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The experience on coronavirus disease 2019 and lung cancer from Regional Center of Pulmonology in Bydgoszcz

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ABSTRACT

In December 2019, an outbreak of 2019 novel coronavirus disease (COVID-19) occurred in Wuhan, Hubei, which has been linked to the severe adult respiratory syndrome coronavirus 2 (SARS-CoV-2). The outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) – related disease (coronavirus disease 2019 [COVID-19]) has spread rapidly to a pandemic proportion. It is characterized by rapid human-to-human transmission from droplet contamination. As of 21May 2020, 20143 COVID-19 cases and 972 deaths have been reported in Poland, representing a global share of 0,41% and 0,29% for incidence and mortality, respectively. We extracted data from the World Health Organization's progress reports. In addition, we retrieved clinical data on patients with cancer and with confirmed COVID-19 in Regional Center of Pulmonology in Bydgoszcz. Here, we report the incidence and outcomes of SARS-CoV-2 infection in cancer patients who were treated at our institution.We reviewed the medical records, including demographic, clinical, and treatment data of 23 patients who were admitted to the Regional Center of Pulmonology, from March 25, 2020, to May 21, 2020 (data cutoff date). COVID-19 pneumonia was diagnosed based on the updated COVID-19 Diagnostic Criteria. Outcomes of COVID-19 among patients with lung cancer were reported and was confirmed in 6 cases (6/23). The median age of infected patients was 69 years (range, 51 to 92 years); 4 of 6 patients (66.7%) were older than 60 years. Cancer has been reported as a major risk factor for adverse outcomes of and death from COVID-19.

Keywords: Cancer, COVID-19, SARS-CoV-2, Coronavirus

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by the newly identified strain of the coronavirus family severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has rapidly evolved into a worldwide pandemic and caused a public health emergency of major international concern (Shi, Han et al. 2020, Chen, Zhou et al. 2020).

In December 2019, an outbreak of respiratory disease caused by a novel coronavirus was first detected in China and has now spread to more than 150 countries (Woldometer, 2020). The virus was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has a phylogenetic similarity to SARS-CoV-1 that caused the SARS pandemic in 2002 (Guan, Ni, 2020). This new type of respiratory illness is characterized by rapid human-to-human transmission, having achieved pandemic spread (Yu, Ouyang et al. 2020). There are currently no therapeutics or vaccines available and, presumably, no pre-existing immunity in the population.

With the World Health Organization (WHO) declaring the novel coronavirus outbreak a pandemic, focus is needed on the impact of this rapidly spreading viral infection on cancer patients (Anderson, Heesterbeek et al. 2020, WHO Director, 2020, WHO, Coronavirus, 2020). Patients with cancer are more susceptible to infection than individuals without cancer, because malignancy and anticancer therapy result in an immunosuppressive state (Liang, Guan 2020). In a retrospective study during the 2009 influenza A (H1N1) virus pandemic, the cancer patient population was at higher incidence of pneumonia (66%) and 30-day mortality (18.5%) compared with the general population (Dignani, Costantini et al. 2014) 10. A recent small case series study that evaluated SARS-CoV-2 in cancer patients found that patients with cancer had worse outcomes from SARS-CoV-2 than other individuals without cancer (Liang, Guan et al. 2020).

This comprehensive reallocation of health resources is of particular concern in patients such as those with underlying chronic diseases, including cancer. In this context, the threat of COVID-19 infection might also factor into decision making – a role which could possibly be lessened by knowledge of the COVID-19 status of patients suitable for anticancer therapy (Ueda, Martins et al.2020). This already dismal scenario seems to be even more severe for patients with lung cancer because of the high risk of interference of COVID-19 with their effective

diagnostic and therapeutic management by treating physicians. Limited studies and research regarding preparedness plans for the patients with during an infectious pandemic exist (Battershill, 2006, ASCO, 2020). In this review, we aim specifically to address challenges associated patients with COVID-19 and concomitant lung cancer during the COVID-19 pandemic.

MATERIALS AND METHODS

PATIENTS

We reviewed the medical records, including demographic, clinical, and treatment data of 23 patients who were admitted to the Regional Center of Pulmonology, from March 25, 2020, to May 21, 2020 (data cutoff date). COVID-19 pneumonia was diagnosed based on the updated COVID-19 Diagnostic Criteria.

We had patients with pneumonia of unknown cause, which was identified as SARS-CoV-2 soon after.

In this program, all consecutive patients with confirmed COVID-19 admitted to the Regional Center of Pulmonology in Bydgoszcz from March 25, 2020, to May 21, 2020 were enrolled. All patients with COVID-19 enrolled in this study were diagnosed and admitted in accordance with the guideline of the polish recommendations (Flisiak, Horban et al. 2020, Zalecenia, 2020).

The final date of follow-up was May 21 2020.

Of these 23 patients with Covid-19, 6 confirmed lung cancer, which was diagnosed in four patients during current hospitalization, in two with this diagnosis established earlier.

DATA COLLECTION

We reviewed clinical charts, nursing records, laboratory results for all patients.

Epidemiological, clinical, imaging, and serological records and treatment and out-comes data were collected from the electronic medical network of hospital.

REAL-TIME REVERSE TRANSCRIPTION POLYMERASE CHAIN REACTION (RT-PCR) TESTS

The confirmation of COVID-19 is achieved by RT-PCR detection of throat swab samples of suspected patients. by the Polish recommendation (Zalecenia, 2020).

STATISTICAL ANALYSIS

Categorical variables were reported as number and percentages, and comparisons between groups were made using the Chi-squared test. Nominal two-tailed statistical significance was set at 0.05. All analyses were performed using programmes Statistica and Excel.

RESULTS

The enrolled 23 patients were all confirmed infected with SARS-CoV-2 with PCR tests of throat swabs. The median age of the patients was 66,6 years (35.0-92.0) (tab. 1). Median age were similiar in both group. The median age of lung cancer group was 64 years, whereas the median age without lung cancer group was 67 years.

9 patients (39%) were men, and 14 patients (61%) were women. In group patients with lung cancer domniated women (83%). Of the 23 patients, almost all had comorbidities (21 [91%]), including malignancy (6 [26%]), hypertension (9 [39%], cardiovascular disease (8 [35%]), and diabetes (7 [30%]), and so forth. Patients of malignancy group showed more underlying comorbidities when compared non malignancy group, such as hypertension (4 [67%] vs 5 [29%], $P < 0,001$). The incidence of other comorbidities was comparable in both groups.

Table 1. Characteristics and Symptoms of Patients Infected With SARS-CoV-2

	All Patients (N = 23)	**With lung cancer (n = 6)**	**Without Lung cancer (n = 17)**	***P* Value**
Age (y)	66,6 (35-92)	64,0 (51- 92)	67 (35 - 90)	NS
Sex				
Male	9 (39%)	1 (17%)	8 (47%)	<.001
Female	14 (61%)	5 (83%)	9 (53%)	
Comorbidity	21 (91%)	6 (100%)	15 (88%)	NS
Malignancy	**6 (26%)**	**6 (100%)**	**0 (0%)**	**<.001**
Hypertension	9 (39%)	4 (67%)	5 (29%)	<.001
Cardiovascular disease	8 (35%)	3 (50%)	9 (53%)	NS
Diabetes	7 (30%)	2 (33%)	6 (35%)	NS
Chronic obstructive Pulmonary disease	4 (17%)	2 (33%)	4 (24%)	NS
hepatopathy	1 (4%)	0 (0%)	1 (6%)	<.001
Fever at onset of illness	17 (74%)	4(67%)	13 (76%)	NS
Symptoms at onset of illness				
Cough	20 (87%)	5 (83%)	15 (88%)	NS
Dyspnea	20 (87%)	5 (83%)	15 (88%)	NS
Fatigue	18 (78%)	3 (50%)	15(88%)	.499
Sputum production	11 (48%)	3 (50%)	8 (47%)	NS
Chest pain	6 (26%)	3 (50%)	3 (18%)	<.001
Oppression in chest	6 (26%)	4 (67%)	2 (12%)	<.001
Anorexia	4 (17%)	3 (50%)	1 (6%)	<.001
Myalgia	4 (17%)	1 (17%)	3 (18%)	NS
Headache	3 (13%)	1(17%)	2 (12%)	NS
Palpitation	3 (13%)	1 (17%)	2 (12%)	NS
Diarrhea	2 (9%)	1(17%)	1 (6%)	NS
Vomiting	2 (9%)	1 (17%)	1 (6%)	NS

The most common clinical feature at the onset of illness was fever (17 [76%]). Other common clinical manifestations included cough (20 [87%]), dyspnea (20 [87%]), and fatigue (18 [78%]). Less common symptoms were sputum production, oppression in chest, dyspnea, diarrhea, headache, and so forth (tab. 1). Compared with the non lung cancer group, patients of the lung cancer group tend to show more frequency of chest pain ,oppresion in chest and anorexia. The frequency of these symptoms among patients with lung cancer can also be explained by the advancement of cancer. The blood counts of patients with lung cancer on admission showed decrease in white blood cells, neutrophils and lymphocytes concurrently to patients of non lung cancer group. The patients with lung cancer showed increase in Lactate dehydrogenase and decrease of aspartate aminotransferase, C-reactive protein compare to patient without lung cancer (tab. 2).

Table 2. Laboratory Records of Patients Infected With SARS-CoV-2 on Admission

	All Patients (N = 23)	**With lung cancer (n = 6)**	**Without Lung cancer (n = 17)**	***P* Value**
White blood cell count, $\times 10^9$/L	3.82(2.98-3.57)	3.57(2.96-4.93)	6.52 (4.30-7.73)	.006
Neutrophil count, $\times 10^9$/L	2.35(1.62-367)	2.16(1.60-2.70)	5.24 (2.90-6.44)	<.001
Lymphocyte count, $\times 10^9$/L	1.15 (0.82-1.46)	0.61 (0.37-1.00)	1.19 (0.95-1.46)	.002
Monocyte count, $\times 10^9$/L	0.31 (0.23-0.44)	0.31 (0.24-0.46)	0.27 (0.14-0.41)	NS
Eosinophil count, $\times 10^9$/L	0.01 (0.00-0.02)	0.01 (0.00-0.02)	0.00 (0.00-0.01)	NS
Hemoglobin, g/L	130.00 (118.00-140.00)	131.00 (121.00-141.00)	128.00 (117.00-136.00)	NS
Platelet count, $\times 10^9$/L	171.00 (142.00-211.00)	172.00 (138.00-206.00)	167.00 (144.00-215.00)	NS
Alanine aminotransferase, U/L	25.00 (17.00-40.00)	24.00 (16.00-40.00)	31.50 (23.00-52.00)	NS
Aspartate aminotransferase, U/L	28.00 (22.00-42.00)	26.00 (21.00-39.00)	40.50 (24.00-62.00)	.03
Lactate dehydrogenase, U/L	224.00 (183.00-291.00)	517.50 (267.00-549.00)	207.00 (181.00-274.00)	.001
C-reactive protein, mg/L	13.20 (6.78-49.00)	11.30 (6.53-26.30)	81.55 (48.85-105.90)	<.001
Procalcitonin, μg/L	0.13 (0.13-0.15)	0.13 (0.13-0.15)	0.13 (0.13-0.15)	NS

So they were not enrolled in the analysis of treatment and prognosis in table 3. The median time from onset of symptoms to admission was 6.0 days. The all of patients needed oxygen suport. All patients received in accordance with Polish recom-mendations. Death occurred signi-ficantly more frequently in the group of patients with lung cancer.

Table 3. Treatments and Outcomes of Patients Infected With SARS-CoV-2

	All Patients (N = 23)	**With lung cancer (n = 6)**	**Without Lung cancer (n = 17)**	***P* Value**
Onset of symptom to admission	6.0 (4.0-9.0)	6.0 (4.0-9.0)	7.0 (4.0-9.0)	NS
Oxygen support	23 (100%)	6 (100%)	17 (100.0%)	NS
Death	7 (30%)	3 (50%)	4 (24%)	<.001

DISCUSSION

Our experience with these 23 patients confirms that COVID-19 is a kind of epidemic pneumonia with fever, dry cough, and fatigue as the most common onset symptoms. Most patients have mild manifestations and excellent prognosis. However, in our group of patients with lung cancer and COVID, the prognosis was significantly worse.

Cancer patients with SARS-CoV-2 infection may have increased morbidity and mortality from COVID-19 than noncancer patients with SARS-CoV-2 infection. Accumulating evidence suggests that cancer patients are at higher risk of COVID-19 infection and more likely to have higher morbidity and mortality than the general population. In a study with a total of 1,524 patients with cancer, cancer patients had a twofold increased risk of COVID-19 infection when compared with the general population (Yu, Ouyang et al. 2020). In another series from a single institution in the Wuhan region, the infection rate of SARS-CoV-2 in patients with cancer was 0.79% (95% CI = 0.3-1.2), which was higher than the cumulative incidence of all diagnosed COVID-19 cases that was reported over the same time period (0.37%, 41,152/ 11,081,000 cases, data cutoff on February 17, 2020) (Yu,Ouyang et al. 2020). The Chinese

Center for Disease Control and Prevention described the epidemiological characteristics of 72,314 COVID-19 cases in mainland China as of February 11, 2020. They reported that 107 patients (0.5%) had cancer, and 6 of them died. The case fatality was 5.6%, which is higher than the overall reported case fatality (2.3%) from COVID-19 (Novel, 2020). Similarly, the WHO-China Joint Mission on COVID-19 identified significantly higher case fatality amongst patients with pre-existing malignancy (7.6%) compared with patients without comorbid conditions (1.4%) (Report,2020). In the series by Liang et al., cancer was associated with higher risk of severe events (i.e., admission to the intensive care unit, invasive ventilation, or death seen in 7 of 18 patients [39%] with cancer vs. 124 of 1,572 patients [8%] without cancer; p = .0003) (Liang, Guan et al. 2020). These findings have been corroborated internationally, as an Italian study assessing the case fatality of COVID-19 found that amongst 355 patients who died and underwent detailed chart review, 72 (20.3%) had active cancer (Onder, Rezza et al. 2020). While these analyses are preliminary and require validation from larger international cohorts, several factors could account for an elevated risk for acquiring COVID-19 and consequent complications amongst cancer patients, including frequent hospital visits and admissions, immunocom-promised state, advanced age, and poor functional status (Yu, Ouyang et al. 2020). In our study the small study sample size, patients in cancer group characterized similiar results a higher death rate and more severe course.

While having cancer and receiving certain cancer therapies remain plausible risk factors for both contracting SARS-CoV-2 infections and having more severe COVID-19 outcomes, existing data do not yet answer these questions. Notably, the early publi-cations in this area include data from a very small number of patients, but have nonetheless had substantial effects. The cited study by Liang et al. is often used as justification for 'a possible increased risk' associated with chemotherapy, despite only two patients in this analysis receiving systemic chemotherapy within the month before COVID-19 diagnosis. Data from Yu et al. have been used to support universal screening of patients with lung cancer for SARS-CoV-2 infections, even though this cohort contained seven patients with lung cancer, six of whom did not have laboratory-confirmed COVID-19 (Yu, Ouyang, 2020). It is difficult to imagine any other context in which data from such small, highly selected, and often flawed case series would be published in major journals and have such a substantial influence on clinical practice and policy.

Patients with lung cancer usually have compromised lung function with associated dyspnea, cough, and polypnea. They might be at higher risk of severe forms of COVID-19 infection due to decreased pulmonary function. In the aforementioned studies that evaluated COVID-19 in a small cohort of patients with cancer, the investigators found that lung cancer was the most frequent type of malignancy in this cohort of COVID-19 – infected patients (five [28%] of 18 patients). Whether this reflects a true increase in the susceptibly of the lung cancer population to SARS-CoV-2 infection or is simply due to the fact that lung cancer is the most cancer in China is yet to be determined (Feng, Zong, 2019). Lastly, other potential causes for the respiratory deterioration of NSCLC patients, which could mimic COVID-19 symptoms, must be considered; these may include obstructive pneumonia, pleural or pericardial effusion, pulmonary embolism, and heart failure; therefore, rapid access to SARS-CoV-2 assays is of utmost importance. Postponing anticancer treatment should be considered according to the patient's risk of infection, performance, and clinical status. Currently, there are no clinical trials to examine the safety and efficacy of antiviral prophylaxis for SARS-CoV-2 in cancer patients.

COVID-19 and the cancer patient is based on the latest information and knowledge available to the medical community at this time. As the COVID-19 pandemic continues to evolve and unfold, it is likely that the health care community will be faced with additional, yet unknown challenges. It is imperative that we stay abreast of all deve-lopments with COVID-19 to provide our most vulnerable COVID-19 and the cancer patient with the care needed for their best chance of to optimal health care.

As the size of this cohort is limited, the statistical analysis results should be interpreted with caution, and the P value without statistical significance does not necessarily reflect the exact situation of the whole population. Larger sample size of clinical studies is needed to

elucidate the epidemiology, clinical characteristics and prognostic factors of COVID-19. Moreover, due to the outcomes data of patients have shown that, the prognosis comparation between the lung cancer group and the nonlung cancer group is much worse.

CONCLUSIONS

The study groups infected with SARS-CoV-2 (with and without lung cancer) differed significantly in several aspects. In group of patients with lung cancer dominated women. Patients of malignancy group showed more underlying comorbidities, such as hypertension and hepatopathy. Patients of the lung cancer group tend to show more frequency of chest pain, oppression in chest and anorexia. Another difference was blood laboratory analysis. The lung cancer group showed decrease in white blood cells, neutrophils, lymphocytes, aspartate aminotransferase and C-reactive protein compared to the non-lung cancer group. The most important difference is the mortality rate in the studied groups. Death occurred significantly more frequently in the group of malig-nancy patients.

Considering the above aspects, it is safe to say that the coexistence of COVID-19 and lung cancer may change the diagnosis, treatment and prognosis of both diseases.

SUMMARY

Our review on COVID-19 and the cancer patient is based on the latest information and knowledge available to the medical community at this time. As the COVID-19 pandemic continues to evolve and unfold, it is likely that the health care community will be faced with additional, yet unknown challenges. Lung cancer associated with COVID-19 is a disease that significantly worsens prognosis. Therefore, patients should be isolated and protected against potentially possible coronavirus disease infection (COVID-19). Early diagnosis, timely isolation, and appropriate treatment are the keys in fighting this infection.

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