Small Cell Lung Cancer:
A Case of Complications & Treatment

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Objectives

- List preferred chemotherapy treatment regimen(s) for extensive stage small cell lung cancer
- Differentiate among chemotherapy regimens for small cell lung cancer based on patient-specific needs
- Recognize signs and symptoms of superior vena cava syndrome
- Identify treatment options for superior vena cava syndrome
Patient Case

- **CC:** LC is a 65 yo WF who presented to the ED with extreme SOB, chest tightness/pain, swelling at head
- **HPI:** Symptoms x 5-7 days, progressively worsening. Increased eyelid, face, side of head veins swelling x 2 days. Headache, usual smoker’s cough. Mild hemoptysis 7 days ago. Facial flushing with occasional purplish discoloration of face.
Patient Case

- **PMH:** Heavy tobacco abuse, HTN, anxiety with panic attacks, chronic lower back pain (degenerative disk disease)
- **Surgical Hx:** Total hysterectomy 12/2013; B breast augmentation surgery
- **FH:** hypertension
- **SH:** 2-3 PPD smoker x 40 yrs, 2-3 cocktails nightly, no illicits
- **Ht 64” Wt 68 kg**
- **IBW 55 kg AdjBW 60 kg**
- **BMI 25.7  BSA 1.73 m²**
Patient Case

- **PE/Vital Signs:**
  - Pale, very ill appearing, anxious, mild distress
  - Poor dentition, extensive swelling of bilateral eyelids and face as well as upper neck area with prominent veins and circulation venous return on head and upper neck
  - Bibasilar crackles
  - BP: 182/88, HR 88, RR 18, O2 sat 97%
Patient Case

- ED Imaging
  - Stat CTA chest (SVC syndrome/PE?)
  - Chest x-ray- **mediastinum and hilar adenopathy** on right; marked changed from 2011; suggest CT
  - CT chest- **bulky right hilar, right paratracheal, and precarinal adenopathy**--lymphoma vs metastatic disease; spread of malignancy?--subtle perihilar infiltrates
  - CTA chest- **right main pulmonary artery compression**; no PE
Patient Case

- Patient admitted secondary to findings of right hilar mass
  - Pulmonary consult
  - Superior vena cava syndrome with pleural effusion
- Hypertension, uncontrolled
- COPD
Patient Case

- Medications ordered on admission:
  - Symbicort
  - Flonase
  - Mucinex
  - Solu-Medrol 60 mg IV q12h
  - Ativan 1 mg IV q4h prn
  - Zosyn 3.375 gm q8h (ext infusion)
  - Dilaudid 1-2 mg IV q4h prn
  - Melatonin 10 mg HS prn
  - Thiamine, MVI, folic acid
  - Hydralazine 10 mg IV q4h prn
  - Diovan 80 mg daily
Patient Case

- **Pulmonology Consult**
  - Bronchoscopy with endobronchial ultrasound (with needle aspiration biopsy) to assess mass
    - Preliminary pathology report indicative of SCLC
  - **Medication Changes**
    - D/C Solu-Medrol
    - Prednisone 40 mg daily
    - Albuterol nebs
    - Spiriva
Lung Cancer

- Lung cancer is the leading cause of cancer deaths in the US and worldwide
  - Non-small cell lung cancer (85%)
  - Small cell lung cancer (15%)

- Small cell lung cancer
  - 31,000 new cases of SCLC were estimated to occur in the US in 2013
  - Primarily due to smoking
  - Female:male ratio 1:1
Small Cell Lung Cancer

- Rapid doubling time
- High growth fraction
- Early development of widespread metastases
  - ~1/3 present with limited disease confined to the chest
- Highly sensitive to initial chemotherapy and radiotherapy
  - Most patients eventually die of recurrent disease
- Typically diagnosed when patients present with symptoms indicative of advanced-stage disease
SCLC: Presentation

- Malignant epithelial tumor
  - Large hilar mass
- Bulky mediastinal lymphadenopathy
  - Cough, dyspnea
- Symptoms of widespread metastatic disease
  - Weight loss, debility, bone pain, and neurologic compromise.
Patient Case

- Oncology Consult
  - Right pulmonary artery compressed at 70-80%
  - SVC at rest: <4 mm diameter lumen
- A/P:
  - “SCLC with SVC syndrome, final pathology pending, clinical presentation suggestive
  - Complete staging with CT abd/pelvis, bone scan, MRI brain
  - If extensive→palliative therapy with carboplatin + etoposide
    - If limited, treat curatively with chemotherapy plus radiation
  - Begin chemotherapy inpatient and then continue outpatient, depending on clinical condition”
- Patient transferred to 4 East
SCLC: Staging

**DIAGNOSIS**

Small cell or combined small cell/non-small cell lung cancer on biopsy or cytology of primary or metastatic site

**INITIAL EVALUATION**

- H&P
- Pathology review
- CBC with differential, platelets
- Electrolytes, liver function tests (LFTs), Ca, LDH
- BUN, creatinine
- Chest/liver/adrenal CT with IV contrast whenever possible
- Brain MRI\(^a,b\) (preferred) or CT with IV contrast whenever possible
- PET-CT scan (if limited stage is suspected)\(^a,c\)
- Smoking cessation counseling and intervention

**STAGE**

**Limited stage**\(^d\)
(T any, N any, M0; except T3-4 due to multiple lung nodules that do not fit in a tolerable radiation field)

**Extensive stage**\(^d\)
(T any, N any, M1a/b; T3-4 due to multiple lung nodules)
SCLC Treatment Goals

- **Limited-stage SCLC**
  - Cure using chemotherapy plus thoracic radiotherapy

- **Extensive-stage SCLC**
  - Chemotherapy alone for palliation of symptoms and prolonged survival
    - Long-term survival rare
Patient Case

Imaging results (to assist with staging):
- MRI brain- **multiple metastatic deposits**, no ventricle involvement
- CT abd/pelvis- no metastases founds
- Bone scan- no bony metastases
Extensive Stage SCLC

STAGE

Extensive stage without localized symptomatic sites or brain metastases
- Extensive stage (T any, N any, M1a/b; T3-4 due to multiple lung nodules)
  - Extensive stage with brain metastases
  - Symptomatic
    - Whole-brain RT to before chemotherapy if not immediate systemic therapy is required
    - Asymptomatic
      - May administer chemotherapy first, with whole-brain RT after chemotherapy

Extensive stage + localized symptomatic sites
- Extensive stage without localized symptomatic sites or brain metastases
  - Extensive stage with localized symptomatic sites
    - Spinal cord compression
      - RT to symptomatic sites before chemotherapy unless immediate systemic therapy is required
        - See NCCN Central Nervous System Cancers Guidelines
        - Chemotherapy ± RT to symptomatic sites
          - If high risk of fracture due to osseous structural impairment, consider palliative external-beam RT and orthopedic stabilization

INITIAL TREATMENT
- Combination chemotherapy including supportive care
  - See NCCN Palliative Care Guidelines
- Individualized therapy including supportive care
  - See NCCN Palliative Care Guidelines
SCLC Treatment

- Clinical trials ideal per NCCN
- Smoking cessation (5 A’s)
- Chemotherapy +/- radiation
  - Stage dependent
- +/- Prophylactic cranial irradiation (PCI)
SCLC Treatment

- Limited stage (maximum of 4-6 cycles):
  - Cisplatin 60 mg/m² day 1 and etoposide 120 mg/m² days 1, 2, 3
  - Cisplatin 80 mg/m² day 1 and etoposide 100 mg/m² 2 days 1, 2, 3
  - Carboplatin AUC 5-6 day 1 and etoposide 100 mg/m² 2 days 1, 2, 3
SCLC Chemotherapy

- Extensive stage (maximum of 4-6 cycles):
  - Cisplatin 75 mg/m² day 1 and etoposide 100 mg/m² days 1, 2, 3
  - Cisplatin 80 mg/m² day 1 and etoposide 80 mg/m² days 1, 2, 3
  - Cisplatin 25 mg/m² days 1, 2, 3 and etoposide 100 mg/m² days 1, 2, 3
  - Carboplatin AUC 5-6 day 1 and etoposide 100 mg/m² days 1, 2, 3
  - Cisplatin 60 mg/m² day 1 and irinotecan 60 mg/m² days 1, 8, 15
  - Cisplatin 30 mg/m² and irinotecan 65 mg/m² days 1, 8 every 21 days
  - Carboplatin AUC 5 day 1 and irinotecan 50 mg/m² days 1, 8, and 15
Patient Case

- Chemotherapy orders:
  - Carboplatin AUC 5 x 1 dose today (= 500 mg)
    - Normally AUC 5-6
  - Etoposide 100 mg/m² daily (=173 mg) x 3 doses
  - BSA = 1.73 m²

- Other medication changes:
  - D/C prednisone
  - Dexamethasone 4 mg PO every 6 hours
Patient Case

- Radiation oncology consult
  - Pt states history of recent altered mentation and incoordination over baseline
  - Slight abnormalities; chronic headaches unchanged

- A/P:
  - SVC syndrome 2/2 presumed SCLC, stabilized
    - Agree with oncologist to start chemotherapy given SVC syndrome
  - Brain metastases
    - No neuro radiation unless neuro abnormalities worsen (“sandwiched” between chemo treatments, if necessary); should improve with systemic therapy
  - SCLC
    - Some evidence for consolidative radiation AFTER good chemotherapy response; TBD later
Patient Case

- **Treatment:**
  - **Day 1:**
    - Carboplatin 500 mg
    - Etoposide 173 mg
  - **Day 2:**
    - Etoposide 173 mg
  - **Day 3:**
    - Etoposide 173 mg
Patient Case

- SIADH developed
- Treatment
  - Free water restriction
  - Bumex IV x 5 doses, Lasix IV x 1 dose
  - Chemotherapy fluid changed to NS
  - Demeclocycline 300 mg every 8 hours
SCLC: SIADH

- **SIADH**
  - SCLC cells produce vasopressin (ADH), adrenocorticotrophic hormone (ACTH)
    - Hyponatremia of malignancy (SIADH & Cushing’s)
    - SIADH > Cushing syndrome.

- Chemotherapy and/or supportive care may also cause hyponatremia

- **Treatment**
  - Fluid restriction
  - Demeclocycline
  - Vasopressin receptor inhibitors ("vaptans")
Extensive Stage SCLC

RESPONSE ASSESSMENT FOLLOWING INITIAL THERAPY

- Chest x-ray (optional)
- Chest/liver/adrenal CT with IV contrast whenever possible
- Brain MRI\(^b\) (preferred) or CT with IV contrast whenever possible, if prophylactic cranial irradiation (PCI) to be given
- Other imaging studies, to assess prior sites of involvement, as clinically indicated
- CBC, platelets
- Electrolytes, LFTs, Ca, BUN, creatinine

ADJUVANT TREATMENT

Complete response or Partial response \[\rightarrow\] Limited or extensive stage: PCI\(^{n,o,p}\) (category 1)

SURVEILLANCE

After recovery from primary therapy:
- Oncology follow-up visits every 3-4 mo during y 1-2, every 6 mo during y 3-5, then annually
  - At every visit: H&P, chest imaging, bloodwork as clinically indicated
- New pulmonary nodule should initiate workup for potential new primary
- Smoking cessation intervention
- PET/CT is not recommended for routine follow-up

Stable Disease

Primary progressive disease

See Subsequent Therapy/Palliation (SCL-6)
Superior Vena Cava Syndrome
Superior Vena Cava Syndrome

- Obstruction within lung or chest wall due to a mass
  - Narrows diameter of SVC*
- Increased venous pressure in upper body
- Decreased venous return
Figure 1. The Superior Vena Cava Syndrome.
Clinical findings in a patient with the superior vena cava syndrome, including facial edema, plethora, jugular venous distention, and prominent superficial vascularity of neck and upper chest, are shown in Panel A. The vascular anatomy of the upper chest, including the heart, superior vena cava, inferior vena cava, and subclavian vessels, is shown in Panel B. The tumor is shown compressing the superior vena cava.
<table>
<thead>
<tr>
<th>Sign or Symptom</th>
<th>Frequency</th>
<th>Range (percent)</th>
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<tbody>
<tr>
<td>Facial edema</td>
<td>82</td>
<td>60–100</td>
</tr>
<tr>
<td>Arm edema</td>
<td>46</td>
<td>14–75</td>
</tr>
<tr>
<td>Distended neck veins</td>
<td>63</td>
<td>27–86</td>
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<tr>
<td>Distended chest veins</td>
<td>53</td>
<td>38–67</td>
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<tr>
<td>Facial plethora</td>
<td>20</td>
<td>13–23</td>
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<tr>
<td>Visual symptoms</td>
<td>2</td>
<td>0–3</td>
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<tr>
<td>Dyspnea</td>
<td>54</td>
<td>23–74</td>
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<tr>
<td>Cough</td>
<td>54</td>
<td>38–70</td>
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<tr>
<td>Hoarseness</td>
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<td>15–20</td>
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<tr>
<td>Stridor</td>
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<tr>
<td>Syncope</td>
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<tr>
<td>Headaches</td>
<td>9</td>
<td>6–11</td>
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<tr>
<td>Dizziness</td>
<td>6</td>
<td>2–10</td>
</tr>
<tr>
<td>Confusion</td>
<td>4</td>
<td>0–5</td>
</tr>
<tr>
<td>Obtundation</td>
<td>2</td>
<td>0–3</td>
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Figure 1. Distribution of malignancies causing superior vena cava syndrome. Data from Wilson et al (9).
SVCS: Oncologic Emergency?

- Emergency
  - Airway obstruction
    - Pharynx, larynx
    - Cough, hoarseness, dysphagia, stridor, dyspnea
  - Cerebral edema
    - Headache, confusion, coma
SVCS by Malignancy: Treatment

- **Cancer treatment**
  - Chemotherapy
  - Complete symptom resolution in 80% of patients

- **Symptomatic relief of obstruction**
  - Elevate patient’s head
    - Decrease hydrostatic pressure, edema
  - Decadron 4 mg every 6 hours
    - Case reports
  - Radiotherapy
    - Tissue diagnosis required
    - Symptom relief in ≥ 72 hours
SVCS by Malignancy: Treatment

- Stent placement
  - Bypass the SVC obstruction
  - Percutaneous
  - Benefit in brain metastases?
    - Decreased cerebral edema
  - Stent placement +/- radiotherapy consideration generally recommended by ACCP and NCCN

- Treatment of SVCS complications
  - Ex: thoracentesis for pleural effusion
Patient Case

- **SVCS**
  - Limiting factor for hospital discharge
  - Chemotherapy
  - Decadron
    - Rx at discharge for tapered regimen

- **Granix**
  - 2 doses prior to discharge
  - Not routinely recommended by NCCN during chemotherapy initiation treatment
Conclusion

- Our patient’s care mimicked NCCN treatment guidelines for SCLC
- SCLC must be staged
  - Treatment relies on stage
  - Cisplatin + etoposide mainstay of chemotherapy
- Cancer and treatment-related complications will arise
  - SVCS may/may not be emergent
References

Questions?