Chapter 14
Small Cell Lung Cancer

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PEARLS

- SCLC accounts for 15–20% of lung cancer cases with decreasing incidence.
- Approximately 1/3 of patients present with limited stage disease and the remainder present with extensive stage disease.
- More than 95% of cases are associated with a history of tobacco exposure.
- Ten to 15% of patients present with brain metastases and 2 year incidence after chemo-RT is 50–80%.
- SCLC is the most common solid tumor associated with paraneoplastic syndromes: SIADH, ACTH production syndrome, and Eaton–Lambert syndrome.
- Histopathologic hallmarks include dense sheets of small, round to fusiform cells with scant cytoplasm, extensive necrosis, and a high mitotic rate.
- Pathologic subtypes (pure or classic, variant, and mixed) carry the same prognosis.
- Most important prognostic factors are stage and performance status.

WORKUP

- H&P.
- Labs: CBC, chemistries, BUN/Cr, LFTs, LDH. Consider bone marrow aspirate/biopsy if LDH elevated.
- Diagnosis: sputum, FNA, bronchoscopic biopsy, or CT-guided biopsy. No need for invasive mediastinal staging after SCLC diagnosis made due to limited role of surgical resection.
- Imaging: CT chest and abdomen, bone scan, and MRI brain (preferred over CT brain). PET optional.
- Additional: PFTs, pathology review, smoking cessation intervention.

STAGING

- See Chap. 15 for details of the AJCC 7th Ed Staging for Lung Cancer.
- In practice, SCLC has been divided into limited stage and extensive stage disease.

Limited stage (LS): disease confined to one hemithorax and regional nodes (historically defined as fitting into a single radiation port)
Extensive stage (ES): any disease not meeting limited stage criteria

TREATMENT RECOMMENDATIONS

Stage	Recommended treatment	Outcome
Limited	Concurrent cisplatin and etoposide (4c every 3 weeks) with early RT during cycle 1 or 2 (45 Gy/1.5 Gy b.i.d. preferred). If CR or near-CR, prophylactic cranial RT (25 Gy in 10 fx) For <5% of patients with cT1-2N0 disease with negative mediastinoscopy (or endoscopic biopsy), lobectomy and mediastinal node dissection/sampling may be performed initially. If pN0, chemotherapy along. If pN+, concurrent chemoradiation as above	MS 20 months, 5-year OS 20–26%
Extensive	Combination platinum-based chemotherapy ± palliative RT to symptomatic sites. For patients with PR or CR to chemotherapy, consider prophylactic cranial RT (25 Gy in 10 fx). If brain metastases present, WBRT (30–37.5 Gy in 10–15 fx)	MS 12 months, 5-year OS <5–10%

STUDIES

LIMITED STAGE (LS-SCLC)

- Pignon et al. (1992): metaanalysis of 13 trials and 2,140 patients with LS-SCLC treated with chemo ± thoracic RT. Thoracic RT improved 3-year OS by 5.4% vs. chemo alone (14.3 vs. 8.9%).
- Metaanalyses of randomized controlled trials performed on LS-SCLC patients receiving chemo and early vs. late timing of thoracic RT demonstrate improved survival for early concurrent integration of RT with platinum-based chemo (Fried et al. 2004; De Ruysscher et al. 2006).
- *INT 0096* (Turrisi et al. 1999): 417 patients with LS-SCLC randomized to concurrent cisplatin/etoposide with either 45 Gy/1.8 Gy QD or 45 Gy/1.5 Gy b.i.d. Twice daily arm decreased local failure

(36 vs. 52%) and increased 5-year OS (26 vs. 16%) compared to QD arm. Grade 3 esophagitis more frequent with b.i.d. regimen (27 vs. 11%).

- *RTOG 0239* (Komaki et al. 2009): phase II trial using accelerated high-dose thoracic RT (AHTRT) with concurrent etoposide/cisplatin. RT was given to large field to 28.8 Gy /1.8 Gy QD, then 14.4 Gy/1.8 Gy b.i.d. (1.8 Gy AP/PA in am; 1.8 Gy boost in pm). Total RT dose 61.2 Gy in 5 weeks. Two-year OS 37%, 2-year LC 80%, and 18% acute severe esophagitis, improved compared to INT 0096. One of three arms in ongoing randomized trial of LS-SCLC RTOG0538/CALGB30610.
- Auperin et al. (1999): metaanalysis of seven trials of SCLC patients in CR comparing prophylactic cranial irradiation (PCI) vs. no PCI. PCI reduced the 3-year incidence of brain metastases (59 vs.33%) and increased 3-year OS (15.3 vs. 20.7). Neurocognitive function not assessed.
- Le Pechoux et al. (2003): 720 LS-SCLC patients in CR to chemo-RT randomized to standard dose (25 Gy/2.5 Gy QD) vs. higher dose (36 Gy/2 Gy QD or 36 Gy/1.5 Gy b.i.d.) PCI. No significant difference in 2-year incidence of brains metastases. Reduced 2-year OS in higher dose group (37 vs. 42%) probably due to increased cancer-related mortality.

IV

EXTENSIVE STAGE (ES-SCLC)

- Jeremic et al. (1999): 210 ES-SCLC patients treated with three cycles cisplatin/etoposide with local PR or CR and distant CR randomized to accelerated hyperfractionated RT (54 Gy/1.5 Gy b.i.d.) and chemo vs. four cycles chemo alone. Patients receiving chemo-RT had improved 5-year OS (9.1 vs. 3.7%) and MS (17 vs. 11 months) vs. those treated with chemo alone.
- *EORTC* (Slotman et al. 2007): 286 patients with ES-SCLC with response to chemotherapy randomized to PCI vs. no further treatment. PCI reduced 1-year incidence of symptomatic brain mets (14.6 vs. 40.4%) and improved OS (27.1 vs. 13.3%) compared to the control group.

RADIATION TECHNIQUES

SIMULATION AND FIELD DESIGN

- High-dose volume to GTV + 1.5 cm margin. Include ipsilateral hilum, and bilateral mediastinum from thoracic inlet to subcarinal region (5 cm below carina or adequate margin on

subcarinal disease). Exclude contralateral hilum or SCV unless involved.

- If RT is preceded by chemotherapy, target volumes should be defined on the RT planning CT scan. However, the prechemotherapy originally involved lymph node regions should be included.

DOSE PRESCRIPTIONS

- 45 Gy in 1.5 b.i.d. fx (preferred) or 50–70 Gy at 1.8–2.0 Gy QD (Miller et al. 2003; Roof et al. 2003; Schild et al. 2004)
- PCI: 25 Gy in 10 fx
- Brain metastases: 30–37.5 Gy in 10–15 fx

DOSE LIMITATIONS

- Spinal cord: limit maximum dose to ≤36 Gy with 1.5 Gy b.i.d. RT or ≤46 Gy at 1.8–2 Gy/fx QD.
- Lung: limit volume receiving ≥20 Gy (V20) to <20–30%. Pneumonitis rates increase rapidly with V20 >25–30%.
- Esophagus: limit 1/3 to 60 Gy, entire esophagus to 55 Gy.
- Heart: limit 50% of volume of heart to <25–40 Gy.
- Brachial plexus: limit maximum dose to <60 Gy.

COMPLICATIONS

- Acute: esophagitis, dermatitis, cough, fatigue.
- Subacute/late: radiation pneumonitis, pulmonary fibrosis, esophageal stricture or perforation, pericarditis, coronary artery disease, Lhermitte's syndrome, brachial plexopathy, rib fracture.

FOLLOW-UP

- Clinic visits every 2–3 months initially (H&P, chest imaging, and blood work at each visit), then decrease frequency to every 3–6 months, then annually.

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