Oncologic Palliative Care

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Financial Disclosures

I have no real or apparent conflict of interest with the information presented in this lecture.
Lecture Outline

- Palliative Chemotherapy
- Palliative Radiotherapy
- Common Symptoms
Palliative Chemotherapy: Why?

- Patient wants to “do something”
- Prognostic uncertainty
- Attempt to decrease symptoms
- Culture promotes treating rather than “doing nothing”
Case #1

- A 75 year-old patient presents with rapid weight loss of 20# in 6 weeks and the onset of Type II diabetes mellitus requiring insulin. The patient’s family indicates that she spends over half her time in bed, has no appetite, and complains of back and abdominal pain. CT scan reveals a large mass in the head of the pancreas and multiple hepatic metastases. The best approach for this patient is
  
  A. Multiagent chemotherapy.
  
  B. Single agent chemotherapy.
  
  C. Gastrojejunostomy to avoid obstruction.
  
  D. Radiation therapy.
  
  E. Supportive care with hospice referral.
Complexity: The Real World

Efficacy

Toxicity
Complexity: Efficacy

Chemosensitive:
Chemotherapy more likely to generate tumor response or improve QOL

- Germ cell tumor
- Lymphoma
- Leukemia
- Ovarian cancer
- Breast cancer
- Colorectal cancer
- Bladder cancer
- Small cell lung cancer
- Prostate cancer

Chemoresistant:
Chemotherapy less likely to generate tumor response or improve QOL

- Non-small cell lung cancer
- Esophageal cancer
- Cervical cancer
- Pancreatic cancer
- Gastric cancer
- Melanoma
- Hepatoma
- Renal cell carcinoma
- Malignant glioma
Complexity: Toxicity

Relatively lower risk for treatment-related toxicity

- Younger age
- Better performance status
- Fewer co-morbidities
- Less prior cancer treatment
- No prior treatment toxicity
- Targeted/hormone therapy

Relatively higher risk for treatment-related toxicity

- Older age
- Worse performance status
- More co-morbidities
- More prior cancer treatment
- Prior treatment toxicity
- Cytotoxic chemotherapy
## Performance Status Tools

<table>
<thead>
<tr>
<th>Karnofsky Performance Scale (KPS)</th>
<th>Eastern Cooperative Oncology Group (ECOG, Zubrod) Performance Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal, no evidence of disease</td>
<td>Normal Activity</td>
</tr>
<tr>
<td>Able to perform normal activity</td>
<td></td>
</tr>
<tr>
<td>with only minor symptoms</td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Normal activity with effort</td>
<td>Symptomatic and ambulatory</td>
</tr>
<tr>
<td>some symptoms</td>
<td>Cares for self</td>
</tr>
<tr>
<td>80</td>
<td>1</td>
</tr>
<tr>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Able to care for self but</td>
<td>Ambulatory &gt; 50% of the time</td>
</tr>
<tr>
<td>unable to do normal activities</td>
<td>Occasional assistance</td>
</tr>
<tr>
<td>60</td>
<td>2</td>
</tr>
<tr>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Requires occasional assistance</td>
<td>Ambulatory ≤ 50% of the time</td>
</tr>
<tr>
<td>cares for most needs</td>
<td>Nursing care needed</td>
</tr>
<tr>
<td>Requires considerable assistance</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>3</td>
</tr>
<tr>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Disabled, requires special</td>
<td>Moribund</td>
</tr>
<tr>
<td>assistance</td>
<td></td>
</tr>
<tr>
<td>Severely disabled</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>10</td>
<td></td>
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</tbody>
</table>
Complexity: Toxicity

Performance Status: ECOG, Karnofsky, others

Better
- Working
- Cares for self
- Ambulatory, out of bed most of the day

Worse
- Not working
- Cannot care for self
- Confined to bed most of the day
Palliative Chemotherapy: General Concepts

- Combination agents - appropriate where chemosensitivity exists and benefit of therapy in improving QOL is established
- Single agents - appropriate where PS is < 3 (ECOG) and chemosensitivity exists and benefit of therapy in improving QOL is established
- Targeted agents - appropriate where PS < 3 (ECOG) and biomarker establishes sensitivity and benefit of therapy in improving QOL is established
Palliative Chemotherapy: General Concepts

- Treatment of patients with poor performance status with chemotherapy is discouraged unless...
  - Tumor with known rapid response to therapy (germ cell tumors, lymphoma)
  - Patient desires treatment and is accepting of toxicities
  - Potential for improved QOL is very real
Case #2

- A 64 year-old man presents with a known history of non-small cell lung cancer presents with rapid onset of confusion. He had an unwitnessed loss of consciousness and there are concerns about a seizure. His re-staging scans demonstrate widespread metastatic disease. An MRI of the brain at the right. The best treatment option at this point is
  A. Craniotomy and resection.
  B. Multiagent chemotherapy.
  C. Whole brain radiation.
  D. Intrathecal chemotherapy.
  E. Stereotactic radio surgery.
Palliative Radiotherapy Basics

↑ cancer volume needs ↑ radiation dose for cure

<table>
<thead>
<tr>
<th>Radiation Dose (180-200 cGy/day fractions)</th>
<th>Probability of Tumor Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-35 Gy</td>
<td>60-70% subclinical</td>
</tr>
<tr>
<td>40 Gy</td>
<td>80-90% subclinical</td>
</tr>
<tr>
<td>50 Gy</td>
<td>&gt;90% subclinical</td>
</tr>
<tr>
<td>70 Gy</td>
<td>90% palpable axillary nodes 2.5-3 cm, 65% primary tumors 2-3 cm</td>
</tr>
<tr>
<td>70-80 Gy</td>
<td>30% primary tumors &gt; 5 cm</td>
</tr>
<tr>
<td>80-90 Gy</td>
<td>~55% primary tumors &gt; 5 cm</td>
</tr>
<tr>
<td>90-100 Gy</td>
<td>75% primary tumors 5-15 cm</td>
</tr>
</tbody>
</table>
**Palliative Radiotherapy Basics**

↑ radiation dose causes ↑ risk to normal tissues

<table>
<thead>
<tr>
<th>Normal Tissue</th>
<th>Dose (cGy)</th>
<th>Side Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td>&gt; 6000</td>
<td>necrosis</td>
</tr>
<tr>
<td>Lens</td>
<td>&gt; 500</td>
<td>cataracts</td>
</tr>
<tr>
<td>Optic chiasm</td>
<td>&gt; 5000-5500</td>
<td>blindness</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>&gt; 5000</td>
<td>paralysis</td>
</tr>
<tr>
<td>Parotids</td>
<td>&gt; 3200</td>
<td>xerostomia</td>
</tr>
<tr>
<td>Lung</td>
<td>&gt;1800-2000</td>
<td>pneumonitis</td>
</tr>
<tr>
<td>Skin</td>
<td>&gt;5500-6000</td>
<td>telangiectasia</td>
</tr>
<tr>
<td>Small bowel</td>
<td>&gt;5000</td>
<td>adhesions, SBO</td>
</tr>
</tbody>
</table>
Ideal dose balances probability of tumor control and normal tissue injury.
Palliative Radiation Therapy

- Painful bony metastases - most common reason
- Bone is most common metastatic site
- 65-75% advanced breast/prostate Ca
- 30-40% advanced lung Ca
- Treatment given as multiple fractions over 2-3 weeks or as single dose
Uses for Palliative Radiation Therapy

- Spinal cord compression
- Impending/Pathologic fracture
- Control of massive hemoptysis in lung cancer
- Control of pelvic bleeding in cervical, vaginal, vulvar, endometrial, colorectal cancers
- Brain metastases
Uses for Palliative Radiation Therapy

- NOT valuable…
  - Death imminent
  - One symptom among many
  - Unable to give informed consent
  - Retreatment exceeds normal tissue tolerance
  - Lengthy treatment course
  - Therapy facility unavailable
Common Symptoms

- Nausea/Vomiting
- Dyspnea
- Depression/Anxiety
Nausea/Vomiting

- Affects ~60% of all terminal cancer patients with 40% in last 6 weeks of life
- 71% of patients admitted for control of symptoms
- History…focus on character of N/V, associated symptoms, medication history, prior therapies, past medical history
Nausea/Vomiting

- Common findings…
  - Chemical abnormalities 31% - electrolyte abnormalities, acidosis/alkalosis, infection
  - Impaired gastric emptying 44%
  - Visceral/serosal causes 31% - bowel obstruction, GI bleeding/PUD, enteritis, constipation
Nausea/Vomiting

- Common findings…
  - Medications 51%
  - 83% of these due to opioids
- Best way to control N/V is an understanding of the 4 pathways of N/V
- Chemoreceptor Trigger Zone, Cortex, Peripheral Pathways, Vestibular System
Nausea/Vomiting

- Non-pharmacologic therapy
  - Avoid strong smells or other triggers (perfume, cologne)
  - Small, frequent meals
  - Limit oral intake during severe episodes
  - Relaxation techniques
  - Acupuncture and acupressure including wrist bands
Dyspnea

- Affects 50-70% of cancer patients with life-limiting illness

Etiologies…

- Concomitant lung disease
- Deconditioning
- Cachexia (weakens respiratory muscles)
- Pleural effusion
- Obstruction from tumor - atelectasis, “functional” lobectomy, etc.
- Lymphangiitic metastases
Dyspnea

- Recognition of Symptoms
  - Only reliable measure is patient self-reporting
  - Respiratory rate, pO$_2$, SaO$_2$ do not consistently correlate with symptom of dyspnea
  - Focus on identification and treatment (if possible) of underlying cause
Dyspnea - Potential Cause/Treatment

- Airway obstruction
  - Tumor: stent, laser, RT, resection, steroids, chemotherapy
  - COPD: bronchodilators, steroids
- Pneumonia
- Antibiotics
- Heart failure
  - Diuretics, decrease afterload
Dyspnea - Potential Cause/Treatment

- Treatment-related Pneumonitis
  - Glucocorticoids
- Massive ascites
  - Drainage, diuretics
- Anemia
- Transfusion
Malignant Pleural Effusion

- Drainage
  - Thoracentesis, Pleurx catheter
- Pleurodesis
  - Talc, intrapleural chemotherapy (bleomycin, others)
Dyspnea - Symptom Management

- Opioids
  - Improves sensation of breathlessness
  - Central and peripheral action (opiate receptors in lung and in pleura)
- Oxygen
  - Powerful symbol of medical care
  - Fan may do as well
  - Monitor CO$_2$ retainers!
An 82 y/o man with NSCLC and pain from spinal metastases comes in with his wife. The wife reports that the patient is sleeping more and no longer wants to go out to restaurants or church with her. Patient indicates that these activities are too painful. What is the patient’s underlying problem?

A. Anxiety disorder.
B. New onset depression.
C. Expected changes at end-of-life.
D. Poorly controlled pain.
E. Grief reaction.

Additional information…the patient no longer enjoys anything
## Depression/Anxiety

### Prevalence of depression and anxiety at the end of life


<table>
<thead>
<tr>
<th></th>
<th>Cancer</th>
<th>Community Elderly</th>
<th>NH Residents</th>
<th>Base Rates</th>
<th>PC/Hospice Inpatient Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>6-8%</td>
<td>2-10%</td>
<td>10%</td>
<td></td>
<td>60-70%</td>
</tr>
<tr>
<td>Depression</td>
<td>14-31%</td>
<td>2% (47% post-CVA)</td>
<td>10-25%</td>
<td>2-5%</td>
<td>14%</td>
</tr>
</tbody>
</table>
Depression

- Impact of depression
  - Reduces ability to find meaning and purpose
  - Impairs quality of life
  - Shortens survival in some illnesses
  - Worsens physical symptoms (pain)
  - Bereavement outcomes worse in family members of depressed patients
Depression

- Medications that can cause depression...
  - Steroids
  - Interferon
  - Interleukin-2
  - Tyrosine kinase inhibitors
  - Zidovudine
  - Vinblastine
Depression

- Screening tools for depression: 2 questions (97% sensitive, 67% specific)
  - “During the past month, have you been bothered by feeling down, depressed or hopeless?”
  - “During the past month, have you been bothered by little interest or pleasure in doing things?”
- At EOL Sensitivity of 55%, specificity of 75%
Depression

- Separating grief from depression...
  - Normal Grief
    - The emotional response is intense early on after a loss, but gradually diminishes in intensity
    - May come in waves – ‘pangs of grief’
  - Depression
    - Persistent low mood, loss of interest in everyday activities, feelings of hopelessness, worthlessness or guilt, and suicidal ideation
Treatment of Depression

- Aggressively treat other physical symptoms
- Consider psychotherapy/counseling
- Encourage exercise
- Antidepressants (SSRIs) for a life expectancy over two months
- Psychostimulants
Treatment of Depression

- **SSRIs**
  - Good for co-morbid anxiety and irritability
  - Nausea, diarrhea, and sexual side-effects
  - Potential for QTc prolongation (citalopram dose > 40mg)

- **SNRI**
  - Can be effective if there is co-morbid pain or hot flashes
  - Often increases blood pressure (venlafaxine)
Treatment of Depression

- TCA’s
  - Can assist with appetite, pruritus, neuropathic pain and sleep
  - Inexpensive
  - Anticholinergic (constipation, dry mouth, orthostatic hypotension)
  - Generally contraindicated in cardiac disease or liver failure
  - Worsen symptoms of BPH
- Other
  - Mirtazepine (Remeron) can increase appetite and improve sleep, increases warfarin levels
  - Bupropion (Wellbutrin) can reduce fatigue but also lowers the seizure threshold
Benefits of Psychostimulants

- Response often seen within 2 days
  - 73% response in cancer pts (noncontrolled)
- Discontinuation from side effects <10%
- Augment opioid analgesia
- Diminish opioid sedation
- May increase appetite
- Can be used in conjunction with SSRIs
- Start with methylphenidate 5mg q am, q noon and double if no effect in 2 days, stop if no improvement in a week
- Can go up to 60mg bid
Anxiety

- Generalized anxiety disorder and anxiety 2º to a medical condition most common
- Medications that can cause anxiety
  - Caffeine
  - Steroids
  - Nicotine
  - Antidepressants, antipsychotics, stimulants
  - Phenylephrine (Sudafed)
  - Synthroid over replacement
<table>
<thead>
<tr>
<th>Potential Sources of Anxiety Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Actual underlying anxiety disorder</td>
</tr>
<tr>
<td>● Fear of death and the dying process</td>
</tr>
<tr>
<td>● Spiritual or existential concerns</td>
</tr>
<tr>
<td>● Chronic coping or personality style</td>
</tr>
<tr>
<td>● Medication side effects (akathisia from antiemetics)</td>
</tr>
</tbody>
</table>

<p>| |</p>
<table>
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<th></th>
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</thead>
<tbody>
<tr>
<td>● Undertreated symptoms (pain,</td>
</tr>
<tr>
<td>dyspnea, sepsis)</td>
</tr>
<tr>
<td>● Withdrawal states (sedatives,</td>
</tr>
<tr>
<td>opioids)</td>
</tr>
<tr>
<td>● Delirium</td>
</tr>
<tr>
<td>● Anticipatory response to</td>
</tr>
<tr>
<td>repeated aversive treatment</td>
</tr>
<tr>
<td>(chemo)</td>
</tr>
</tbody>
</table>
Pharmacological Anxiety Treatment

- Benzodiazepines: drugs of choice at EOL
  - Ativan (lorazepam) 0.5-2 mg q4-6hrs prn
  - Xanax (alprazolam) 0.25-0.5 mg q4-6hrs prn
  - Klonopin (clonazepam) for long-acting coverage
  - Can cause sedation, confusion, tolerance, abuse, disinhibition, gait instability, falls

- Trazodone (Desyrel)
  - Sedating but can be given in low doses during the day (12.5-50 mg q4hrs prn)

- Buspirone (BuSpar)
  - Should be scheduled, takes 4-6 weeks to see an effect (7.5-10 mg BID-TID)
Pharmacological Anxiety Treatment

- Consider antipsychotics
  - More sedating
    - Chlorpromazine (Thorazine) 12.5-50 mg q 4 hrs prn
    - Olanzepine (Zyprexa) 2.5-5 mg q 4 hrs prn
    - Quetiapine (Seroquel) 12.5-50 mg q 4 hrs prn
  - Less sedating
    - Haloperidol (Haldol) 0.5-2 mg q 4 hrs prn
    - Risperidone (Risperdal) 0.25-1 mg q 4 hrs prn

- Anti-histamines can be beneficial
  - Hydroxyzine 25-50mg q 6 hrs prn (may also potentiate effects of morphine)
Pharmacological Anxiety Treatment

- Antidepressants if life expectancy > 8 weeks
  - SSRI’s
    - Sertraline (Zoloft) 25-200 mg qd
    - Citalopram (Celexa) 10-40 mg qd
    - Escitalopram (Lexapro) 5-20 mg qd
  - Mirtazepine (Remeron)
  - Also helps with sleep and appetite
  - Antidepressants to avoid
    - Paroxetine (Paxil): anti-cholinergic
    - Venlafaxine (Effexor): withdrawal
    - Bupropion (Wellbutrin): seizure risk
  - Start low and go slow to avoid increasing anxiety
Non-pharmacological Anxiety Treatment

- Explore fears/concerns in non-judgmental fashion
  - Listen, acknowledge, normalize, remain available
- Reassurance not usually effective
  - Can make highly anxious pts more anxious
- Supportive-expressive therapy
  - Aims to reduce symptoms and maintain coping not cure
- Consider psychiatric referral
Anxiety Pearls

- Anxiety is very common
- Benzodiazepines are the drug of choice in hospice patients (need caution since they can cause delirium)
- Can decrease by effectively managing other symptoms (pain/dyspnea)