

Peer Review File

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Reviewer A

Iatrogenic Harlequin Syndrome is rare and it is interesting enough. But, I judged reject for this paper, because this patient was not undergo imaging examinations of the head and spinal cord to rule out the possibility of hidden diseases (for example, metastasis of advanced colon cancer.)

I appreciate your wish to contribute to this journal and cordially hope that you will consider submitting your papers to the journal in the future.

Reply 1:

Unfortunately, due to the patient's indwelling metal contraceptive ring, and due to her poor physical strength, the patient and her family refused to undergo MRI examination of the central nervous system after developing harlequin syndrome. I have added specific explanations to the article as well.

Furthermore, no definite space-occupying lesions were found based on the results of the patient's preoperative contrast-enhanced head CT and trunk CT.

I think what is unique about this report is that this cases presented with harlequin syndrome on different sides of the body in a short period of time, which is obviously more likely to be related to the clinical intervention.

With the above-mentioned manifestations, even there was another cause, this case is unique enough to be published.

Changes in the text:

Added in line 62-66, page4 “And no definite space-occupying lesions were found from the patient's preoperative contrast-enhanced head CT and trunk CT. Unfortunately, due to the patient's indwelling metal contraceptive ring; and due to poor physical strength, the patient and her family refused to undergo further MRI examination of the central nervous system after developing harlequin syndrome.”

Reviewer B

This is an interesting case of Harlequin Syndrome induced by intraspinal analgesia, self-limited, with the peculiarity that the symptoms changed to the opposite site of the face within the same episode of intraspinal analgesia.

Please find below some comments:

- Introduction 35-36 “Sometimes the arms and trunk may also be affected.”. Please cite some

example such as doi: 10.1016/j.nrl.2016.04.006.

Reply 2:

Thanks for the suggestion. We have added relevant further explanations and literature citations to the Discussion section (line 93-96, page5).

- Case report:

Was/Is the patient under follow-up so you can assure that the symptoms haven't recurred?
Did you consider to perform an outpatient MRI?. It should be mandatory to rule out malignancy and abnormalities in the nervous system and the authors may highlight this point in the discussion.

Did you consider to perform neurophysiological studies?

Reply 2:

As showed in line 75-76, page4, except for the two episodes described in the article, the patient did not have Harlequin Syndrome symptoms in the subsequent follow-up.

Unfortunately, due to the patient's indwelling metal contraceptive ring, and due to her poor physical strength, the patient and her family refused to undergo MRI examination of the central nervous system after developing harlequin syndrome. I have added specific explanations to the article as well.

We did consider neuro-EMG or EEG for the patient. Again, due to her poor physical strength, the patient and her family refused the test.

Changes in the text:

Added in line 62-66, page4 "And no definite abnormalities or space-occupying lesions were found from the patient's preoperative contrast-enhanced head CT and trunk CT.

Unfortunately, due to the patient's indwelling metal contraceptive ring; and due to poor physical strength, the patient and her family refused to undergo further MRI examination/EMG/EEG after developing harlequin syndrome."

Added in line 76-77, page4-5 "The patient continued her palliative care in our hospital for the next 45 days, after which the patient passed away. "

- Discussion. The following paragraph should be placed in the Case report section. "Limited to the conditions at the time, the patient in this case did not undergo MRI examination of the head and spine. Instead, the patient's CT scan of the head and spine did not show clear lesions. However, it is impossible to rule out the possibility of abnormalities in the nervous system and accompanying blood vessels caused by cervical spine disease. This is an unsatisfactory part of this case."

Reply 2:

One of the necessary requirements for the implantation of the central nervous system analgesic pump is to exclude the possibility of the nervous system and accompanying vascular abnormalities caused by cervical spondylosis. We have ruled out the possibility of related lesions by preoperative contrast-enhanced CT of the head and trunk.

- Discussion. I don't find appropriate the statement "At present, many institutions still cannot fully distinguish it from Horner syndrome.". Symptoms are quite different between Harlequin syndrome and Horner syndrome, and authors may highlight that Harlequin syndrome can be accompanied by Horner syndrome (myosis and ptosis) when the oculosympathetic innervation is affected.

Reply 2:

In agree with this comment,we had change the statement into:"Drug stimulation may also cause Horner syndrome-related manifestations". (line 110, page6)