Peer Review File

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<mark>Reviewer A</mark>

Prophylactic laminoplasty may be a good treatment when spinal stenosis is present, as oedema and inflammation following radiotherapy of intramedullary tumours can exacerbate spinal symptoms.

The fact that there was no improvement in spinal symptoms after the initial radiotherapy and that there was improvement in spinal symptoms after laminoplasty eight years later suggests that there were also spinal symptoms due to spinal canal stenosis.

A little more mention should be made of the possibility that myelopathy associated with spinal stenosis was also present in the discussion.

See paragraph 5 of observations.

<mark>Reviewer B</mark>

Concept:

Spinal cord compression can be caused by postradiation inflammation. This is a case of prophylactic laminoplasty for avoidance of postradiation inflammatory pseudoprogression. Laminoplasty may be more appropriate than laminectomy with duraplasty for prophylactic mitigation of postradiation inflammation.

Questions:

Has anyone else done a prophylactic laminoplasty for postradiation inflammatory pseudoprogression? -Yes they talk about prophylactic duraplasty but only one study. Are there more?

Reply: We have been unable to find any more studies that use prophylactic laminoplasty.

This patient already had severe cervical stenosis and improved because of a laminoplasty, which is an established outcome. Can the authors comment on what improvement was due to treatment of the cervical stenosis vs. mitigating the postradiation inflammation?

Reply: Given his cancer and spinal cord metastasis diagnosis all his clinicians have ascribed all of his weakness to the spinal cord lesion and not to stenosis. It would be difficult to prove, with two separate pathologies going on, the stenosis and intramedullary tumor, that one was exclusively causing the weakness and not the other. Because the focus had been treating the tumor there was reluctance to undergo surgical treatments for his stenosis as well the degree of stenosis was underestimated by his prior clinicians. So, it is unlikely that the patient would have undergone any treatment because of the sole focus on his intramedullary tumor as being his primary cause of weakness, therefore the only aspect of intervention. As well, the treatment of the patient's cancer might make them a less desirable surgical candidate with complication and wound healing. However, when we saw how much stenosis he had and knowing there would be edema from the radiation treatment we knew that is they did not get the laminoplasty prior to that treatment given out stenotic they were, they would have gotten worse not better.

Changes to text: We have reworded Introduction paragraph 3 to better convey this message

How many of these patients have complications d/t postradiation inflammation? If it is low, then is it expected that this patient had no worsening? Or was this patient expected to have

Reply: Given the patients existing cervical stenosis the determination that while significant postradiation inflammation is somewhat rare, any inflammation would have a significant impact on this patients quality of life.

There is no large study that we could find with patients with significant stenosis who undergo radiation therapy.

Comments:

Introduction – Irrelevant inclusions like when laminoplasty was invented, and Lhermitte's sign. Failed to mention treatment of postradiation inflammation with steroids (<u>https://pubmed.ncbi.nlm.nih.gov/27231814/</u>).

Reply: Added postradiation inflammation with steroids.

Changes to text: "High-dose corticosteroids have shown regression of the lesions; but"

Case – Highlights pertinent history and symptoms prior to laminoplasty. Highlights reason for laminoplasty (severe, symptomatic cervical stenosis). Highlights improvement after laminoplasty. Appropriately mentions timing.

Discussion – Highlights the point that prophylactic laminoplasty was only indicated because of concomitant severe cervical stenosis. Can they discuss further the point made in paragraph beginning on line 144? Talk about the outcomes from the paper cited. Were they similar to what the authors observed? Are there any other studies like this one?

Reply: We have been unable to find similar studies like this one so we have made edits to more concisely reflect that as well as more detail about its outcomes.

Grammar:

Line 64 – spelling, Lhermitte's sign. Changes to the text: Corrected spelling

Line 127 – "If" is capitalized.

Changes to text: Corrected capitalization

Conclusion:

I think they should use the abstract and introduction to better highlight their points. Overall lacks citations and evidence.

They do not show MRI and post-radiation MRI and discuss the comparison. If there was no postradiation inflammation in the post-operative MRI then their claim that the laminoplasty helped is not true. If the post-radiation MRI demonstrates inflammation then that would provide strong evidence for the claim. If the post-op MRI has no postradiation inflammation then we should assume the patient's improvement was due to the decompression from the laminoplasty.

<mark>Reviewer C</mark>

The authors describe a case of prophylactic cervical canal expansion prior to receiving radiotherapy for the management of a neuroendocrine malignancy affecting the cervical spine. Specific comments follow:

Line 48 - 50: In describing the history of cervical laminoplasty, there are both open door and French door/double door methods (Kurokawa's method). You have mentioned only the former type which has been favoured by surgeons.

Reply: Described more specifically.

Changes to text: added "The open door method"

Line 62-68: One may be led by these lines to equate radiation myelopathy with perilesional edema causing cord compression. Paragraph would benefit from an additional sentence or two clarifying the pathophysiology of radiation myelopathy (not just secondary to mechanical compression, but also radiation-induced damage to cells) and forms of radiation myelopathy (i.e. acute delayed).

Reply: See reviewer B question 2 reply.

Line 72: Manuscript is not a study, it is a case report. **Reply: Corrected Changes in text: study changes to "case report"**

Lin 82-86: Not clear how much worse the neurology is. Would help if there is motor grading of important myotomes from the prior and present presentation, i.e. according to the MRC scale.

Reply: We do not have motor grading for this patient.

Line 100: Should state the indication for the foraminotomies – were they prophylactic due to radiological stenosis or did the patient had associated radicular symptoms at those levels?

Reply: Foraminotomies were irrelevant to the case.

Changes to text: Removed "right-sided foraminotomies at C-2/3 and at C7/T1"

Line 103: Wasn't described what his sensory status was pre-op this should have been elaborated previous (i.e. the distribution, severity etc) to clarify what 'improved' means. **Reply: Added pre-op sensory status**

Changes to text: "with bilateral numbness and tingling"

104 - 106: Why the wait of 1.5 months, and what was the RT field? Usual practice is to initiate RT within ~ 2-3 week when the wound has healed. Was steroid cover used? I am also not familiar with this regimen so would benefit from some brief discussion within the context of neuroendocrine tumour management.

Reply: Standard of care is 6 weeks from procedure to start radiation therapy when doing full beam radiation if incision area is within the radiation field. This is to reduce the incidence of wound complications

Ln 115: I am not sure how laminoplasty / RT would have helped with lower back symptoms unless there was some indication that the pathology related to the cervical spine, i.e. parasthesia / dysaesthenic component from the neck down, Lhermitte sign positive etc.

Reply: We have found that some patient will see lower back pain improvement with cervical laminoplasty. Here is a paper that found this as well https://pubmed.ncbi.nlm.nih.gov/19721149/

Ln 127: 'If' capitalized where it should not be.

Reply: Corrected

Ln 129-132: Disagree with this statement as in the context of malignancy and instability (i.e. according to SINS score), fusion may be favoured, or consequent to the need of wide decompression, so these don't dictate a preference for laminoplasty. Pros and cons for each surgical technique towards selection should be clarified.

Reply: SINS is gross instability not progressive instability. Laminoplasty because they don't require a fusion to has a successful outcome are preferable when there is going to be some treatment that may impair somebody's ability to heal from a fusion

Ln 136: rephrase 'bony degeneration and lesion enhancement'. Reply: Corrected Change to text: "bone deterioration and lesion advancement."

Ln 138 - 139: Should find and quote any literature on the incidence and amount of expansion of the spinal cord subsequent to RT. Also should mention here the rationale for corticosteroids and any guidelines for their use in such a context.

Added corticosteroids to introduction. See reviewer B comments

Ln 152: grammatical error.

Corrected

Figure 1: Arrows / arrowheads will help to demarcate the pathology. Figure legend also seems incongruent with the main text which only appears to describe intramedullary / leptomeningeal metastasis. If the hyperintense signals within the vertebral bodies are compatible with 'diffuse tumour involvement' as described in the legend, then this should be added to the main text.

Added arrows. And corrected text to find with the rest of the case report. Change to text: Removed "diffuse tumor involvement at this level with contrast enhancement.