



PALLIATIVE CARE CASE OF THE MONTH

“Mucositis in Head and Neck Cancer”

by

Mamta Bhatnagar, MD

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Case: WF was a 53-year-old man with squamous cell carcinoma of the head and neck who was admitted with nausea, vomiting and odynophagia after concurrent chemotherapy and radiation therapy. Patient reported sharp pain in his throat which was worse with swallowing and talking. He was on a fentanyl patch 150 µg and hydromorphone 3 mg IV prn every 3 hours in the hospital. Despite the titration of the fentanyl patch his pain failed to abate.

Discussion: Therapy for head and neck cancer, both radiation and chemotherapy, damage the rapidly proliferating cells of the oral mucous membranes.¹ This causes a series of side effects including mucositis, saliva changes, taste alterations, infection and bleeding. It is estimated that 60% of patients receiving radiotherapy and more than 90% of patients receiving combined chemotherapy and radiation will develop severe oral mucositis. Mucositis in head and neck cancer typically starts 7-14 days after treatment is started and lasts for 2 to 6 weeks depending on the dose and duration of therapy.² Mucositis is a major dose-limiting side effect which has the potential to cause treatment interruption and premature treatment termination

Symptoms of treatment-induced mucositis include mouth and throat sores, difficulty swallowing, pain, and lost or altered taste (dysgeusia). Excessive secretions may lead to gagging, nausea, and vomiting. Weight loss and aspiration occur in a third of patients.³ The most common grading systems to judge the severity of mucositis are the WHO Mucositis scale and the National Cancer Institute Common Terminology Criteria for adverse events (NCI-CTC).⁴

WHO Mucositis Scale	NCI-CTC
0: No clinical features	Grade 1: Asymptomatic/mild symptoms No intervention is indicated
1: Soreness/erythema	Grade 2: Moderate pain not interfering with oral intake. A modified diet is indicated
2: Erythema, ulcers but able to eat solids	Grade 3: Severe pain, interfering with oral intake likely resulting in hospitalization
3: Ulcers requiring liquid diet	Grade 4: Life-threatening consequences for which urgent intervention is indicated requiring care in the ICU
4: Oral intake is not possible	Grade 5: Death

The NCI-CTC Grade 3-4 mucositis is seen in more than half of the patients receiving regimens other than conventional radiation therapy (usually a regimen of 50-70Gy over 4-6 weeks).²

Given the high rates of mucositis, recent attention has focused on how to prevent mucositis. The most common prophylactic treatments are systemic and topical antimicrobials and anti-inflammatory agents, cryotherapy, radioprotectors and systemic biologic agents.

These are utilized as the cancer treatments are initiated. Evidence on select agents is summarized below. Overall, none of these interventions have shown improvement in patient-reported pain or hospitalizations or opiate use even while they reduced the severity and duration of mucositis. While it is not backed by strong evidence, basic oral supportive care with the use of a soft toothbrush, bland rinses and flossing are recommended.⁵

Cryotherapy has been shown to be effective in preventing mucositis in patients receiving 5-Fluorouracil or melphalan infusions. There is insufficient evidence to support its use in the absence of these chemotherapeutic agents.⁶

Amifostine is a pharmacologic radiation protector which binds to free radicals produced by radiation and interferes with their oxygen binding, which is essential to DNA damage. Data for its use in mucositis from radiation therapy to the head and neck is limited.⁷ Topical benzydamine has been shown to be beneficial to head and neck cancer patients receiving less than 50Gy dose of radiation.⁵

Randomized controlled trials of Low Level helium neon Laser Therapy (LLLT) has proved to be well tolerated, with the intervention groups reporting lower pain and mucositis scores after six weeks of radiation.⁸ Laser therapy is a non-invasive technique that involves local application of a high density monochromatic narrow-band light source to the oral mucosa.

Finally, the keratinocyte growth factor (palifermin) stimulates the differentiation of mucosal cells and has proved effective in preventing mucositis in patients undergoing stem cell transplantation but not in the head and neck cancer population.^{9,5}

Among natural agents, such as antioxidants, there is some evidence to support the use of zinc supplementation and pilocarpine. The latter agent treats the hyposalivation commonly seen among head and neck cancer patients.⁵

Once a patient has developed mucositis, the only treatments are supportive. Anesthetic agents such as lidocaine or antihistamines such as diphenhydramine may provide symptomatic relief from the pain of mucositis, but these agents can be irritating when initially applied to ulcerated mucosa. Other side effects include anesthesia-induced loss of taste, oral sensitivity, and a negative effect on the ability to eat and swallow. Topical anesthetic agents have often been combined with coating agents, such as milk of magnesia, aluminum hydroxide gel, or calcium carbonate to produce a "magic mouthwash." Studies of these combination rinses have generally found no benefit for these combined agents over saline rinses. Topical NSAIDs such as benzydamine were also ineffective even though it is recommended for prophylaxis.⁶ Guidelines using bland rinses or single topical anesthetics rather than these mixtures only show LLLT some benefit in reducing the severity of mucositis¹⁰.

Personal details in the case published have been altered to protect patient privacy.

For palliative care consultations please contact the Palliative Care Program at PUH/MUH, 647-7243, beeper 8511, Shadyside Dept. of Medical Ethics and Palliative Care, beeper 412-647-7243 pager # 8513, Perioperative/ Trauma Pain 647-7243, beeper 7246, UPCI Cancer Pain Service, beeper 644 –1724, Interventional Pain 784-4000, Magee Women’s Hospital, beeper 412-647-7243 pager #: 8510, VA Palliative Care Program, 688-6178, beeper 296. Hillman Outpatient: 412-692-4724. For ethics consultations at UPMC Presbyterian-Montefiore and Children’s page 958-3844. With comments about “Case of the Month” call Dr. Robert Arnold at (412) 692-4834.



(Discussion Continued)

The mainstay of treatment of oral mucositis remains supportive care with opioids, tricyclic antidepressants, and enteral feeding. Tricyclic antidepressants have been used with modest success in treating mucositis, although not superior to opiates.¹¹ Providing supportive care for anxiety with pharmacologic and non-pharmacologic means of patient and families might be a useful adjunct.¹

Resolution of Case: WF was started on a PCA to try to control his pain. Given his high oral morphine equivalents (> 1000), WF was initiated on methadone therapy, a short-term hydromorphone PCA and then transitioned to oral opioids as tolerated. He was then discharged home. Over the next four weeks, WF required three hospitalizations largely for pain control, eventually needing a feeding tube for oral intake.

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