Oncologic Palliative Care

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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

- Palliative Chemotherapy: Why?
  - Patient wants to “do something”
  - Prognostic uncertainty
  - Attempt to decrease symptoms
  - Culture promotes treating rather than “doing nothing”
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

Non-small cell lung cancer
Esophageal cancer
Cervical cancer
Pancreatic cancer
Gastric cancer

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

Melanoma
Hepatoma
Renal cell carcinoma
Malignant glioma
### Complexity: Toxicity

<table>
<thead>
<tr>
<th>Relatively lower risk for treatment-related toxicity</th>
<th>Relatively higher risk for treatment-related toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger age</td>
<td>Older age</td>
</tr>
<tr>
<td>Better performance status</td>
<td>Worse performance status</td>
</tr>
<tr>
<td>Fewer co-morbidities</td>
<td>More co-morbidities</td>
</tr>
<tr>
<td>Less prior cancer treatment</td>
<td>More prior cancer treatment</td>
</tr>
<tr>
<td>No prior treatment toxicity</td>
<td>Prior treatment toxicity</td>
</tr>
<tr>
<td>Targeted/hormone therapy</td>
<td>Cytotoxic chemotherapy</td>
</tr>
</tbody>
</table>
### Karnofsky Performance Scale (KPS)

<table>
<thead>
<tr>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal, no evidence of disease</td>
<td>100</td>
</tr>
<tr>
<td>Able to perform normal activity with only minor symptoms</td>
<td>90</td>
</tr>
<tr>
<td>Normal activity with effort, some symptoms</td>
<td>80</td>
</tr>
<tr>
<td>Able to care for self but unable to do normal activities</td>
<td>70</td>
</tr>
<tr>
<td>Requires occasional assistance, cares for most needs</td>
<td>60</td>
</tr>
<tr>
<td>Requires considerable assistance</td>
<td>50</td>
</tr>
<tr>
<td>Disabled, requires special assistance</td>
<td>40</td>
</tr>
<tr>
<td>Severely disabled</td>
<td>30</td>
</tr>
<tr>
<td>Very sick, requires supportive treatment</td>
<td>20</td>
</tr>
<tr>
<td>Moribund</td>
<td>10</td>
</tr>
</tbody>
</table>

### Eastern Cooperative Oncology Group (ECOG, Zubrod) Performance Scale

<table>
<thead>
<tr>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Activity</td>
<td>0</td>
</tr>
<tr>
<td>Symptomatic and ambulatory Cares for self</td>
<td>1</td>
</tr>
<tr>
<td>Ambulatory &gt; 50% of the time Occasional assistance</td>
<td>2</td>
</tr>
<tr>
<td>Ambulatory ≤ 50% of the time Nursing care needed</td>
<td>3</td>
</tr>
<tr>
<td>Bedridden</td>
<td>4</td>
</tr>
</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
## 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>
</tbody>
</table>
| 70 Gy                                     | 90% palpable axillary nodes 2.5-3 cm  
|                                           | 65% primary tumors 2-3 cm    |
| 70-80 Gy                                  | 30% primary tumors > 5 cm    |
| 80-90 Gy                                  | ~55% primary tumors > 5 cm   |
| 90-100 Gy                                 | 75% primary tumors 5-15 cm   |
## 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>
Palliative Radiotherapy Basics

Ideal dose balances probability of tumor control and normal tissue injury

- Failure rate
- Side effects

Radiation dose
Uses for 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

Chemoreceptor Trigger Zone (CTZ) → Cortex

Vomiting center → Vestibular apparatus

GI tract

Neurotransmitters
- Serotonin
- Dopamine
- Acetylcholine
- Histamine

from AOA ELC course
Nausea/Vomiting

- Mechanism-based therapy
  - Careful assessment to determine etiology
  - Use knowledge of pathophysiology to determine receptors underlying symptoms
  - Choose antiemetic to block appropriate receptors
<table>
<thead>
<tr>
<th>Antiemetic</th>
<th>Receptor Antagonized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoclopramide (po, IV, SC)</td>
<td>D2 (GI tract)</td>
</tr>
<tr>
<td></td>
<td>5HT3 (at high doses)</td>
</tr>
<tr>
<td>Haloperidol (po, IV, IM, SC)</td>
<td>D2 (CTZ)</td>
</tr>
<tr>
<td>Prochlorperazine (po, IV, rectal)</td>
<td>D2 (CTZ)</td>
</tr>
<tr>
<td>Chlorpromazine (po, IV, IM, rectal)</td>
<td>D2 (CTZ)</td>
</tr>
<tr>
<td>Promethazine (po, IV, rectal)</td>
<td>H1, Achm, D2 (CTZ)</td>
</tr>
<tr>
<td>Antiemetic</td>
<td>Receptor Antagonized</td>
</tr>
<tr>
<td>------------------------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Diphenhydramine (po, IV, SC)</td>
<td>H1</td>
</tr>
<tr>
<td>Scopalamine (po, patch, gel)</td>
<td>Achm</td>
</tr>
<tr>
<td>Hyoscyamine (sl, po, SC, IV)</td>
<td>Achm</td>
</tr>
<tr>
<td>Ondansetron (po, IV)</td>
<td>5HT3</td>
</tr>
<tr>
<td>Mirtazapine (po)</td>
<td>5HT3</td>
</tr>
</tbody>
</table>
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\textsubscript{2} retainers!
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 do gradually diminish 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 (CBT)
- 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
  - Buproprion (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
Potential Sources of Anxiety Symptoms

- Actual underlying anxiety disorder
- Fear of death and the dying process
- Spiritual or existential concerns
- Chronic coping or personality style
- Medication side effects (akathisia from antiemetics)
- Undertreated symptoms (pain, dyspnea, sepsis)
- Withdrawal states (sedatives, opioids)
- Delirium
- Anticipatory response to repeated aversive treatment (chemo)
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 25-50 mg 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)