



PALLIATIVE CARE CASE OF THE MONTH

“Let me clear my throat”:

A Review of Antitussives for a Malignancy-Related Cough

by

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Case: Ms. P, a 74-year-old female, presented to the hospital with a 6-month complaint of cough and evolving gynecologic mass. A CT scan of chest, abdomen, and pelvis revealed bilateral pulmonary masses consistent with metastatic disease. Ms. P’s most distressing symptom was persistent and constant cough that resulted in poor sleep, difficulty eating, and thoracic back pain. She had tried OTC cough syrup, guaifenesin, and was prescribed a codeine-based medication but perceived little benefit.

Clinical Question(s): What medications/treatments are available for malignancy-related cough? Is there a standard therapeutic approach to a cough related to malignancy?

Discussion: Cough is a common symptom that occurs across many specialties in medicine and may suggest a diagnosis of asthma, COPD, or GERD. The prevalence of a cough in the general palliative care population can be as high as 52%, and in the context of lung cancer, the symptom is present in >90% of patients.^{1,2} Unfortunately, treatment of cough is often not as easy as starting a proton pump inhibitor in a patient with acid reflux. Treatment of the underlying etiology of cough is the standard of care. When related to malignancy, cancer-specific treatments including radiation of tumors, chemotherapies, and/or endobronchial therapies should be offered if indicated. Despite the frequency of the symptom, guidelines for treating a cough related to malignancy are not readily available. Most recommendations are based on limited data or the result of expert opinion.

Treatments for cough have either peripherally-acting or centrally-acting mechanism of action. When determining a treatment approach, it can be helpful to revisit the cough reflex. It begins with the mechanical or chemical irritation of cough receptors, most of which are found in the upper airway (larynx, trachea, and carina). The sensation travels centrally to the cough center in the medulla oblongata by way of the vagus nerve and its branches. Efferent motor nerves carry the subsequent signal to the respiratory musculature resulting in a cough. In a case related to malignancy, underlying inflammation and mechanical irritation from the mass often causes the cough.

Peripherally-Acting Agents:

Depending on the etiology of a patient’s cough, targeting receptors or triggers in the respiratory system may be ideal. A commonly prescribed medication is benzonatate, which is thought to desensitize stretch receptors in the lung and pleura, thus decreasing the cough reflex. Studies have shown mixed results, with some case studies showing improvement of a cough when combined with opiates.⁵ Corticosteroids may also be helpful by targeting malignancy-related inflammation within the airway.

Consensus from an expert panel in the United Kingdom recommended a two-week trial of prednisolone 30 mg daily,³ which equates to approximately 4 mg of dexamethasone daily.

Although data is limited, expert opinion supports the use of anticholinergic medications such as scopolamine or homatropine when increased respiratory secretions are present. Mucous may be produced by the malignancy itself, or may be a result of a patient’s inability to control their normal production of secretions.

Sweet syrups are often incorporated into elixirs, which may or may not include a centrally acting agent. Alone, syrups are thought to create a mucoprotective layer in the pharynx to thus diminishing irritation contributing to the cough. An example of sweet syrup is honey, which in itself has limited data for utilization.⁶ In the same vein, expectorants like guaifenesin are often recommended for productive cough, yet their application in patients with advanced cancer is limited by data.⁷ Lastly, the use of nebulized anesthetics is often discussed in palliative medicine literature. There is data in favor for the use of nebulized anesthetics, such as bupivacaine and lidocaine, in patients with cough and asthma,⁸ thus cancer patients with a possible component of bronchospasm may be considered for this treatment.

Centrally-Acting Agents:

Suppression of cough reflex within the brain is also an important mechanism to target. The mechanism of action, as well as the availability of data, differs amongst the centrally-acting antitussive medications: opiates, dextromethorphan, and gabapentin.

Dextromethorphan can be found in many different combinations in over-the-counter medications. It is related to an isomer of a codeine analog and works in the medulla oblongata to suppress the cough reflex. Reviews of studies have found that dextromethorphan has been consistently better than placebo in improving both the severity and frequency of chronic cough.⁷ The maximum daily dose is 120mg/day, with a relatively low concern for potential side effects. The most serious adverse effect noted in case reports is the possibility of serotonin syndrome in patients on SSRIs.

Opiates remain a cornerstone in the treatment of cough, especially in the palliative care where they are often already being used for the management of pain. It is generally accepted that all medications within the opiate class are helpful in treatment. Many opiates have been studied (i.e. codeine, hydrocodone, and long-acting morphine) for chronic cough and have been shown to help in either the severity or frequency of cough when compared to placebo. Arguably, codeine has the most data, however a recent study showed the use of 5-10 mg of extended release morphine sulfate twice daily also improved chronic cough.^{7,9}

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)

Finally, gabapentin was recently studied in a small randomized trial as a potential centrally-acting antitussive for refractory chronic cough in non-cancer patients. A dose of 1800 mg/day was found to improve the cough compared to placebo.¹⁰ This may be an agent to consider in a patient who also suffers from neuropathic pain.

Treatments should be individualized based off the suspected underlying mechanism of cough, and considering medications that may have dual purpose may be beneficial in palliative care patients in the hopes of minimizing polypharmacy and pill burden. Overall expert consensus and review articles recommend an approach that includes both peripherally-acting and centrally-acting therapies for optimal control of cough.³

Resolution of Case: With the addition of hydrocodone/homatropine elixir, oxycodone, dexamethasone, and benzonatate in a stepwise manner, Ms. P, noted a mild improvement in cough over the course of her hospitalization. Additionally, radiation therapy was used to target the larger pulmonary masses that were likely the etiology of the cough.

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