Case Report

Possible role of aprepitant for intractable nausea and vomiting following whole brain radiotherapy—a case report

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Abstract: Radiation-induced nausea and vomiting (RINV) is one of the most distressing symptoms that adversely affects quality of life (QOL) as well as the ongoing management plan of cancer patients. Although there are protocols for management of chemotherapy induced nausea and vomiting (CINV) but such guidelines are still lacking for RINV. Various agents like 5-hydroxy tryptophan 3 (5-HT3) antagonist, dexamethasone, metoclopramide and haloperidol are used in clinical practice for RINV but the results are not very encouraging. Because of proposed similarity in the mechanism of nausea and vomiting following chemotherapy and radiotherapy, aprepitant, a substance P neurokinin 1 receptor antagonist can be an optimal agent for RINV on account of its unique pharmacological property. We report a case of metastatic carcinoma breast with bilateral cerebellar metastasis. She presented with complaints of headache and intractable nausea and vomiting. A single fraction whole brain radiotherapy (WBRT) was given for bilateral cerebellum metastasis which further precipitated her symptoms. The prophylactic and therapeutic efficacy of antiemetic used for RINV may be enhanced by adding aprepitant before starting radiotherapy in high risk cases as in ours.

Keywords: Aprepitant; radiation induced nausea and vomiting (RINV)

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Introduction

Nausea and vomiting are most distressing and debilitating symptoms encountered in cancer patients with intracranial metastasis or due to complications of cancer treatment. The overall incidence of radiation induced nausea and vomiting (RINV) is 28 percent in patients receiving different kinds of radiotherapy without concurrent chemotherapy (1). In addition to decreasing compliance of ongoing treatment, it results in dehydration, electrolyte imbalances and malnutrition leading to decreased quality of life (QOL) (2-4). Because of increased incidence of nausea and vomiting after whole brain radiotherapy (WBRT), different antiemetic agents had been tried with mixed results (5). Newer agents like aprepitant, a substance P neurokinin 1 receptor antagonist which is approved for prevention of chemotherapy induced nausea and vomiting (CINV), may have a role in the management of radiotherapy induced nausea and vomiting considering the fact that there is a similarity between the underlying mechanism of CINV and nausea and vomiting after WBRT (6,7). As in CINV, the best understood mechanism of RINV is chemoreceptor trigger zone (CTZ)/area postrema (AP) stimulation (direct or indirect); stimulation of gastrointestinal (GI) mucosal nerves, neurotransmitter release, direct or indirect stimulation of various "pro-emetic" receptors; cortical or vestibular mechanisms: altered smell/taste; and/or release of emetic mediators from the tumour area (6,7).

Case presentation

A 48-year-old female, presented to the palliative care unit (PCU) with complaints of headache and intractable

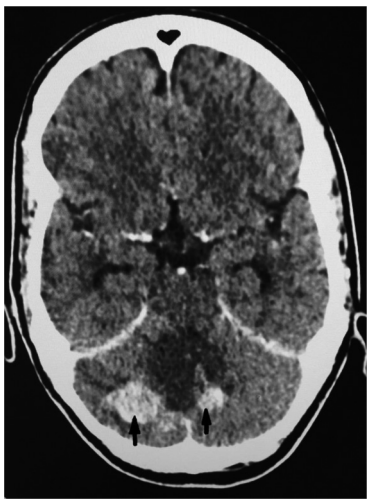

Figure 1 CT showing bilateral cerebellar metastasis. CT, computed tomography.

nausea and vomiting. She has a 2-year history of metastatic carcinoma of breast and was on regular follow up. The headache was of recent onset, holocranial in distribution and throbbing in character which gets worse in the morning. The nausea and vomiting started 1 day after headache, was of sudden onset and projectile in nature. The intensity of headache on numerical rating scale (NRS) was 10 (out of 10) and that of nausea and vomiting was 3 (out of 3) with 4–6 episodes of vomiting in a day which increased in frequency with movement or exposure to light.

She underwent left modified radical mastectomy (MRM) with axillary lymph node dissection 2 years back. She had received six cycles of neoadjuvant chemotherapy (docetaxel, epirubicin, endoxon) preoperatively and local-regional radiotherapy (50 Gy/25#) in the postoperative period. She was started on tablet tamoxifen and put on regular follow up. One year after MRM surgery, she presented with recurrence. The computed tomography (CT) scan showed subpleural nodules in apical segments of both lungs suggestive of metastasis. She received four cycles of second line chemotherapy (vinorelbine, capecitabine, trastuzumab) for metastatic disease.

In the PCU, she was started on morphine based analgesic titration. After 3 mg bolus of injection morphine, an infusion of injection morphine 1.5 mg/h was started. For nausea and vomiting, injection metoclopramide 10 mg thrice a day was started. Her headache was reduced in intensity but the nausea and vomiting was still persisting. Considering her complaints of headache and nausea and vomiting, she was advised Contrast enhanced computerized tomography (CECT) of brain to rule out any intracranial metastasis. The CECT brain revealed intensely enhancing well defined lesion in bilateral cerebellar hemispheres with adjacent edema. The lesion on right cerebellum was of 3.6 cm and larger than left side (*Figure 1*). There was mild mass effect, compression of fourth ventricle and mild upstream hydrocephalus. She was put on cerebral decongestive therapy with injection mannitol 100 mL thrice a day and injection dexamethasone 8 mg twice a day. In consultation with the radiation oncologist, a single fraction WBRT of 8 Gy was given to her. One day after WBRT, her headache had reduced in intensity but total number of vomiting episodes increased to 10–12/day. She was complaining nausea and vomiting even on opening her eyes. So an additional antiemetic, 5-HT_3 antagonist was added. Since she was on opioid analgesic for pain relief (Morphine) which could be another cause, so the doses of Morphine were reduced. But complaints of nausea and vomiting was still persisting and adversely affecting her QOL. Injection haloperidol 0.5 mg twice a day was advised as an additional antiemetic to rule out opioid induced nausea and vomiting. Even with use of three different classes of antiemetics, her nausea and vomiting was not controlled. As there is similarity between CINV and RINV, it was decided to start her on aprepitant, a substance P neurokinin 1 receptor antagonist. She was started on three day regimen of oral aprepitant, 125 mg on first day, followed by 80 mg per day on two consecutive days. There was a dramatic response after first dose of aprepitant, her nausea and vomiting had reduced both in intensity and frequency. After second dose, there was complete response to aprepitant with resolution of nausea and vomiting (*Figure 2*). She was discharged with antiemetic 5-HT_3 antagonist on as on required basis. In the follow up period after 1week, she had no complaints of nausea and vomiting.

Discussion

Nausea and vomiting as a consequence of radiotherapy is a common side effect and needs urgent management (1,8). The onset of nausea and vomiting after WBRT may be acute or delayed. It may present acutely with a latent period of 0.5–4 hours or can be delayed by 2–3 days in up to 40% of patients (9,10). The incidence and severity of RINV remains high after WBRT, but has been significantly reduced due to the introduction of targeted radiotherapy technique as the overall radiation exposure to the normal

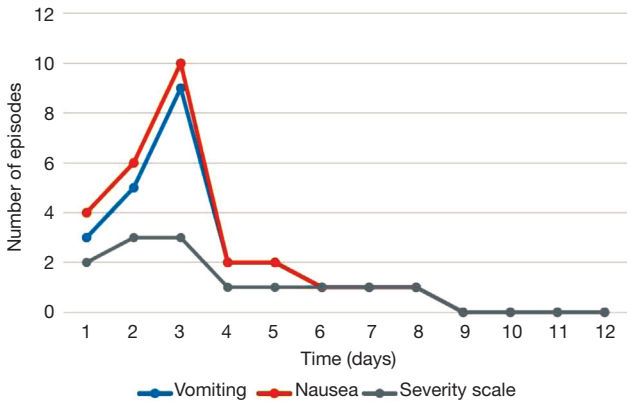

Figure 2 Graphical representation of severity of nausea and vomiting.

surrounding tissue is reduced. In our case, there was an increased risk of RINV due to ongoing nausea and vomiting prior to palliative WBRT. However, in special clinical conditions as in our case, bilateral cerebellar metastasis with compression of fourth ventricle and raised intracranial pressure (ICP), the chances of emetogenic effect of radiation is very high. As the CTZ lies in the floor of fourth ventricle (AP), any cerebral metastasis near CTZ may cause precipitous increase in nausea and vomiting even after trivial stimulus. Since brain is one of the highly susceptible organs for emetogenic response following radiotherapy, Prophylactic antiemetic should be administered to patients at increased risk of RINV (11). The individual risk factors for RINV like age <55 years, female sex, presence of anxiety, previous history of nausea and vomiting, increased ICP and use of opioids as in our case can further predispose the patients for RINV (12).

In a study by Wu and Liaw, the addition of aprepitant as a secondary antiemetic prophylaxis in patients who failed to respond on primary antiemetic prophylaxis with 5-HT_3 antagonists plus dexamethasone has significantly reduced the RINV (13).

In an another study, the combined efficacy of aprepitant and granisetron (5-HT_3 receptor antagonist) in patients suffering from RINV after receiving moderately emetogenic RT for thoracolumbar bone metastases was superior to granisetron alone (14).

Conclusions

Nausea and vomiting is a common side effect after WBRT. The approach for the management of nausea and vomiting following radiotherapy must consider the site of intracranial metastasis and the associated risk factors for its occurrence. Large cerebellar lesions with compression of fourth ventricle can increase the incidence and severity of nausea and vomiting, the role of prophylactic therapy is needed to be explored. Since aprepitant can be given by oral route, faster onset even after first dose (within hours), no dose titration over wide range of body weight and minimal side effects and limited drug interaction, hence its use in such high risk cases as a prophylactic as well as therapeutic agent can be justified as in our case. In clinical conditions where there are high chances of RINV because of associated risk factors; aprepitant may be used as a primary prophylaxis rather than a second line therapy. Also, a single agent approach using aprepitant may offer a better response to RINV which require further studies to prove this hypothesis.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Informed Consent: Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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