



The Role of Surgery in Small Cell Lung Carcinoma-Limited Disease

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Abstract

Small cell lung carcinoma represents about 10% to 15% of all lung cancers. It exhibits an aggressive behavior and potential for early distant metastasis. Systemic chemotherapy with or without radiotherapy are the cornerstones of treatment in most patients with small cell lung carcinoma. However, in cases of limited stage disease and in selected patients, pulmonary resection surgery may be an option. In this study, we present three cases of small cell lung carcinoma that underwent pulmonary resection surgery in 2019, 2017 and 2015, respectively. At the time of writing, none of these patients presented recurrence of the disease.

Keywords: Surgery; Limited disease; Small cell lung carcinoma

Introduction

Small Cell Lung Carcinoma (SCLC) currently accounts for 10% to 15% of all lung cancer diagnoses [1]. SCLC is characterized by rapid growth, early spread to distant sites, and high sensitivity to chemotherapy and radiation. One third of patients will present with Limited Stage (LS) SCLC at the time of diagnosis [2], a potentially curable disease. The management of these patients requires effective coordination of the Multidisciplinary Team (MDT). SCLC is still commonly staged using the Veterans Administration Lung Study Group system [3]. LS SCLC is confined to one hemithorax and can be encompassed in a safe conventional radiotherapy field. Since the seventh edition of the Union for International Cancer Control TNM Classification of Malignant Tumors (2009) it is recommended the use of the TNM classification for staging SCLC, which has demonstrated prognostic value [4,5]. LS SCLC corresponds to T1-4N0-3 M0 tumors, whereas Extensive Stage (ES) SCLC have spread to distant organs. Despite some reservations, surgery is an option for T1-2N0 SCLC in current guidelines after appropriate staging [2,6]. It is important that radical treatment, including the option for surgical resection and its potential extent, are previously discussed with the MDT and invasive mediastinal staging and cardiopulmonary function testing should always be performed. Unlike stage I disease, there is no consensus for surgery in stage II and stage IIIA SCLC and current guidelines state that patients with disease exceeding T1-T2, N0 do not benefit from surgery [7]. However, several recently published population-based studies have shown that surgery was significantly associated with improved survival also in patients with stage II and stage IIIA SCLC. Lobectomy is the surgery of choice in patients who can tolerate the procedure, and clearly [8,9], a complete excision (R0) needs to be achieved. ES SCLC is incurable and systemic platinum-based chemotherapy (ChT) is used to improve quality of life and prolong survival [10]. Current overall 5-year survival rates for LS disease are 48% for stage I, 39% for stage II and 15% for stage III, respectively [11]. Patients with ES disease that were given combination ChT have a complete response rate of more than 20% and a median survival longer than 7 months; however, only 2% are alive at 5 years [12].

Case Presentation

Case 1

A 60-year-old man, former smoker with a 60 pack- year history and previously diagnosed with Chronic Obstructive Pulmonary Disease with moderate bronchial obstruction (FEV1 2.34L, 72% and DLCO 61% of predicted). He had no symptoms other than chronic productive cough and exertional dyspnea. In 2016, he performed a Chest CT and a subsolid pulmonary nodule (13 mm × 12 mm) in

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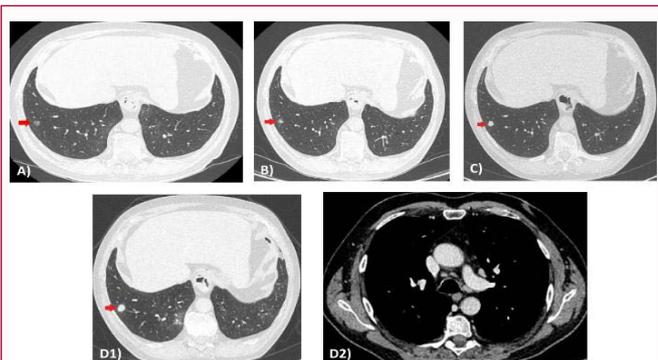


Figure 1: A) Chest computed tomography showing the evolution of the nodule in the right lower lobe over 2016, B) 2017, C) 2018 D) 2019 D2 (mediastinal window) with subcarinal lymphadenopathy.

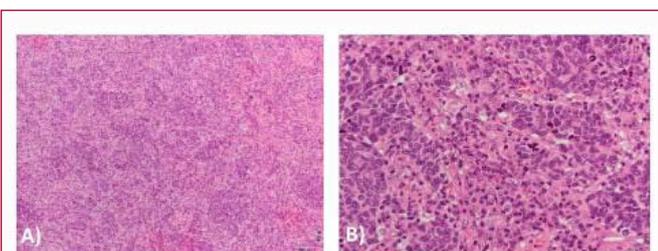


Figure 2: Microscopic examination of SCLC, with hematoxylin and eosin stain. A) Clusters of cells arranged in nests. B) Small cells with salt and pepper nucleus and high mitotic index. Immunohistochemistry (not shown) positive for CK AE1/AE3 (in dot), CD56 and Synaptophysin. Ki67 was expressed in 100% of the cells.

the right lower lobe was detected. The nodule was of difficult access for biopsy and clinical follow-up was recommended. Despite initial regression (8 mm × 7 mm) and stabilization of the lesion, the nodule became solid and increased in size (15 mm × 10 mm) after three years of surveillance. Mediastinal lymph nodes (right paratracheal and subcarinal) were observed on Chest CT, without PET-CT uptake and no distant lesions were detected (Figure 1). The Eastern Cooperative Oncology Group Performance Status (ECOG PS) was grade 1 and after negative mediastinal staging by mediastinoscopy (with sampling lymph nodes of stations 4R, 4L, 7), the patient was submitted to atypical pulmonary resection. The extemporaneous examination identified carcinoma and right lower lobectomy with lymph node dissection (stations 4R, 7 e 8) was performed. The final anatomopathological diagnosis revealed SCLC-pT1b N2 (stage IIIA), with neoplastic infiltration of station 7; R0 was achieved (Figure 2). Adjuvant ChT with Cisplatin and Etoposide (CE) was initiated and concurrent with the second and third cycle of CE, he performed mediastinal Radiotherapy (RT) with 60 Gy. The patient stopped ChT at the fourth cycle due to severe febrile neutropenia. No evidence of relapse to date, with a disease-free survival of nine months.

Case 2

A Female, 45 years old, non-smoker with previous diagnosis of Gaucher disease. During weight loss evaluation, a lung mass in the right upper lobe (43 mm × 33 mm) was detected and biopsy showed a SCLC in stage IIA (cT2bN0M0) (Figure 3). The ECOG PS was grade 0 and the patient began ChT with CE, suspended on second cycle by severe pancytopenia (probably aggravated by hypersplenism of Gaucher disease). The MDT, concluded she had contraindication to ChT and after restaging the lesion was found to have progressed locally, but no lymph nodes or distant metastasis were detected

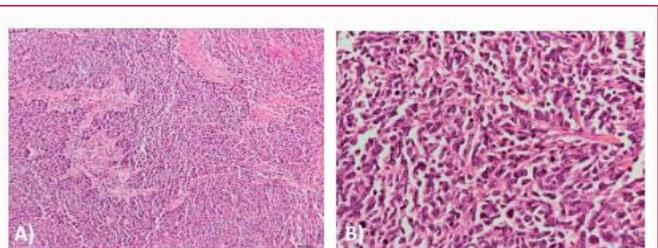


Figure 3: Microscopic examination of SCLC, with necrotic areas, with hematoxylin and eosin stain (A & B).

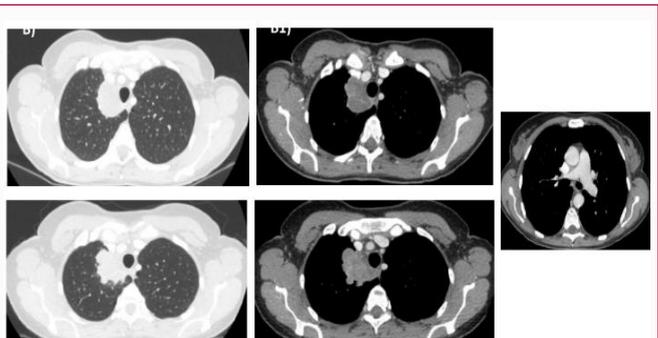


Figure 4: Chest computed tomography showing the lung mass on the right upper lobe. A) Mass with 43 mm × 33 mm at diagnosis and A1) In the mediastinal window, close mass contact with mediastinum and subclavian artery, without invasion. B) Progression of mass (65 mm × 49 mm) after two cycles of ChT. B1). In the mediastinal window, close contact with mediastinum, esophagus and vessels. B2) No mediastinal or hilar lymphadenopathy.



Figure 5: Chest computed tomography, 32 months after surgical resection, with no recurrence of cancer.

(Figure 4). The patient was submitted to right upper lobectomy with lymph node dissection (stations 4R, 7 e 9R). The preoperative diagnosis-SCLC pT2b N0 (stage IIA) was confirmed and R0 surgery was achieved. She underwent prophylactic cranial irradiation with no further adjuvant ChT. There is no evidence of relapse to date, with a disease-free survival of 36 months (Figure 5).

Case 3

A 79-year-old male, former smoker with a 40 pack year history. He had previously been diagnosed with diabetes mellitus, acute ischemic stroke and bilateral carotid occlusive disease. During admission due to ischemic stroke in 2013, the patient performed a Chest CT that showed a pulmonary nodule in upper right lobe with 27 mm × 12 mm. The biopsy revealed SCLC. The ECOG performance status was grade 1 and he was proposed for ChT which he refused. After ten months without any treatment, there was no disease progression and surprisingly the tumor dimensions had reduced (18 mm × 12 mm) (Figure 6). Following MDT discussion and in agreement with

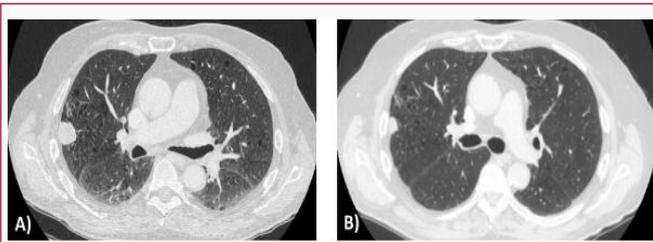


Figure 6: A) Chest computed tomography showing SCLC in upper right lobe, at diagnosis B) and after ten months, without any treatment.

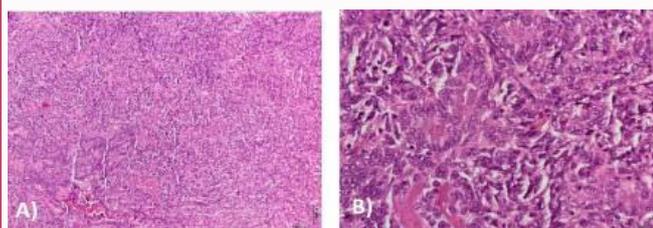


Figure 7: Microscopic examination of SCLC (fusiform morphology) combined with adenocarcinoma areas, with hematoxylin and eosin stain (A & B).

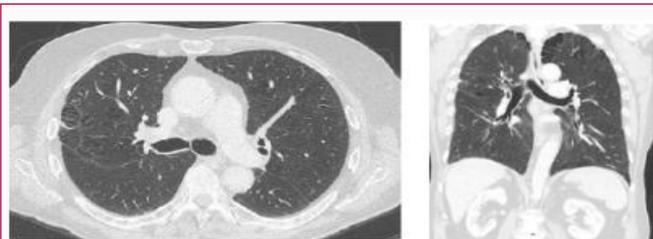


Figure 8: Chest computed tomography, 50 months after surgical resection, with no recurrence of cancer.

patient preference, he was submitted to atypical pulmonary resection (surgical technique limited by poor lung function (DLCO 50% predicted) and comorbidities). The definitive anatomopathological diagnosis was SCLC combined with areas of adenocarcinoma, pT1Nx and R0 surgery was achieved (Figure 7). Once again, he refused adjuvant therapy. There is no evidence of relapse to date, with a disease-free survival of 54 months (Figure 8).

Conclusion

SCLC presents multiple interdisciplinary challenges with several paradigm shifts in its treatment in recent years. Despite the minor role of thoracic surgery in the treatment of SCLC, in cases of LS disease, the most recent studies have already shown good results, either as an initial approach (followed by adjuvant ChT) for stage I SCLC or following induction ChT or chemoradiotherapy in stage II and

stage III disease. The multidisciplinary approach in SCLC is essential and in these three cases it was decisive given the particularities and complexity of each patient. We believe that, as treatment of SCLC continues to evolve and more research is done, surgical resection may play a greater role than current guidelines suggest.

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