

Characteristics and outcomes of patients with cancer and COVID-19: results from a cohort study

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Introduction

The COVID-19 pandemic has transformed clinical care around the world with elective procedures being postponed and regular medical care being compromised by patient isolation and repeated testing. Data on the impact of COVID-19 on the clinical course in cancer patients is still limited [1]. The incidence of SARS-CoV-2 infections was shown to be increased in patients with cancer compared to the general community, and in some, but not all, studies affected patients were more likely to deteriorate into severe illness than those without cancer [2–4].

Patients with hematologic malignancies may harbor the highest risks due to the inherent immunosuppression of the underlying disease and immunosuppressive treatments [1,5]. Previous studies on the clinical course of hematologic patients with concurrent COVID-19 showed a high fatality rate [3,6]. The aim of the present study was to analyze the characteristics and outcomes of patients with cancer and COVID-19 diagnosed at the peak of the 2020 pandemic in the area of Munich, Germany.

Material and methods

All patients with cancer and a laboratory-confirmed diagnosis of COVID-19 treated in four collaborative hematology and oncology centers from the greater Munich area between 01 March and 31 May 2020 were included in this study. The medical records were retrospectively reviewed. We obtained written informed consent for scientific evaluations when feasible. For critically ill patients informed consent was waived by the Internal Review Board due to the urgency of the matter. The study was approved by the Internal Review Board and adheres to the tenets of the declaration of Helsinki.

At the onset of the COVID-19 pandemic in Germany in early March 2020, only patients with symptoms suggestive of COVID-19 were tested for the presence of SARS-CoV-2 RNA

in a deep nasal and pharyngeal swab specimen. As from 01 April 2020 all hospitalized patients were screened for SARS-CoV-2 RNA at our institutions by Roche Cobas 6800 polymerase chain reaction (PCR).

To determine the immune competence of individual patients, absolute numbers of CD4+ T-cells, CD8+ T-cells, CD19+ B-cells, and CD16+/CD56+ NK cells were determined by flow cytometry in the peripheral blood.

The Chi-square test was used for comparison between groups.

Results

A total of 17 patients, 12 (71%) with hematologic malignancies and 5 (29%) with solid tumors, were included in the study. SARS-CoV-2 infections were diagnosed between 24 March and 11 April 2020. Patients characteristics are summarized in Table 1.

Initial findings

Twelve of 17 patients (71%) had symptoms consistent with COVID-19 (Table 1). The median age at diagnosis of SARS-CoV-2 was 72 years (range, 42–81) in patients with hematologic malignancies and 37 years (range, 27–82) in solid tumors. The test for SARS-CoV-2 was performed at the onset of symptoms in 9 of 12 hematology patients (75%) and as a routine measure in three. CT scans revealed atypical bilateral pneumonia in 9 of 11 patients evaluated. Three of 5 patients with solid tumors had symptoms of COVID-19 while two were routinely tested for SARS-CoV-2 (Table 1).

Clinical course of SARS-CoV-2 infections

Seven of 12 hematologic patients (58%) developed progressive respiratory failure, of whom two survived. Two patients with uncontrolled acute myeloid leukemia (AML) and

Table 1. Patient characteristics, treatment, and outcomes.

No.	Sex	Age (years)	Diagnosis	Prior antineoplastic treatment	Status at COVID diagnosis	Comorbidity	Time from antineoplastic treatment to positive SARS-CoV-2 result (d)	Initial symptoms, reason for testing	Bilateral pneumonia	Mechanical ventilation	Further complications	Outcome COVID-19	Time from 1st positive PCR to next treatment (d)
1	M	72	Multiple myeloma	4 × CyBorD, cydo, HD-Mel + ASCT	PR	Arterial hypertens.	8	Sore throat	Yes	No	None	Resolved	none
2	M	72	Multiple myeloma	3 × VRd, cydo, HD-Mel + ASCT	VGPR	None	18	Fever	Yes	Yes	ARDS, pulmonary embolism; secondary graft failure; infarction of left middle cerebral artery	death	n.a.
3	M	73	Multiple myeloma	Bortezomib + RT	n.d.	Arterial hyperten., diabetes, depression	10	Deteriorat. of general condition, fever	Yes	No	Respiratory failure	Death	n.a.
4	M	68	Multiple myeloma	3 × CyBorD, cydo, HD-Mel + ASCT, LenDex	Relapse	Atrial fibrillation	0	Fever	Yes	No	Stroke	Resolved	86
5	F	62	Multiple myeloma	4 × BorCyDex	PR	Arterial hypertens., fractures vertebrae	8	Dyspnea, diarrhea,	Yes	No	None	Resolved	42
6	F	69	sAML	5-azacitidine, vyxeos® induction	Blast persistence	Diabetes, arterial hypertens., obesity	12	Fever	Yes	No	Fungal pneumonia	Death	n.a.
7	F	81	APL	ATRA/ATO hydroxyurea dexameth.	Differentiat. syndrome	Hypothyreosis, migraine	0	Fever	Yes	Yes	Duodenal ulcer bleeding; BAL positive for HSV1-DNA and aspergillus antigen	Death	n.a.
8	F	78	tAML	Decitabine	SD	Emphysema, prior Hodgkin lymphoma, prior colorectal cancer	8	Routine	Yes	No	None	Resolved	33
9	F	74	sAML	Decitabine	PD	Depression, gastric ulcer disease, multiple prior infections	277	Routine	No	No	Transfusion dependent thrombocytopenia; intracerebral hemorrhage	Death	n.a.
10	F	42	CML lymphoid last crisis	Prephase cyclo/dexa, induction with vincr/dexa/ imatinib/ith therapy	Hematologic response	Arterial hypertens., smoking	0	Routine	Yes	No	None	Resolved	39
11	F	42	PCNSL, HLH	Rituximab/HD-MTX/ara-C/thiotepa for PCNSL, prephase cyclo/dexa, induction with vincr/dexa/ imatinib/ith. therapy/VP16/ pred/ dexa/CSA for HLH	PR	Autoimmune hepatitis, liver cirrhosis	24	Cough, fever	Yes	No	None	Resolved	45
12	M	80	Follicular lymph.	Obinutuzumab bendamustin c1, obinutuzumab c2d1	Clinical response	Arterial hypertension, diabetes, prostate cancer	31	Fever, dyspnea	Yes	Yes	ARDS	Death	n.a.
13	M	37	Germ cell tumor	4 × VIP, 1 × TIP/2 × TI + 3 × HD-CE/ASCT, 2 × TIP	PD	None	5	Fever	Yes	No	None	Resolved	28
14	M	31	Germ cell tumor	None	n.a.	None	n.a.	Ageusia, dysphagia	No	No	None	Resolved	8
15	M	27	Germ cell tumor	None	n.a.	None	n.a.	Routine	No	No	None	Resolved	16
16	F	79	Pancreatic cancer	Gemcitabine	SD	Gastritis,	9	Fever, dyspnea	Yes	No	None	Resolved	43
17	F	82	NSCLC	Nivolumab	SD	Parkinsons disease, atrial fibrillation, COPD, diabetes, renal insufficiency, arterial hypertension, depression	15	Routine	No	No	None	Resolved	57

VRd: bortezomib, cyclophosphamides, dexamethasone; HD-Mel: high dose melphalan; ASCT: autologous stem cell transplantation; RT: radiotherapy; APL: acute promyelocytic leukemia; PCNSL: primary CNS lymphoma; HLH: hemophagocytic lymphohistiocytosis; Cyclo: cyclophosphamide; pred: prednisolone; dexa: dexamethasone; TIP: paclitaxel, ifosfamide, cisplatin; Ti: paclitaxel, ifosfamide; VIP: etoposide, ifosfamide, cisplatin.

multiple myeloma, respectively, were not ventilated according to the patient's decision and died of respiratory failure. Three patients were mechanically ventilated for a median duration of 20 days (range 7–32 days). All died 9, 25, and 63 days following the diagnosis of COVID-19 and 7, 21, and 36 days following the start of mechanical ventilation, respectively. Another patient with sAML who had not responded to five cycles of decitabine never experienced respiratory symptoms and succumbed to massive intracerebral hemorrhage 11 days after diagnosis of COVID-19. Thus, 6 hematologic patients (50%) died a median of 10 days (range, 9–63 days) after diagnosis of COVID-19 and 16 days (range, 9–63 days) after the onset of symptoms. Two patients, one each with multiple myeloma and primary central nervous system lymphoma, had subfebrile temperatures or mild cough for 15 and 25 days after the first positive PCR, respectively, before they experienced respiratory failure.

Three of 5 patients with solid tumors were hospitalized for COVID-19 but none experienced respiratory deterioration. All patients recovered.

Outcome and altered immunologic parameters

Six out of 17 patients proved positive for SARS-CoV-2 at repeated testing for a median of 18.5 days (range, 12–58 days). The median time to negativity was 22 days (range, 8–36 days).

The cellular immune status was determined in four patients with hematologic malignancies and in one with germ cell tumor (GCT), at a median of 12 days (range, 5–19) following the diagnosis of SARS-CoV-2. The median neutrophil count was 2900/ μ l (range 0–11,000/ μ l, normal range 1800–6200/ μ l), and the median lymphocyte count 481/ μ l (range 74–6890, normal range 1100–3200/ μ l). Further, the median CD4-, CD8-, NK-cell, and B-cell count was 110/ μ l (50–1530, normal range 580–1960/ μ l), 400/ μ l (10–1020, normal range 280–900/ μ l), 20/ μ l (2–1460, normal range 35–850/ μ l) and 30/ μ l (0–1300, 70–800/ μ l), respectively. Four of 5 patients eventually cleared SARS-CoV-2 RNA after a median of 24 days (range, 19–39). A patient with multiple myeloma remained positive during repeat testing and died of respiratory failure on day 63.

Comparing cancer and non-cancer patients

Of 4800 patients admitted to Red Cross Hospital Munich from 1 March to 31 May, 345 (7.2%) were diagnosed with cancer. Overall, 102 of 4800 patients (2.1%) tested positive for SARS-CoV-2, 11 of 345 patients (3.2%) with and 91 of 4455 patients (2.0%) without cancer. The difference between both groups is not statistically different ($p = 0.067$). However, 5 of 345 cancer patients (1.4%) died of COVID-19 compared to 20 of 4455 patients (0.4%) with a non-cancer diagnosis ($p = 0.002$). Finally, 5 of 11 cancer patients with COVID-19 (45.5%) died compared to 15 of 80 non-cancer patients and COVID-19 (18.8%) ($p = 0.044$). Thus, cancer patients had a significantly higher risk of dying from COVID-19 than patients without cancer.

Restart of systemic therapy

Ten patients started or restarted chemotherapy after recovery from COVID-19 after a median of 39 days (range, 8–86 days). Two GCT patients were diagnosed with SARS-CoV-2 before the start of curative treatment with 3 cycles of PEB (cisplatin, etoposide, bleomycin). One of both developed an atypical pneumonia negative for SARS-CoV-2 under PEB so that bleomycin was replaced by ifosfamide in cycle 3. The 3rd GCT patient went through an asymptomatic SARS-CoV-2 infection and did not experience any specific toxicity after salvage chemotherapy was initiated on day 28.

A 42-years old female with lymphoid blast crisis of chronic myelogenous leukemia (CML) experienced fever and mild cough during induction therapy. Chemotherapy was withheld and restarted 39 days following the first positive test but imatinib was continued over the entire period without any complication. Decitabine/venetoclax were restarted in a patient with tAML 33 days, and azathioprine in a patient with hemophagocytic lymphohistiocytosis 45 days after diagnosis of COVID-19. Further, lenalidomide/dexamethasone and BorCyDex were safely restarted in two patients with multiple myeloma 86 and 42 days following the first positive test, respectively. All patients with solid tumors (re)started anti-neoplastic therapy without any specific toxicity.

Discussion

There are some remarkable findings from our study on patients with cancer and COVID-19. First, the case fatality rate in patients under antineoplastic therapy is 35% overall and 50% in patients with hematological malignancies. This is similar to results from a recent study on 13 patients with hematologic malignancies reporting a case fatality rate of 62% with a median survival of 11 days from onset of coronavirus-related symptoms [7]. Other studies on patients with hematological malignancies found case fatality rates of 37% and 50%, respectively [3,8]. However, uncontrolled underlying diseases may have contributed to the fatal outcome in our series as patients with AML were either refractory to prior treatment ($n = 1$), died of intracerebral hemorrhage in the presence of prolonged thrombocytopenia or of ischemic cerebral infarction ($n = 2$), experienced a severe differentiation syndrome as a result of therapy with ATRA ($n = 1$) or also suffered from fungal pneumonia ($n = 1$). Of note, cases of severe intracranial hemorrhage in critically ill patients with COVID-19 have also been reported recently [9,10].

Moreover, at the largest of the participating institutions (Red Cross Hospital Munich), cancer patients had a significantly higher risk of dying from COVID-19 than patients without cancer.

Second, antileukemic therapy can be safely restarted at least in a proportion of patients with acute leukemia. Notably, imatinib was given throughout the entire course of COVID-19 in a patient with lymphoid blast crisis from CML. Thus, treatment with tyrosine kinase inhibitors (TKI) may be safely continued as also shown by recent case reports [11,12]. Based on our experience chemotherapy can be safely

restarted in patients with two consecutive negative PCR tests and if they are symptom-free for at least 48 h.

Third, in terms of cellular immunity all analyzed patients that eventually recovered showed a marked decrease of either lymphocytes, granulocytes, or both. Thus, at least in this small cohort, the level of immunosuppression did not correlate with the severity of COVID-19.

Finally, apart from small patient numbers younger age and controlled underlying diseases may have contributed to the superior outcome of patients with solid tumors. Previous studies reported an increased risk of severe or even fatal outcome of COVID-19 in patients with uncontrolled cancer [1,13,14], and this may particularly be true in patients with hematologic malignancies [3,5,8,15]. Thus, effective treatment of the underlying malignancy seems critical.

In contrast to our findings, recent results from a matched cohort study indicate similar outcomes between patients with and without cancer and COVID-19 [4]. However, the percentage of patients with hematologic malignancies was markedly lower than in our cohort (36% compared to 70%) as was the number of patients receiving cytotoxic cancer treatment (44% compared to 82%). Thus, the higher number of patients at high risk included in our study may explain the differences in outcomes between both studies. Some studies found recent antineoplastic therapy to be a risk factor for adverse outcomes [16] while others did not [3,14,17]. However, in our cohort 9 of 14 patients (64%) resolved their infection despite having received antineoplastic therapy most recently indicating a limited impact of prior antineoplastic therapy on the outcome of COVID-19. By contrast, given the 50% case fatality rate in patients with hematological malignancies, delaying/discontinuing chemotherapy seems appropriate at least in this high-risk group as well as in patients with solid tumors undergoing intensive chemotherapy [1]. Therefore, routine testing for SARS-CoV-2 is mandatory for in-patients at our institution.

Limitations of the present study are its retrospective design and the small sample size. Also, the cohort was not population-based as the number of all cancer cases in the greater Munich area during the study period is not available. However, our analysis provides some additional new data on the clinical outcomes of patients with cancer and COVID-19.

In conclusion, this study underlines, that individuals with hematological malignancies are at higher risk for a severe course of COVID-19 while the prognosis may be more favorable in patients with solid tumors. Antineoplastic therapy can be safely restarted after recovery from SARS-CoV-2.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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