hope that our revisions have satisfactorily addressed their concerns.

Sincerely,
Keith Lawrence Uy, on behalf of all authors

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