A 75-Year-Old Female Smoker with Advanced Small-Cell Lung Cancer and Eastern Cooperative Oncology Group Performance Status 2 who Responded to Combination Immunochemotherapy with Atezolizumab, Etoposide, and Carboplatin

Michał Dębczyński
Damian Mojsak
Beata Kuklińska
Robert Marek Mróż

Corresponding Author: Michał Dębczyński, e-mail: michal.debczynski@gmail.com

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Patient: Female, 75-year-old
Final Diagnosis: Small cell lung cancer
Symptoms: Hemoptysis
Medication: —
Clinical Procedure: —
Specialty: Pulmonology

Objective: Unusual clinical course
Background: Atezolizumab is an immune checkpoint inhibitor used as first-line treatment with carboplatin and etoposide chemotherapy for advanced small cell lung cancer. Immunochemotherapy treatment decisions can be affected by patients' physical ability. Because of the exclusion of patients with an Eastern Cooperative Oncology Group Performance Status (ECOG PS) ≥2 from clinical trials, treatment outcome evidence in this group is limited.

Case Report: We present the case of a 75-year-old woman with an ECOG PS of 2 admitted with respiratory symptoms and diagnosed with advanced small-cell lung cancer. After managing exacerbation of COPD and decompensated heart failure, atezolizumab with carboplatin and etoposide was administered. After 2 cycles of immunochemotherapy, deterioration of health was observed, including anemia and thrombocytopenia. Because of the good response in imaging tests and restored balance of the patient condition, immunochemotherapy was continued. After 4 cycles of combined treatment, complete regression was achieved. No another adverse effects were observed. The patient was qualified for maintenance therapy with atezolizumab. In follow-up CT scan after 2 cycles of atezolizumab, progression was observed and patient was qualified for second-line treatment.

Conclusions: This report presents the case of an older patient with advanced small cell lung cancer and an ECOG status of 2 who responded to combined immunochemotherapy with atezolizumab, etoposide, and carboplatin. Adverse effects observed during immunotherapy were not a reason for discontinuation of the therapy. The assessment of the effectiveness of immunotherapy in patients with ECOG PS ≥2 is difficult owing to the insufficient representation of this group in clinical trials.

Keywords: Antineoplastic Combined Chemotherapy Protocols • Case Reports • Immunotherapy • Physical Functional Performance • Small Cell Lung Carcinoma

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Background

Small-cell lung cancer (SCLC) accounts for 15% to 20% of all lung cancer cases. Most of the patients diagnosed with this cancer are ≥65 years old, and the median age is 67 years [1,2]. SCLC is a cancer with an unfavorable prognosis [3]. The 3-year survival rate before the combined treatment era was 12% to 25% in the limited disease stage and did not exceed 2% in the disseminated disease stage [3]. SCLC is a highly tobacco-dependent cancer, as most of the patients diagnosed with SCLC are former or current cigarette smokers [4]. It is characterized by a high mitotic index and thus a rapid growth rate. Often, distant metastases are found at diagnosis. The limited form of the disease affects only 30% of patients [5]. The main method of treating patients with SCLC is chemotherapy based on etoposide and platinum derivatives. Recently, new therapeutic options have emerged in first-line treatment, with the addition of immunological drugs to standard chemotherapy. In some cases, the addition of an immune checkpoint inhibitor drug is associated with an increase in overall survival and progression-free survival [6]. There are still ongoing medical trials being conducted to more accurately define the safety and efficacy of atezolizumab in combination with carboplatin and etoposide in patients with untreated extensive-stage SCLC [7,8]. When qualifying patients for treatment, it is very important to accurately and individually assess the degree of performance status (PS) of patients, distinguishing whether a poor PS score results from the neoplastic disease itself and its complications or from concomitant diseases [9].

PS is a tool often used by oncology healthcare professionals to assess the fitness of patients for systemic anticancer therapy and to predict prognosis in advanced malignancy. The Eastern Cooperative Oncology Group Performance Status (ECOG PS) scoring system (Table 1) is considered an effective and reliable scale, which shows no significant variations in PS assessment by different healthcare professionals [10].

In a meta-analysis, Dall'Olio et al noticed that the high level of heterogeneity for overall survival analysis in the PS ≥2 population with advanced non-small cell lung cancer (NSCLC) treated with immune checkpoint inhibitors could be the result of the patient heterogeneity within the PS 2 population and the subjectivity of the ECOG PS assessment. They indicate that poorer PS is correlated with lower immunotherapy efficacy [12].

Most case reports in the literature refer to the immunotherapy in NSCLC. There are reports of using chemotherapy with atezolizumab in an 80-year-old male patient with extensive-stage SCLC undergoing hemodialysis [13]. Authors of another case report also suggested that SCLC patients outside of clinical trials are typically in a poor ECOG state but could also benefit from immunotherapy [14].

In the presented study, we report a case of a 75-year-old female patient with advanced SCLC and an ECOG PS of 2 who responded well to combination immunotherapy with atezolizumab, etoposide, and carboplatin. We draw attention to the qualification and benefits of combination therapy: immunochemotherapy in a patient with SCLC at an older age and an ECOG PS of 2 and the impact of possible adverse effects on this type of treatment.

Case Report

A 75-year-old woman who was an active smoker (about 30 pack-years), reported reduced exercise tolerance, exercise dyspnea, and periodic chest pain. She had been experiencing a gradual deterioration in her health for about 3 weeks. The patient associated respiratory system ailments with a past infection. She was taking symptomatic medications with no significant improvement. Two weeks prior, the patient noticed hemoptysis; therefore, she went to the family doctor. She was prescribed antibiotic therapy (amoxicillin) on an outpatient basis, and experienced no noticeable improvement. Then, she went to the Department of Lung Diseases. The patient was referred to the Department of Lung Diseases.

Table 1. Eastern Cooperative Oncology Group (ECOG) performance status [11].

| Grade | ECOG performance status |
|-------|--------------------------|
| 0     | Fully active, able to carry on all pre-disease performance without restriction |
| 1     | Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, eg, light housework, office work |
| 2     | Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours |
| 3     | Capable of only limited self-care, confined to bed or chair more than 50% of waking hours |
| 4     | Completely disabled, cannot carry on any self-care, totally confined to bed or chair |
| 5     | Dead |
Reported comorbidities included chronic obstructive pulmonary disease, arterial hypertension, ischemic heart disease, and previous infection with SARS-CoV-2 2 months prior to admission. She had a mild course of COVID-19 and was treated at home only. For several years, the patient had been taking ipratropium bromide, salbutamol, temporarily, and angiotensin-converting enzyme inhibitor (ramipril).

The physical examination on admission showed increased blood pressure (160/90 mmHg), 95% oxygen saturation, bilateral edema of the lower limbs, and tachycardia, and chest auscultation showed diminished respiratory sound on the right side, with soft wheezing. The result of the ECOG PS score was 2, based on the patient’s daily activity: unable to carry out any work activities; up and about more than 50% of waking hours. In laboratory tests, the abnormalities found were increased parameters of inflammation, hypoxemia without hypocapnia, and increased level of NT-proBNP.

A chest X-ray was performed (Figure 1), followed by a contrast-enhanced computed tomography (CT) scan of the chest and abdominal cavity. A tumor in the hilum of the right lung with mediastinal lymphadenopathy and hypodense areas in the liver, corresponding to metastases, were found (Figure 2).

Bronchoscopy showed a neoplastic, submucosal wall infiltration of the right main bronchus, covered with necrotic masses. In the upper lobe bronchi, segment 1 was narrowed, and segments 2 and 3 were unchanged. The intermediate bronchus...
was narrowed and was circularly infiltrated with neoplasm masses (Figure 3). In the histopathological examination, SCLC was diagnosed (Figure 4).

A CT scan of the central nervous system with contrast was performed and no metastases were found. The stage of disease was defined as cT4N2M1, stage IV.

Because of the exacerbation of chronic obstructive pulmonary disease and the features of decompensated heart failure, the current treatment was changed, and olodaterol + tiotropium, diuretics, and beta-blockers were used. The patient also received antibiotic therapy (levofloxacin) owing to the increase in inflammatory parameters. After 10 days of therapy, clinical improvement was achieved. There was no lower limb edema, no signs of pulmonary edema or airway obstruction, and the heart rate was regular at 70 beats per min. The ECOG PS was rated as 1.

The multidisciplinary council discussed whether the patient was eligible for combination treatment with immunochemotherapy. The discussion concerned the patient’s age, comorbidities, and general condition and the advancement of the disease.

Due to the improvement of the patient’s general condition after the described treatment, it was decided to administer the combination therapy every 21 days as follows: atezolizumab: 1200 mg on day 1; etoposide: 130 mg on days 1-3 (100 mg/m²); and carboplatin 330 mg (AUC: 5) on day 1.

After 2 cycles of immunochemotherapy, the patient came to the clinic with a worsened general condition (ECOG PS of 2). The patient reported weakness and dizziness. Physical examination revealed pale skin and a Common Terminology Criteria for Adverse Events (CTCAE) scale grade 1 maculopapular rash, which did not require treatment. After completion of the combined treatment, the therapy was continued with atezolizumab alone. After 2 cycles of atezolizumab, progression was observed in a follow-up CT scan. The patient was qualified for second-line treatment with topotecan in a minimal dose, but owing to observed pancytopenia and worsening of the patient’s general condition, she was qualified for best palliative care.

During hospitalization, a control contrast-enhanced CT of the chest and abdominal cavity showed a significant regression of the underlying disease (Figure 5).

In a subsequent follow-up after 4 cycles of combined treatment, complete regression was achieved. There were no treatment adverse effects, except for CTCAE grade G1 maculopapular rash, which did not require treatment. After completion of the combined treatment, the therapy was continued with atezolizumab alone. After 2 cycles of atezolizumab, progression was observed in a follow-up CT scan. The patient was qualified for second-line treatment with topotecan in a minimal dose, but owing to observed pancytopenia and worsening of the patient’s general condition, she was qualified for best palliative care.

Discussion

The assessment of the effectiveness of immunotherapy in patients with an ECOG PS ≥2 is difficult owing to the insufficient representation of this group of patients in clinical trials. There is an ongoing clinical trial for these patients, which addresses this problem and perceives it as important and actual issue, but recruitment is still in progress and no results have been published yet [15].

The sparse case reports in the literature show that an elderly patient undergoing hemodialysis safely received this kind of treatment [13] and describe a good response in a patient with poorer PS scores and indicate that there is a lack of research in this group [14].
Yan Wu et al [14] reported the case of a 68-year-old patient who was a cigarette smoker and was admitted to the pulmonary hospital with a cough, chest tightness, and asthma, similar to our present case. Physicians found the patient's right neck lymph nodes were enlarged. After 4 cycles of treatment, which was similar to that used in our patient, partial regression was achieved and the patient's quality of life improved significantly. The authors mentioned moderate adverse events but did not describe them.

The first-line treatment of patients with disseminated SCLC was based solely on etoposide and platinum derivatives [3]. The breakthrough came in 2019 when new therapeutic options appeared, including immunotherapy, which was added to classic chemotherapy. The simultaneous use of chemotherapy and immunotherapy may lead to an increase in the effectiveness of anti-cancer treatment in patients with SCLC and improve their quality of life [16,17]. Combined treatment increases tumor immunogenicity. It should be emphasized that combined treatment does not increase the toxicity of the drugs used, which shows that such a combination is well tolerated [6].

Currently, in Poland, we commonly use 2 drugs that are monoclonal antibodies directed against the ligand of programmed cell death: atezolizumab and durvalumab. Atezolizumab has been approved for treatment under the Ministry of Health’s drug program since July 2021, and durvalumab is available under the Emergency Access to Drug Technologies program.

In the phase III study IMpower 133, a group of 403 patients with stage IV SCLC was treated with first-line chemotherapy etoposide and carboplatin with or without atezolizumab. Overall survival was 2 months longer in the group receiving the additional immunocompetent drug [18]. The efficacy of durvalumab in combination with chemotherapy in the treatment of patients with SCLC was also demonstrated in the Caspian phase III clinical trial. A total of 805 patients with extensive-stage SCLC were divided into 3 groups, and an advantage in terms of overall survival was demonstrated in patients additionally receiving immunotherapy compared to chemotherapy alone [19].

Extending overall survival when combining atezolizumab or durvalumab with platinum-based chemotherapy in first-line treatment improves the prognosis and should be the standard of care in the treatment of patients with disseminated SCLC [20].

It is worth noting that also in the case of NSCLC, patients with an ECOG PS of 2 constitute a huge, heterogeneous group of patients, including approximately 40% of patients [21]. Data on the benefits of immunotherapy with lower performance levels are limited and most often refer to patients with NSCLC. In a study regarding the use of immunotherapy in patients with an ECOG PS 2 score, Mojsak et al [22] showed that these patients may benefit from this approach in terms of increased overall survival and progression-free survival. This benefit is modest compared to that in people with a better PS score, but given the low toxicity profile and proven safety of such therapy, it is an option that should be considered in patients with NSCLC. It seems that these conclusions can be applied in a similar way to patients with SCLC; however, data on this subject are sparse and further research is needed. In the case of SCLC, the group of patients with an ECOG PS of 2, as shown by personal observation, is larger than that of patients with NSCLC, and the disease is most often diagnosed in an extensive stage [4]. In the event of adverse effects of therapy, they can be effectively treated and do not have to lead to the termination of therapy.

In our case report, the patient was not disqualified from immunochemotherapy because of her age and comorbidities. The patient’s treatment for chronic diseases was optimized, thus improving her general condition. The symptoms of cancer may also be alleviated after therapy administration. Each such case should be treated individually and the decision should be made by a multidisciplinary council.

Conclusions

This report has presented a 75-year-old patient with advanced small cell lung cancer and an ECOG PS of 2 who responded to combined immunochemotherapy with atezolizumab, etoposide, and carboplatin. The adverse effects observed during immunotherapy were not always the reason for discontinuation of the therapy. In the described case, combined immunochemo-therapy treatment turned out to be safe for the patient and resulted in a beneficial effect in the form of complete remission in the lungs and the liver. After completion of the combined treatment, maintenance therapy with atezolizumab, and then second-line treatment, the patient was qualified for best palliative care because of worsening of her general condition.

The use of immunochemotherapy in older adults with SCLC appears to be a viable option that may benefit these patients. It should be emphasized that advanced age or comorbidities do not determine the qualification for such treatment; rather, this is determined by the general condition of the patient. The compensation of comorbidities improved the PS score in our patient. The assessment of the effectiveness of immunotherapy in patients with an ECOG PS ≥2 is difficult owing to the insufficient representation of this group of patients in clinical trials.

Declaration of Figures’ Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.
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