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Palliative Treatment for Asymptomatic Patients

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Head and neck cancer; palliative care; shared decision making

Case Description

Ms. JW is a 47-year-old woman who presented with symptoms of neck adenopathy, headache, and nasal congestion. She was diagnosed with locoregionally advanced nasopharyngeal carcinoma, and workup confirmed biopsy-proven liver metastases. Given her distant metastatic disease, systemic chemotherapy was initiated. She had a partial response, and her initial symptoms of headache and congestion improved. Concern for local tumor progression with eventual cranial nerve involvement and skull-base invasion prompted discussion of radiation therapy to the primary site. Here, an *asymptomatic* patient with *incurable* disease is faced with a difficult decision whether to pursue local cancer-directed therapy at this time.

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Point

The patient should receive radiation therapy to improve local control of disease that is anticipated to become symptomatic

In the case of patients with incurable cancer, goals of treatment aim to prolong life or to mitigate symptoms and improve quality of life. The ways in which these treatments can be delivered range in intensity and aggressiveness, and often can achieve both endpoints. For example, aggressive surgical management of brain metastases followed by radiation therapy, can both prolong life and delay the onset of neurologic symptoms, thereby improving quality of life, and this is considered a palliative intervention.¹ On the other end of the spectrum, early palliative care intervention without tumor-directed therapy itself was similarly shown to improve quality of life and prolong overall survival.² Regardless of overall prognosis, there are no standards that define which interventions are too aggressive and which ones are not aggressive enough when it comes to palliative care.

In many cases, tumors continue to grow in patients with advanced cancer who do not receive cancer-directed therapy. If the trajectory of symptoms due to a growing tumor can be reasonably predicted, and other sites of disease are controlled, it may be worthwhile to offer cancer-directed therapy before the patient experiences symptoms. This is based on two main assumptions: (1) The patient will eventually become symptomatic in a way that is distressing due to morbid symptoms and (2) palliating a patient prior to symptom onset would ultimately result in less suffering than waiting to palliate when symptoms are established and potentially more difficult to alleviate.

Radiation oncologists, routinely offer palliative treatments prior to true symptom onset, whether it is offering palliative radiation for small brain metastases or even offering prophylactic whole brain radiation to patients with small cell lung cancer,³ to areas that threaten to evolve into true symptomatic cord compression, and for impending pathologic fractures that fulfill radiologic criteria in weight-bearing areas but are not necessarily fractured or causing pain.^{4,5} These recommendations are tempered by a holistic sense of the individual's performance status, competing risks, prognosis, and the anticipated side effects of treatment. In the case of patients with head and neck cancer, the anticipated side effects of treatment are a key component of the discussion of risks and benefits.⁶

More than other disease sites, the progression of advanced cancers of the head and neck can have significant impact on both physical and psychosocial symptoms.⁷ With advanced imaging techniques and ability to detect regions of local tumor extension, these side effects *may be* predictable. Tumor extension into the skull base may cause cranial neuropathies resulting in visual disturbances, hearing loss, and facial pain. Tumors may ulcerate through skin and facial structures leading to disfigurement, which can lead to social isolation and distress. Tumor extension into pharynx and cranial nerve involvement may lead to feeding difficulties, nutritional deficiencies, and may eventually necessitate a feeding tube. Hypopharyngeal or laryngeal invasion may prevent a patient from communicating effectively. These effects can be reasonably anatomically predicted, which suggests that whether palliative cancer-directed interventions are employed preventatively or when the patient becomes symptomatic is simply a matter of time.

In the case of Ms. JW, the location and extension of her primary tumor into the skull base are concerning for the development of cranial neuropathies and compromised function, which ultimately may necessitate more aggressive treatments to maximize comfort or pain medications that can lead to somnolence and constipation. Early palliative radiation may obviate the need for feeding tubes, as well as mitigating potential side effects associated with radiation therapy. If the patient receives palliative radiotherapy when the gross disease is limited to the skull base, she could expect minimal mucosal and parotid irradiation, which would result in less mucositis and xerostomia,⁸ and would likely be well tolerated. However, should the primary tumor progress, then these symptoms would likely be worse due to the need to irradiate a larger area. If the goal for palliative treatment is to maximize comfort and minimize the extent of interventions, it is logical to offer radiation treatment prior to symptom onset.

The role of clinicians in empowering Ms. W to make informed decisions includes a detailed discussion of treatment intent (palliative versus curative), the risks and benefits of any treatment *as well as* the alternative of forgoing further disease directed treatment. In addition to fully informing patients of expected side effects and duration of treatment, it would be remiss to ignore the fact that many standard palliative measures including pain control are often insufficient to adequately manage the symptoms of head and neck cancers such as vision loss, inability to communicate, and physical disfigurement which can be distressing at the end of life for both patients and their family members.⁹

The ethical principles that drive the rationale for offering treatment are to maximize beneficence to the patient and to empower patient autonomy through shared decision-making.¹⁰ If in line with the patient's overall goals of care, it would be reasonable to offer a course of palliative radiation therapy prior to symptom onset, to prevent symptoms related to tumor progression and to mitigate side effects of future palliative treatment. All of these nuances should be discussed with the patients in the context of the unique clinical situation, and the proposed therapies must be aligned with patient and family goals.

Counterpoint

Because the trajectory of the patient's clinical course cannot be accurately predicted, the patient should only receive palliative radiation when she is symptomatic

In managing progressive incurable cancer, it is critically important to define the intent of care and patient-centered goals in the context of their prognosis. As discussed, palliative care can encompass a variety of interventions, but the tradeoffs of toxicity and time must be balanced with potential benefits of the intended outcome. One of the most important factors in balancing these considerations is expected prognosis.

The clinical trajectory of incurable head and neck cancer is variable, and life expectancy cannot be reliably predicted.¹¹ In this case, while her nasopharyngeal tumor may progress over an unknown period of time, she may ultimately succumb to regional or distant metastatic disease. Local radiation therapy delivered prior to symptom onset over the last months of her life could subject her to a course of treatment that would not be beneficial, at the expense of both treatment-related side effects as well as unnecessary time spent under

treatment. If she were to progress locally with associated symptoms, there would be more robust justification to initiating cancer-directed therapy. This uncertainty in the natural history of cancers at the end of life further underscores for frequent evaluation and multidisciplinary input through tumor board, conferences, and consultations.^{12,13} This also allows for a range of palliative interventions that can be readily initiated when the patient becomes symptomatic.

Cancer-directed palliative interventions may or may not improve the natural history of the disease, but they almost certainly will subject the patient to adverse effects in the immediate future. Indeed, all local treatment modalities for patients with head and neck cancer can be associated with troublesome symptoms, regardless of curative versus palliative intent. Therefore, there must be a candid discussion to facilitate informed decision-making specifying the treatment dose and interval needed to provide meaningful palliation, as well as the anticipated side effects and efficacy. There are a litany of palliative radiation therapy regimens and fractionation schemas designed to shorten both the length of treatment and the resulting consequences. Like palliative radiation, palliative surgical intervention to a site of disease has its own risks and may be more justified in cases with a clear indication and clinical endpoint, such as control of hemorrhage or establishing an airway. Pain control, one of the most significant goals of palliative care, can often be achieved without cancer-directed therapy, and thus avoid the significant risks and morbidity associated with surgical intervention or radiation therapy to the head and neck.

Shared decision making with identification of specific patient and family goals is a vital part of cancer care, especially in incurable settings.¹⁴ Offering no active cancer-directed treatment must always be considered as a valid option in the context of one's treatment options, reiterating that palliation is itself a worthy endpoint.¹⁵ For patients with estimated life expectancies measurable in months, the burden of time in treatment should not be minimized, and is not a trivial toxicity. With the onset of symptoms, the balance between relative risks and benefits of treatment may be skewed in favor of treatment. However, in the absence of current symptoms, we may subject a patient to assume risks without a predictable or necessarily proportionate benefit. The therapeutic imperative to treat a tumor simply because it is present must be mitigated.

Patients who receive palliative cancer-directed therapy commonly believe their treatment is curative.¹⁶ Such beliefs may conflate the patient's expectations regarding prognosis and may be psychologically damaging. Appropriately, National Comprehensive Cancer Network guidelines recommend consideration of clinical trials (versus best supportive care) for patients with metastatic disease and good functional performance status.¹⁷ Still, clinical trial enrollment requires particular attention to informed consent, including a discussion to avoid the *therapeutic misconception* that may occur when the patient does not appreciate the difference between research and treatment. Henderson *et al* posit that in these circumstances there must be a clear understanding that the defining characteristic of research is to create generalizable knowledge rather than to administer personalized treatment.¹⁸

Indeed, the role of palliative care is commonly misconceived by both physicians and patients alike and is often only considered in the setting of end of life or hospice care. Likewise, the

need for psychosocial counseling and social support, is also underestimated by physicians despite its critical role for patients with advanced cancers.¹⁹ The benefits of palliative care supported by a large body of evidence and include better symptom control, lower rates of emergency room visits and hospital admissions, more efficient healthcare spending, improved quality of life, improve satisfaction with care, lower rates of depression, and less invasive interventions at the end-of-life.² In this case, palliative care must be considered separately from end of life care, and thus initiation of palliative care services should not depend on the patient's prognosis or pursuit of life-prolonging treatments at any stage in her care.

There are several considerations that must underpin decisions in a palliative framework: (1) How much is she suffering at present? (2) What is a reasonable estimation of her prognosis? (3) What are the side effects of palliative interventions? (4) What are her immediate and longer term goals? Based on these questions, it may not be justifiable to deliver aggressive therapies that may cause disproportionate toxicity. In the latter case, extended survival without meaningful quality of life constitutes low-value palliative care.²⁰ As is often the case in end-of-life care, patients and physicians alike are tasked to make decisions with limited knowledge of future events and clinical trajectories.

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