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Clinical and Imaging Characteristics of Cancer Patients with COVID-19: A Pilot Study

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Abstract

Background: Malignancy is a known risk factor of coronavirus disease 2019 (COVID-19) severe involvement. Information about this infection in patients with cancer is limited.
Objectives: This study aimed at reporting the clinical and imaging characteristics of COVID-19 infection in patients with cancer.
Methods: All the patients were known cases of a solid tumor with COVID-19 infection in one center, between February and May 2020. Clinical presentation and imaging involvement of COVID-19 infection in addition to cancer features were documented from medical records/patient interviews.
Results: Thirty-one patients with solid tumors and COVID-19 involvement were included. The most prevalet presentation was fever, cough, and myalgia. Breast and gastrointestinal malignancies were the most common cancer types. The mortality rate was 22.5% and all deceased patients suffered from stage 4 of their underlying cancer disease. Lung computed tomography scan (CT scan) features in these patients were not different from the non-cancer patients with COVID-19.
Conclusions: COVID-19 involvement in patients with cancer seems to be more severe with higher mortality rates especially in patients with other comorbidity and in metastatic cases. Treatment modifications during the pandemic era sound to be logical in decreasing the infection rate.

Keywords: Cancer, SARS-CoV-2, COVID-19, CT Scan, Infection

1. Background

After the identification of SARS-CoV-2 (COVID-19) infectious disease in December 2019 in China, its effect on our lives became obvious as a health emergency. Preliminary studies have shown that people with comorbidities, especially cancer, are at higher risk for severe infection (1). Patients with Cancer are expected to be more prone to severe infections due to their immunodeficiency conditions compared to the general population. However, there are limited data about the SARS-CoV-2 infection in this group. The effect of factors such as the type of cancer, its stage, and related treatments on this infection is unknown.

2. Objectives

This study was conducted to describe the characteristics of the patients with cancer and their imaging features, who were infected by SARS-CoV-2 and referred to our clinic during the pandemic era.

3. Methods

3.1. Patient Population and Study Design

It is a retrospective study focusing on cancer patients with COVID-19 infection admitted in Shohada-e-Tajrish hospital in Tehran, Iran. It is a general hospital that admitted COVID-19 patients from the first days of the pandemic while chemotherapy and radiotherapy services were also provided. The records of the patients were collected from February to May 2020. Patients with COVID-19 infection and a history of solid tumors were included. The patient's data consisted of cancer type, stage, and treatments in addition to clinical, laboratory, and imaging findings

of SARS-CoV-2 infection which were extracted from medical records. Information about deceased patients was obtained from their medical files or companions.

All the patients underwent a low-dose chest CT scan during the disease course. Low dose chest CT images were obtained at 1.5 mm slice thickness and processed in lung parenchymal and mediastinal reformat. An expert radiologist reviewed these images and recorded the following imaging features in a datasheet: unilateral/bilateral involvement, ground-glass opacities/ consolidation/ nodular opacities/ bronchial wall thickening; with associated pleural effusion, lymphadenopathy.

3.2. Study Definitions

COVID-19 diagnosis was established based on the clinical findings in addition to positive chest CT scans and/or positive reverse transcription polymerase chain reaction (RT-PCR) tests due to the limited number of Real-time PCR Kits in the first days of the epidemic in Iran. Patients with normal lung CT scans but positive RT-PCR were also included in the current study. Disposition of the disease is categorized based on the need to be hospitalized or intensive care unit (ICU) admission. The severity of the disease was considered mild when a patient was managed in an outpatient setting, moderate when the patient needed to be hospitalized, and severe when the patient required mechanical ventilation or had death outcomes. The patient's outcome was defined as death or recovery if he/she died of infection or was discharged after the symptoms improved. Patients were asked about using the mask outdoors from the beginning of the pandemic until the onset of the disease. Considered comorbidities were the patient's body mass index (BMI) and their previous history of ischemic heart disease, diabetes mellitus, and hypertension. The ethic committee of Shahid Beheshti University of Medical Sciences approved this study.

3.3. Statistical Analysis

Categorical variables are presented as numbers (percentage) and continuous variables are presented as mean (standard deviation). Regression statistical test (Binary Logistic) with a confidence level of 95% (P-value < 0.05) was conducted to investigate the effect of risk factors on COVID-19 indued death. Statistical analysis was performed by using SPSS software (version 24; IBM, New York, NY).

4. Results

Data of 31 patients with cancer were collected. The mean age of considered patients was 56 (range of 31 - 88) years. The most common symptom of COVID-19 at presentation was fever (58%) followed by cough (45.1%) and myalgia (38%) (Table 1). The infection of 8 patients was mild and managed as an outpatient, while others (23 cases) were admitted to the hospital.

Two patients were admitted to the hospital with a decreased level of consciousness. Among the hospitalized patients, 6 patients were admitted to ICU. Seven patients died of infection, 5 of them were admitted to the ICU and 2 inwards. All deceased patients were at stage 4 of their cancer disease and 4 had gastrointestinal malignancies.

Table 1. Clinical Patients' Characteristics (N:31)

Characteristic	No. (%)
Age	56 (range: 31 - 88)
Sex	
Male	15
Female	16
BMI	
< 20	7 (22.5)
20, 25	8 (25.8)
25, 30	12 (38.7)
30 <	4 (12.9)
Comorbidity	13 (41.9)
Ischemic heart disease	6 (19)
Diabetes mellitus	3 (9.6)
Hypertension	2 (9.6)
Hypertension + diabetes	2 (6.4)
Used mask	20 (64.5)
Signs and symptoms	
Fever	18 (58)
Cough	14 (45.1)
Myalgia	12 (38.7)
Nausea & vomiting	9 (29)
Cough	8 (25.8)
Sweating	7 (22.5)
Headache	6 (19.3)
Chill	6 (19.3)
Diarrhea	5 (16.1)
Disposition	
Outpatient	8 (25.8)
Hospitalized	23 (74.1)
ICU addition	6 (19.3)
Outcome	
Recovery	24 (77.4)
Death	7 (5 of them in ICU) (22.5)

The risk of death in cases with abnormal body mass in-

dex (BMI) was about 1.9 times higher than normal ones, however, it was not statistically significant (P-value: 0.59, OR: 1.87). Other aforementioned comorbidities consisting of ischemic heart disease, hypertension, and diabetes mellitus were observed in 13 patients. The risk of death in cases without diabetes mellitus (DM) was about one-third of the diabetic patients (P-value: 0.322, OR: 0.70). The most common underlying morbidity was ischemic heart disease (IHD). Patients with IHD had a 1.6 times higher risk of death than the normal group (P-value: 0.701, OR: 1.58). The relationship between death and the number of abnormal CT scan features was investigated. It was found that with increasing any type of feature, the chance of death increases 2.3 times, although it was not significant (P-value: 0.08, OR: 2.27). Hypertension had low correlation with infected patients' death (P-value: 0.91, OR: 0.14). However, the obtained odds ratios were statistically non-significant which could be due to the low sample size.

Based on the patient's self-claiming, 64.5% of them used a mask as protection before infection during the pandemic.

The most common cancer types were breast cancer (25.8%) and gastric cancer (19.3%). However, gastrointestinal malignancies were the prevalent type (35.4%). Among the patients, 48.3% were at stage 4 of cancer disease and the others were at stage 1to 3. Three patients had simultaneous pulmonary metastasis.

Only 8 patients were under follow-up step after their previous cancer treatments, others infected during chemotherapy (13 cases), radiotherapy (5 cases), or chemoradiation (5 cases). The mean time interval between the last chemotherapy (or concurrent chemotherapy) session and the onset of COVID-19 symptoms was 9 days (Table 2).

The mean value of the white blood cell count (WBC) of the patients was 6.6×10^9/L. A total of 29 patients underwent a chest CT scan. The findings are summarized in Table 3. The chest CT scan of 5 patients with positive SARS-COV-2 RT-PCR was normal. Pulmonary embolism and COVID-19 involvement of lung were found concurrently in the chest CT scan of a patient with rectal cancer and for another patient with a metastatic bladder tumor who was admitted to the emergency room with deep vein thrombosis as the first presentation of infection of SARS-COV-2. One patient with a history of chondrosarcoma who was under follow-up, presented with COVID-19 and pulmonary metastasis simultaneously that was established based on tissue sampling.

Table 2. Baseline Characteristics of the Patients with Cancer (N:31)

Characteristic	No. (%)
Cancer type	
Breast	8 (25.8)
Gastric	6 (19.3)
Lymphoma & thymoma	3 (9.6)
Sarcoma	3 (9.6)
Rectal cancer	2 (6.4)
Esophagus cancer	2 (6.4)
Brain tumor	1 (3.2)
Unknown primary tumor	1 (3.2)
Head and neck cancer	1 (3.2)
Uterine	1 (3.2)
Bladder	1 (3.2)
Colon	1 (3.2)
Lung	1 (3.2)
Cancer stage (except one brain tumor)	
Stage 1 - 3	15 (48.3)
Stage 4	15 (48.3)
Time between the last cancer treatment and onset of COVID-19, days	
Mean time of last chemotherapy (or concurrent chemotherapy)	9.1
Current cancer treatment	
Radiotherapy	5 (16.1)
Chemotherapy	13 (41.9)
Chemoradiation	5 (16.1)
Follow up	8 (25.8)

Table 3. Chest CT Scan Features of the Patients (N = 29)

Characteristics	No. (%)
Normal appearance	5 (17.2)
Presence of GGO	7 (24/1)
Presence of consolidation	3 (10.3)
Presence of GGO + consolidation	9 (31)
Bilateral lung disease	14 (45.1)
Lymphadenopathy	2 (6.4)
Pleural effusion	4 (13.7)
Pulmonary nodule	5 (17.2)
Bronchial wall thickening	4 (13.7)
Pulmonary metastasis	3 (31)

5. Discussion

This case series included 15 males and 16 females with a mean age of 56 (range: 31 - 88). In other case series of cancer patients with COVID-19 the reported mean age was more than 60 years (2-10) except one study, consisting of the hematologic malignancies, which reported the mean age of the patients was 35. Gender differences have been

seen in previous studies and male gender has been predominant, but in the present study, female patients were the most which could be related to the most frequency of breast cancer in our clinic.

However, 80% of patients were under treatment (Chemotherapy, Radiotherapy, or Chemoradiation) at the time of diagnosis of COVID-19. However, in a previous study, only 28.6% of the patients had a nosocomial infection (3) but in another cohort study of 218 patients, 61% of deceased cases interacted with health care workers (5). before any treatment decisions, physicians should consider that, more hospitals visits may expose patients to infection.

The clinical presentation of COVID-19 in our patients was not different from the general population. Fever and cough were the most symptoms. Nausea and vomiting were seen in 29% of our cases while the mean interval of last chemotherapy and onset of COVID-19 was 9 days. However, chemotherapy-induced nausea and vomiting are expected to occur within 5 days after chemotherapy. Therefore, it is possible that nausea and vomiting of COVID-19 are considered chemotherapy-induced side effects. Patients should be educated about the presentations of COVID-19 and chemotherapy sequelae.

This study consisted of infected cancer patients that were managed in the hospital or outpatient settings. Patients who did not need to be hospitalized were categorized as a mild disease. It was found that 23, 6, and 7 of our patients with cancer were admitted to the hospital, ICU/ventilated, and died of disease, respectively. Two patients presented with loss of consciousness at first. In another case study, no patient was required to ventilation or ICU admission, and in the other, 53.6% of the patients developed a severe infection, and 28.6% died of the infection (3, 4). In a cohort study consisting of 218 cancer patients with COVID-19, a mortality rate of 25% was reported for patients with solid tumors (5).

This study demonstrated that 12 (38.7%) of included patients had other comorbidities in addition to cancer. The most prevalent comorbidity was ischemic heart disease. Only one patient with severe infection had another comorbidity. According to the finding of the present study and the previous reports, cancer patients with other underlying diseases need more attention during the pandemic. Revised consensuses and guidelines should be considered in the management of patients with cancer during the pandemic era (11).

In previous studies, lung cancer was the most common type of infected cancer among the patients (3-7, 12). In the other study in 37 patients, the most commonly reported cancer was colorectal (29.7%) (2). In a cohort study consisting of 800 cancer patients with COVID-19, the most common type of cancer was the digestive tract (13). In the presented study, breast cancer was the most seen type. On the other hand, gastrointestinal cancers consisting of gastric, esophagus, and colorectal were the most cancer types. This discrepancy could be due to the fact that lung cancer is not a prevalent type among the malignancies that are referred to the oncology clinic of our hospital. Eventually, it cannot be stated with certainty that a specific type of cancer can make patients more predisposed to infection or severe infection, but lung tissue damages caused by cancer probably make it more sensitive to infection.

Only 8 (25.8%) patients were under follow-up of their malignancies, the others were receiving oncology treatments. COVID-19 involvement occurred 9 days after the last chemotherapy or concurrent chemotherapy of chemoradiation in 58% of cases. Five (16.1%) patients were developed COVID-19 during radiotherapy. In 2 studies by Mehta et al. that were conducted on 218 and 37 patients, most of the patients were receiving chemotherapy or radiotherapy (2, 5). On the other hand, a cohort study contained 800 patients, showed that 35% of cases received chemotherapy for 1 month before COVID-19 involvement and chemotherapy had no effect on the mortality rate (13).

Only 8 patients in our study had a normal BMI, others were overweight/obese or underweight. It is revealed that obesity not only is a risk factor for cancer development (14, 15) but also is a risk factor for COVID-19 involvement and the severity of the disease (16-18). We did not find any significant correlation between any underlying disease and COVID-19 death but it could be due to the small sample size of the study population.

It has been clear that thrombosis and microangiopathy are important components of COVID-19 pathogenesis (19). The incidence of thrombosis among COVID-19 patients is higher than in the general population (20, 21). On the other hand, malignancy itself is a major cause of thrombosis in cancer patients (22). Thromboembolic events were found in 2 patients, one with rectal cancer and the other one with a bladder tumor. More research are required to show if there is any correlation between increasing the chance of thrombosis and history of malignancy for COVID-19 infected cases.

This study presented that a combination of ground-glass opacities and consolidation together is the most common imaging finding of COVID-19 infection in cancer patients, followed by ground-glass opacities alone. Among the patients, 45.1% had bilateral involvement. On the other hand, nodular opacities, pleural effusion, and lymphadenopathy are not typical features in involved individuals (23). Bilateral peripheral ground-glass opacities and consolidations are the imaging hallmark of COVID-19 infection in the non-cancer population too (21). It seems that imaging characteristics of immunosuppressed patients with a previous history of solid tumors do not significantly different compared to the general population. Moreover, a combination of low-dose CT findings and clinical features

of infection can help in prompt diagnosis of infection like otherwise healthy individuals.

5.1. Conclusions

COVID-19 involvement in cancer patients seems to be more severe with high mortality rates especially in patients with other comorbidity and in metastatic cases. Treatment modifications during the pandemic era sound to be logical in decreasing the infection rate. As the first step, this can be achieved by decreasing these patients' hospital exposure.

Footnotes

Authors' Contribution: A.J: Study concept and design, acquisition of data, and drafting of the manuscript.Z. MF: The acquisition of data and editing of the manuscript. Z.S: The acquisition of data and drafting of the manuscript. A.R: The acquisition of data and drafting of the manuscript. S.M: The acquisition of data and editing of the manuscript. A.F: The acquisition of data and editing of the manuscript. M.MF: The acquisition of data and editing of the manuscript.

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Ethical Approval: IR.SBMU.REC.1399.012. (Link: ethics.research.ac.ir/EthicsProposalView.php?id=153123)

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