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Cancer and Covid-19 in the Department of Internal Medicine and Medical Oncology at the National Teaching Hospital Hubert Koutoukou Maga of Cotonou, about 4 Cases: A Review of the Literature

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Abstract

Coronavirus Disease-19 (COVID-19) manifests itself by a respiratory attack that can go from mild to severe forms. The factors favoring the severe forms are age, arterial hypertension, diabetes mellitus, and cancer. We report 4 cases of COVID-19 on cancer, followed in the Department of Internal Medicine and Medical Oncology of National Teaching Hospital Center Hubert Kougougou Maga (NTHC-HKM). Case 1: A hypertensive 65-year-old female patient with a severe form of COVID-19 on an FIGO (International Federation of Gynecology and Obstetrics) IVB endometrioid adenocarcinoma with pulmonary metastasis: unfavorable evolution under treatment with death. Case 2: A 56-year-old hypertensive patient with severe COVID-19 with pulmonary metastatic recurrence of SBRIII, HER2 positive invasive ductal carcinoma of the left breast: favorable evolution with cure of COVID-19, subsequent death related to active tumor. Case 3: A 37-year-old patient with a moderate form of COVID-19 with hepatocellular carcinoma complicating post alcoholic cirrhosis, CHILD C: favorable evolution with cure of COVID-19, patient lost to follow-up. Case 4: A 56-year-old patient, hypertensive, type II diabetic, presenting a severe form of COVID-19 on a field of ovarian serous adenocarcinoma of high grade FIGO IV A with pleuro-pulmonary metastasis: favorable evolution with cure of COVID-19, subsequent stroke, patient followed in

palliative home hospitalization. The diagnosis of COVID-19 in cancer with pulmonary metastases is difficult. The pulmonary location of tumors seems to be a factor favoring severe forms.

Keywords

COVID-19, Cancer, NTHC-HKM

1. Introduction

Since December 2019, SARS-CoV-2 (severe acute respiratory syndrome corona virus 2) has spread in two successive waves around the world [1]. On March 11, 2020, the World Health Organization declared the 2019 coronavirus disease (COVID-19) a pandemic [2]. According to data compiled by the U.S. Johns-Hopkins University as of May 19, 2021, 163.61 million people have tested positive for COVID-19 worldwide and nearly 3,390,000 people have died [3].

This disease is characterized by rapid human-to-human transmission of contaminating droplets [4]. It can affect all ages [5]. Patients most at risk of developing complications are frail patients over 65 years of age and those with co-morbidities (hypertension, diabetes mellitus, obesity), as well as immunocompromised patients, including those being treated for cancer [2] [4]. Cancer patients would be likely to develop severe disease during COVID-19, due to immunosuppression related to both the disease and anticancer treatment (chemotherapy, biotherapy, immunotherapy, radiotherapy) [4].

Given the complex and heterogeneous health situations related to COVID-19, the management of cancer patients suffering from COVID-19 represents a challenge especially in low-resource countries with difficulty in reorganizing oncological care [4]. This has an impact on the follow-up and evolution of patients who may develop complications related either to the extension of their cancer or to COVID-19, the outcome of which may be fatal [6].

Through this work, we describe the cases of 4 cancer patients who were followed in hospital and in whom SARS Cov-2 infection was diagnosed in the Internal Medicine and Medical Oncology Department of the National Teaching Hospital Center Hubert Kougougou Maga (NTHC-HKM) of Cotonou.

2. Observations

2.1. Observation 1

Mrs. H.F, 65 years old, hypertensive, known to be on a calcium channel blocker (amlodipine 5 mg), followed in palliative care for a moderately differentiated tubulo-papillary endometrioid adenocarcinoma classified FIGO stage IVB (2018) in terminal stage, with pulmonary metastases. In terms of carcinological care, she was off treatment after 3 cycles of carboplatin AUC 5 + Paclitataxel 175 mg/m², stopped for Grade 4 mucositis diarrhea and vomiting. Follow-up in palliative

care was mainly pain management and transfusion support. During her check-ups, she presented a dry cough with slight dyspnea without desaturation. Biological tests showed an anemia of 8.3 g/dL normocytic (VGM 86.2fL) normochromic (CCMH 34.1%), a predominantly neutrophilic hyperleukocytosis (WBC 8.7 PN 7.56 G) and a disturbed inflammatory balance (CRP: 30.7 mg/l). On the bacteriological and virological level, the GeneXpert test of the gastric tubing fluid for the *Mycobacterium tuberculosis* gene was negative. The covid RT PCR performed on the nasopharyngeal swab came back positive. Chest radiography showed balloon-like images and massive right pleurisy (Figure 1).

The diagnosis of a moderate form of COVID-19 was made (**Table 1**) and the patient was transferred to the severe COVID-19 case management center. The evolution was marked by progressive worsening of dyspnea, and the patient died from a severe form of COVID-19. The duration of management in the center was 10 days, the treatment received was in accordance with the severe protocol (**Table 2**).

2.2. Observation 2

Mrs. A.A aged 56 years hypertensive for 24 years, currently on a combination of converting enzyme inhibitor and calcium channel blocker (Perindopril-amlodipine), followed up for SBR III infiltrating ductal carcinoma of the left breast, RE and RP negative, HER2 positive, Ki67 at 60%. At initial diagnosis in 2017, the tumor was classified as cT3N2M0 (AJCC2018) and the patient had received neoadjuvant chemotherapy followed by left total mastectomy and radiotherapy and had regular follow-up. She was referred to internal medicine in August 2021 for a febrile dyspnea associated with a dry cough, evolving for 3 months.

The physical examination noted an altered general condition with a WHO IPS of 2, a temperature of 36.7°C, a BP of 150/80 mmHg, and a HR of 120 beats/min. Respiratory rate was 46 cycles per minute with an oxygen saturation of 72% on room air. Respiratory distress syndrome (supra-sternal draft, decreased chest expansion) and pleural fluid effusion syndrome (watery dullness in the lower 2/3 of the right lung field) were observed.



Figure 1. Pulmonary metastase of endometrioid carcinoma with massive right pleurisy in the setting of SARS-Cov2 superinfection (Case 1).

Table 1. Definition of the forms of COVID-19 in force in Benin [11].

Simple case	Asymptomatic	Any patient who tests positive for COVID-19 by RT-PCR or RDT, and who is asymptomatic, without respiratory distress and without comorbidities, and under 60 years of age Any patient who tests positive for COVID-19 by RT-PCR or RDT, without comorbidities, under 60 years of age, without respiratory distress and who presents with signs other than respiratory distress.	
	Symptomatic	Any patient testing positive for COVID-19 by RT-PCR or RDT, without respiratory distress but with comorbidities and/or age greater than 60 years.	
	A		
Moderate case	В	Any patient tested positive for COVID-19 by RT-PCR or TDR, with comorbidities and/or age over 60 years without respiratory distress and whose radiological images show pulmonary involvement	
	Grade I	I A: patient under a mask (O ₂ requirement between 1 and 4 L/min)	
		I B: patient under simple face mask (O_2 requirement between 4 and 9 L/min)	
Severe case	Grade II	II A: patient with high concentration mask (O_2 requirement between 9 and 15 L/min)	
		II B: patient with an O_2 requirement >15 L to <50 L (high concentration mask or OHD system)	
	Grade III	III A: patient on OHD system at more than 50 L/min; patient on NIV	
		III B: intubated patient	

Biologically, the hemoglobin level was 13.1 g/dl, and there was a hyperleukocytosis of 8.9 G WBC (6.586 G PNN). Renal and liver function tests were normal. The thoracic CT scan showed multiple bilateral pulmonary nodules of secondary appearance, a large tumor mass in the lower lobe of the right lung with liquid pleural effusion, nodular thickening of the pleura, and multiple mediastinal adenopathies of secondary appearance (Figure 2).

The covid test by RT PCR on nasopharyngeal swab was positive. The diagnosis of pulmonary metastatic recurrence of SBR III ductal carcinoma of the left breast, complicated by COVID-19 was retained.

She was put on NIV and antiretroviral treatment in the center for the management of severe cases of COVID-19 according to the protocol in force in Benin (**Table 2**). Control covid tests performed at D7 and D10 were negative. The patient was declared cured of COVID-19 and transferred for further palliative

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Table 2. Treatment of COVID-19 in force in Benin [11].

	Standard	therapy	Adjuvant therapy	
	Adult	Child	Adult	Child
Simple case	 CHLOROQUINE PHOSPHATE 250 mg or CHLOROQUINE HYDROXIDE 200 mg tablet: 01 tablet every 12 h for 10 days AZITHROMYCIN 250 mg tablet: 01 tablet every 12 hours (7 a.m. and 7 p.m.) on Day 1; 01 tablet per day at 7 a.m. from Day 2 to Day 5 STAVIRAL (if contraindication to chloroquine): 02 tablets every 8 hours until cure CEFIXIM 200 mg (if symptomatic): 01 tablet every 12 hours for 7 days 	- CHLOROQUINE PHOSPHATE 250 mg: 5 mg/kg every 12 hours for 10 days - AZITHROMYCIN 250 mg tablet: 15 mg/kg at D1 either as a single dose or in two doses morning and evening; then 7.5 mg/kg at fixed time from D2 to D5 STAVIRAL SIROP	 VITAMIN C: 02 g/day VITAMIN D: 4000 IU/day ZINC: 45 mg/day for 10 days 	VITAMIN C: 250 mg/day for 10 days (under 7 years); 500 mg/day for 10 days (over 7 years) ZINC: 10 mg/day for 10 days (under 6 months); 20 mg/day for 10 days (over 6 months) VITAMIN D: 2000 IU/day
Moderate case	 CHLOROQUINE PHOSPHATE HYDROXIDE 200 mg tablet: 01 t AZITHROMYCIN 250 mg tablet and 7 p.m.) on D1; 01 tablet per c STAVIRAL: 02 tablets every 8 ho CEFIXIM 200 mg: 01 tablet every DEXAMETHASONE (if moderated days then stop if no signs of respirated.) 	tablet every 12 h for 10 days : 01 tablet every 12 hours (7 a.m. day at 7 a.m. from D2 to D5 urs until recovery 12 hours for 7 days te case B): 20 mg/24 h during 5	VITAMIN C: 02 g/day VITAMIN D: 4000 IU/day OMEPRAZOLE 40 mg: tablets if ulcer ZINC: 45 mg/day for 10 days	
Severe case	 LOPINAVIR/RITONAVIR tablet: 400 mg/100 mg every 12 h for 14 days RIBAVIRINE injection tablet: 400 mg every 12 hours for 14 days DEXAMETHASONE injection: 20 mg/8 h for 5 days, then 20 mg/12 h for 5 days, then 20 mg/12 h for 5 days, then 20 mg/24 h for 5 days NB: the dose of DEXAMETHASONE may vary on a case-by-case basis depending on the evolution of the inflammatory process STAVIRAL: 02 gelules/8 h until healing ENOXAPARINE injection: at a preventive dose (0.4 ml/24 h) or curative dose (0.1 ml/kg/12 h) according to the thromboembolic risk NB: in case of renal insufficiency, use UFH/Calciparin Antibiotic coverage CEFTRIAXONE OR CEFOTAXIME: 02 g in IVD as a single injection for 3 days then relay with CEFIXIM 200 mg 01 table t/12. Imipenem 1 g/8 h + vancomycin 1 g in microinfusion of 1 h then 2 g in IVSE during 24 h in case of documented resistance Anxiolytic and antidepressant (if necessary) HYDROXYZINE: 50 - 100 mg/day in 02 doses FLUVOXAMINE: 50 - 300 mg or FLUOXETINE (Prozac) 20 mg/day in case of major depressive episodes PROMETHAZINE: 25 - 50 mg if insomnia is proven 		 OMEPRAZOLE: 40 mg/day ALBENDAZOLE: 400 mg to be repeated after 15 days Potassium and calcium intake under control of the blood ionogram VITAMIN C: 02 g/day VITAMIN D: 4000 IU/day ZINC: 45 mg/day for 10 days 	

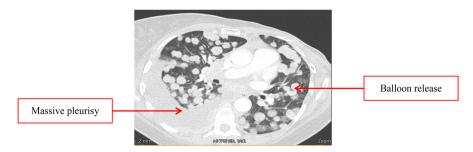


Figure 2. Chest CT: balloon release of an infiltrating ductal carcinoma of the breast in a patient with SARS COV2 infection.

care. Palliative mono-chemotherapy with vinorelbine was considered. Unfortunately, the patient presented with respiratory distress with a large right pleurisy. Pleural drainage was indicated. The patient died in the intensive care unit with severe respiratory distress.

2.3. Observation 3

Patient A.R, 37 years old, was admitted to the department in March 2021 for the exploration of an acute fever evolving in the context of chronic painful hepatomegaly (7 months). The history notes an increase in the volume of the abdomen and edema of the lower limbs with the progressive installation. A pain of the right hypochondrium estimated at 8/10 on the numerical scale. In addition, she had been drinking alcohol at 40 g/day for 7 years.

The initial clinical examination revealed an altered general condition with a WHO IPS of 2, sarcopenia, and palmoplantar jaundice. An oedemato-ascitic syndrome (ascites of average abundance and bilateral OMI taking the bucket). A painful hepatomegaly, with smooth surface, with a foamy lower border, a collateral venous circulation (portal hypertension).

The biology notes a normal fasting blood sugar level at 0.85 g/l, a normocytic normochromic regenerative anemia at 9.4 g/dl, a leukocyte at 9 G/l with neutrophilic predominance (PNN at 6.8 G/L), a disturbed inflammatory balance (VS accelerated to 50 mm, CRP increased to 289 mg/l, a polyclonal hypergammaglobuninemia) On the functional hepatic level, there was a slight cytolysis (ASAT 111 UI/l (<42); ALAT 66 UI/L (<45 UI)), icteric cholestasis (total bilirubin 75 µmol/l Alkaline phosphatase at 855 UI/L (100 - 280); GGT at 911 UI/L (<40)), hepatocellular failure (hypoalbuminemia at 25.8 g/L (40.2 - 47.6); normal PT at 86.2%).

Morphologically, the abdominal ultrasound showed a hepatomegaly with an irregular contour, heterogeneous with a mass developed on the left liver and multiple daughter nodules, as well as portal hypertension. The dosage of alpha fetoprotein was 722 ng/ml (<15 ng/ml), making a hepatocellular carcinoma suspicious. Serum protein electrophoresis showed a beta gamma block suggestive of chronic liver disease. The virological work-up (HBsAg and anti-HCV serology, HIV) was non-contributory.

The diagnosis of hepatocellular carcinoma complicating post alcoholic cirrhosis (Child Pugh C), decompensated on an ascitic mode was retained. In view of the acute fever, a complementary infectious assessment was performed. The ascites fluid puncture brought back a protein-rich (35 g/l) lemon-yellow fluid, without germs. A GeneXpert test of the ascites fluid and gastric tubing fluid for *Mycobacterium tuberculosis* DNA was negative. COVID PCR on nasopharyngeal swab came back positive.

The diagnosis of a moderate form of COVID-19 was made and the patient was transferred to the center for the management of severe cases of COVID-19. The course was favorable to treatment according to the moderate protocol (Table 2) and he was declared cured and discharged on the basis of two negative RT-PCR tests. Readmitted to palliative care for pain management, the patient decided to return home against medical advice and was lost to follow-up. It should be noted that, in carcinological terms, the extension work-up was not performed and that the management was palliative.

2.4. Observation 4

Patient S.A. 56 years old, hypertensive for 3 years and controlled on a conversion enzyme inhibitor (Enalapril 20 mg 1/2 cp per day), type 2 diabetic for 3 years and balanced on Metformin 500 mg (two tablets per day), admitted to hospital for exploration of a left pleural effusion.

The history notes a beginning of the symptomatology going back to 6 months with respiratory discomfort with recent aggravation (dyspnea stage IV of the NYHA two weeks before admission) secondarily associated with a dry cough. The whole evolved in a context of progressive increase of the volume of the abdomen and an alteration of the general state made of weight loss, asthenia, and anorexia.

The initial physical examination revealed a preserved general state (WHO IPS: 1), a temperature of 36.5°C, a polypnea of 24 cycles/min without signs of struggle, a pulsed oxygen saturation of 75% on room air corrected to 95% with 9 L of O²/min. Hemodynamically, BP was 128/78 mmHg and heart rate was 106 bpm.

The patient presented with bilateral bucketing edema of the lower limbs, bilateral left-predominant pulmonary condensation syndrome, and bilateral pleural fluid effusion syndrome. There was moderate ascites, smooth painful hepatomegaly of firm consistency, and an umbilical nodule.

Biologically, the CBC showed a microcytic anemia at 8.6 g/dl and a predominantly neutrophilic hyperleukocytosis (WBC = 8.78 G/L PNN 5.19 G/L). Liver function tests were unremarkable (AST = 45 IU/L, ALT = 21 IU/L, total bilirubin 30 μ mol/L, PT 82%, albumin 38 g/L). There was a biological inflammatory syndrome with a CRP: 346 mg/l.

Morphologically, the abdomino-pelvic ultrasound showed an abdominal mass developed over the left ovary and the extension work-up (thoracic-abdominal-pelvic CT scan), bilateral pleurisy of moderate size, bilateral diffuse frosted lenses, multiple secondary hepatic and peritoneal nodules, and moderate ascites (Figure 3).

Cytologically and histologically, the biological fluids (ascites and pleural) had a serum-like appearance, without suspicious cells on cytology, while the histology of the biopsy specimen of the umbilical nodule showed a high-grade serous adenocarcinoma of ovarian origin (Figure 4 and Figure 5). The diagnosis of high-grade ovarian serous adenocarcinoma FIGO IV A (2018) was retained. A decision was made to treat the patient with palliative chemotherapy based on platinum salt (carboplatin-paclitaxel).

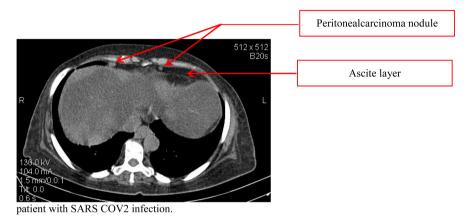


Figure 3. Abdominal CT: peritoneal carcinoma module and ascite layer.

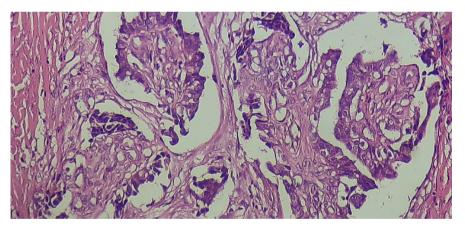


Figure 4. Carcinomatous proliferation with fenestrated appearance and papillary architecture (HE \times 10) (image by cornelly AHOUSSOUSSI, anatomopathologist, laboratory ADECHINA of Cotonou (Benin)).

The pre-chemotherapy infectious workup was oriented towards respiratory infectious pathology, given the frosted glass lung lesions contemporary with symptomatology (GeneXpert of pleural fluid and gastric tubing fluid for *Mycobacterium tuberculosis* DNA, RT-PCR COVID performed on nosopharyngeal samples) and revealed a SARS-COV2 pneumopathy added to the clinical picture.

The patient was transferred to the center for the management of severe cases of COVID-19. The patient was put on a severe COVID-19 protocol (Table 1 and

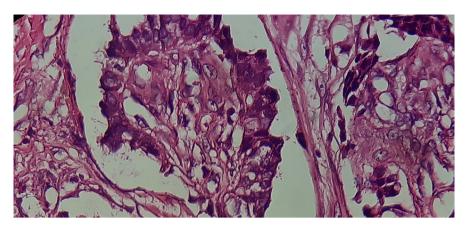


Figure 5. Tumor cells with enlarged, irregularly outlined and nucleated nuclei (HE ×40) (Image by MD, Cornelly AHOUSSOUSSI, anatomopathologist, Laboratory ADECHINA of Cotonou (Benin)).

Table 3. Summary table of the 4 cases in the study.

	1	2	3	4
Age	65 years old	56 years old	37 years old	56 years old
Sex	Female	Female	Male	Female
Comorbidities	НВР	НВР	RAS	HBP DT2
Cancer and stage	Endometrioid tubulo papillary adenocarnoma FIGO IVB (2018)	SBR III infiltrating ductal carcinoma of the left breast, ER and RP negative, HER2+, Ki67 at 60%. cT3N2M0 (AJCC 2018)	Hepatocellular carcinoma complicating post alcoholic cirrhosis Child Pugh C	High-grade serous adenocarcinoma of ovarian origin FIGO IVA (2018)
Lung metastasis	Yes	Yes	No	No
Biological work-up	Anemia at 8.3 g/dL normocytic normochromic Hyperleukocytosis predominantly neutrophilic (WBC: 8.7 G/L NP: 7.56 G/L) CRP: 307 mg/L	Tx Hb 13.1 g/dL Hyperleukocytosis predominantly neutrophilic (WBC: 8.9 G/L NP: 6.586 G/L)	Anemia at 9.4 g/dL normocytic normochromic Neutrophilic hyperleukocytosis (WBC: 9 G/L NP: 6.8 G/L) CRP: 289 mg/L	Anemia at 8.6 g/dL microcytic Hyperleukocytosis predominantly neutrophilic (WBC: 8.78 G/L NP: 5.19 G/L) CRP: 346 mg/L
Grade of COVID-19	Serious case	Severe case	Moderate case	Severe case
Cure of COVID-19	No	Yes	Yes	Yes
Patient outcome	Death	Death	Lost to follow-up	Continuation of palliative care

Table 2); the evolution was favourable with a 02 saturation of 95% on 2 l/min oxygen at D10 of treatment. Two RT-PCR controls were negative at D7 and D10 of treatment. The patient was declared cured and returned to internal medicine

for carcinological follow-up and monitoring of the imbalance of glycemic figures caused by her active tumor and viral infection.

A left hemi-corporeal deficit that occurred during hospitalization led to the suspicion of brain metastases. The brain CT scan showed recent hypodensity areas in the right sylvian territory suggestive of a stroke. Given the comorbidities and the progressive stage of the ovarian tumor, the patient was hospitalized at home for palliative care and physical therapy. The treatment consisted essentially of pain management with morphine derivatives.

These three cases are summarized in **Table 3**.

3. Discussion

We described cases of SARS-Cov2 infection in 4 cancer patients, including 3 women with breast cancer, one with endometrial cancer, and one with ovarian cancer; one man with hepatocellular carcinoma. Almost all patients were at an advanced stage and had lung metastases.

Little work has been done in cancer patients in our setting to highlight the course and difficulties of management of these patients during this period of the COVID-19 pandemic.

Reports published in China, Italy, and the United States since the beginning of the pandemic noted that risk factors for developing severe forms or death from COVID-19 included underlying health problems [2]. These include, but are not limited to, advanced age, comorbidities including diabetes mellitus, hypertension, COPD, coronary artery disease, stroke, smoking, and cancer [1] [2].

Of the 4 patients we described, only one was 65 years old. Nevertheless, hypertension was observed in 2 patients with endometrial and breast cancer; an association of hypertension and diabetes was observed in the patient with ovarian cancer. This makes them susceptible to coronavirus disease.

In addition, cancer patients are more susceptible to infection than people without cancer due to their immunosuppressed state caused by cancer and cancer treatments, such as chemotherapy or surgery [7].

According to the literature, cancer patients in general and lung cancer patients in particular are at increased risk of developing a severe form of Corona virus infection. Other associated solid cancers are breast cancer, gastrointestinal tumors, thyroid tumors, and hematological malignancies [8]. Three of our patients presented with pulmonary metastases and all developed a severe form of COVID-19, including one death directly attributed to the viral disease.

It is difficult to differentiate in this context an aggravation of respiratory symptoms related to secondary pleural-pulmonary tumor progression from an additional COVID-19. On imaging, however, the thoracic CT scan noted, apart from the tumor lesions, recent superadded ground glass images.

In a study performed in China, the images observed on chest CT noted ground glass opacity (75%) and lung condensation (46.3%) in patients with COVID-19 [5].

The severity classification of the patients described was done according to the new national recommendations in Benin (**Table 1**). All patients were managed in the National Center for the Management of Severe Cases according to the protocols in force (**Table 2**).

In the current context of COVID-19, these patients require rigorous follow-up and reorganization of care to avoid transmission of infection to the patient and medical staff, as well as a delay in the management of carcinological follow-up that may be deleterious to patients (case of patient 2) [1] [4] [9] [10].

It is important to understand that cancer patients without respiratory or hemodynamic instability are considered to have a moderate form of SARS Cov2 given the presence of cancer. The vital prognosis in relation to COVID-19 remains good between 90% - 100% (case of patient 3).

4. Conclusion

The description of these patients highlights the difficulty of managing cancer patients with SARS-COV2 infection in our context. It is difficult to differentiate respiratory signs related to complications of advanced cancer, in particular pulmonary metastases, from an additional COVID-19. Lung tumor involvement seems to be a risk factor for a severe form of COVID-19.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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