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Case Report

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Long-Term Sars-Cov-2 of Young Patient with Ewing's Sarcoma Treated with Immunosuppressive Drugs and Radiotherapy

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Abstract

COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS Cov2), has resulted in 176 million infections and 3.8 million deaths by 16 June 2021, globally. Obesity, a critical risk factor for respiratory infection, is increasinglybeing recognized as a predisposing factor in the current coronavirus disease. This has important implications on global health as excess weight, usually represented by a raised body mass index (BMI), affects vast numbers of people worldwide: 39% of adults are overweight (BMI \geq 25.0 to 29.9 kg/m2) and 13% have clinical obesity (BMI \geq 30.0 kg/m2) globally.

Obesity is associated with increased production of inflammatory cytokines such as TNF - α , interleukins and interferons that characterize chronic low - grade inflammation, which impair immune responses, both innate and adaptive. A hyper inflammatory response in which there are raised levels of interleukins and TNF - α has been associated with increased mortality from COVID - 19. The prevalence of obesity in men and women increases with age.

We explore in this Case Report the relationship between excess weight and response to infection with SARS - CoV - 2 the severity and complications of COVID - 19 in a italian patient with Severe Interstitial Pneumonia and co-morbilities.

Keywords: Ewing's Sarcoma; Immunosuppressive Therapy; Long-Term Sars-Cov 2

Introduction

The novel coronavirus disease (COVID-19) caused by the acute and atypical respiratory syndrome coronavirus 2 (SARS-CoV-2) has been declared a global pandemic by the World Health Organization (WHO) on 11th March. As of 10th June 2021, globally infections are crossing 174 million and there are over 3.750.000 fatalities [1]. Many patients, from children to elderly people, affected by primary or metastatic malignancies experienced the tragedy of the disease together with the fear of viral contagion.

Management of cancer patients during the COVID-19 pandemic is challenging. Patients with Ewing's Sarcoma especially are at serious risk for increased chances of morbidity and mortality due to their immunocompromised state. The need of surgery, chemotherapy or radiation therapy places the patients at risk of nosocomial transmission. The myelosuppressive effect of chemotherapy and radiation may increase the morbidity and mortality associated with the coronavirus. Therefore, cancer treatment should be stratified based on the benefits and risk of intervention.

Currently, many oncological societies and cancer networks have assessed the risk of COVID-19 infection for cancer patients

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and formulated practice recommendation for oncological care including neoadjuvant therapy, surgery, adjuvant therapy, immunotherapy, targeted therapy and palliative care. Several soft tissue malignancies have now been stratified according to priority or risk level predicting the need for either urgent intervention, delayed intervention or deferment of intervention after the pandemic [2]. We report a case of Long-Term positivity Sars-Cov-2 of a young patient with Ewing's Sarcoma treated with Immunosuppressive Drugs and Radiotherapy.

Description

Our young Italian patient 25-year-old, male, developed fever up to 38.7 degrees C, asthenia, myalgia, dyspnea, cough, seizure, headache, visual disturbances on 18 Mars 2021. In the Hospital of Alghero, Sardigna, Italy he was admitted immediately after computed tomography scan (CT scan) imaging of his chest showed multiple and bilateral ground-glass opacities located in both subpleural and apico-basal spaces (especially on the left) and extensive left spontaneous pneumothorax with subtotal lung collapse.

Nasopharyngeal swab specimens were collected to detect severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid. The swab specimens were tested by real-time reverse transcriptase–polymerase chain reaction; a positive result was received 6 hours later on 19 Mars 2021. Our patient was diagnosed with COVID-19. He received 100 mg Remdesivir (Veklury) tablets orally, 3 times daily, Tocilizumab was given I.V.400 mg single dose for "cytokine storn", O2 Therapy; Proton Pump Inhibitors (pantoprazole 40 mg , 2 times daily), antibiotics (Piperacillin tazobactam 4.5 g , 3 times daily), antifungal (fluconazole 200 mg), thromboembolic prophylaxis (Enoxaparin 4000UI), Fentanyl transdermal patch (25 g/72 hours), rehydration therapy, Filgrastim 1 f sc/day.

Patient with Ewing's Sarcoma of C7 undergoing decompressive debulking (08/09/2020) and subsequent removal of the lesion (18/12/2020), in ongoing chemo- and radiotherapy treatment. Last radiotherapy session on 06/05/2021.

On Mars 20, 2021 our patient show important sense of encumbrance at the glottic level associated with cough, pharyngodynia, odynophagia, dysphagia for liquids and solids and dysphonia.

Skin erythema of neck and face from radiation therapy. On May 2, 2021 Molecular swab for SARS-CoV-2 always positive (Long-Term Covid-19) Emogasanalysis: FiO₂ 21% (aa) pH 7.43, pO₂ 92.8 mmHg, pCO₂ 40.8 mmHg, SO₂ 97.4% P/F 433

Anesthesiological consultation: no anaphylactic shock diagnosis, but iatrogenic pharyngodynia and edema, consequent to recent radiotherapy. Fibrolaryngoscopic examination: slight edema of the epiglottis, glottic plane in the normal mobility and morphology, good respiratory space. Diffuse pharyngolaryngeal hyperemia, hypertrophy of the posterior commissure compatible as laryngeal mycosis. Our patient received chemiotherapy, radiotherapy for our Ewing's Sarcoma and antiviral therapy for Sars-Cov-2.

On May 12, 2021, our patient was computed tomography (CT) imaging of her chest a complete resolution of bilateral areas of altered density a ground glass after treatment. After 8 day the swab specimens were tested by real-time reverse transcriptase–polymerase chain reaction is negative and asthenia, myalgia, dyspnea, cough, seizure, headache, visual disturbances disorientated have been missing. Fortunately, On May 30, 2021, Nasopharyngeal swab specimens was negative and after the maintenance of intensive medical treatment in hospital computed tomography (CT) imaging of her chest a complete resolution (**Figure 1**). Currently, our young patient continues with complex therapy for Ewing's sarcoma.



Figure 1: efore Therapy after Therapy regression of pneumonia in patient with Sars-Cov-2 and Ewing's Sarcoma.

Discussion

COVID-19 has been shown to develop in a wide spectrum of clinical manifestations, from asymptomatic or paucisymptomatic forms, to severe viral pneumonia with respiratory distress up to systemic dysfunctions and death from multiple organ failure. Multiorgan impact of COVID-19 and frailty from comorbidities are strictly connected, as several risk factors including age, diabetes mellitus, hypertension, and immunosuppression and cancer disease are related to the progression of the viral infection [3].

In our case study, the systemic immunosuppressed state caused by chemotherapy for Ewing's Sarcoma and surgery make our patient more susceptible to infection Long-Term positivy for SARS-CoV-2. Ewing sarcoma was named after James R. Ewing, an eminent American pathologist at Cornell who described the first cases in 1921, is a cancer of the bone or soft tissue that usually affects children and young adults.

Cancer patients who receive chemiotherapy have suppressed immune responses and are more likely to develop SARS-CoV-2-associated complications [4,5]. Immune system dysfunction, including overexpression of immunosuppressive cytokines, impaired maturation of dendritic cells, and elevated numbers of immunosuppressive leukocytes, can lead to cancer development and progression [6].

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In combination with myelosuppressive treatments, immunological dysfunction enables the replication of SARS-CoV-2 in the host's body, which may lead to multiorgan failure and a cytokine storm [7]. On the other hand, diminished cytokine activity and immunosuppression in cancer patients may be beneficial in the context of SARS-CoV-2 infection. Spezzani et al. reported that in a COVID-19 patient with stage 4 breast cancer, receiving immunosuppressive chemotherapy, leucopenia may have contributed to the rapid recovery and prevention of a cytokine storm and other COVID-19 complications [8].

Could prolonged virus positivity have resulted in an amplified response to chemo- and radiation therapy? Or could the immunodepressed condition have promoted long-term positivity? Immune checkpoint inhibitors, monoclonal antibodies as CAR-T, have emerged as promising cancer therapies, exerting potent antitumor effects by unleashing immune responses. However, the influence of new therapies on the course of COVID-19 remains undetermined. Even though immune modulation may provide an advantage in eliminating SARS-CoV-2, it could also intensify the cytokine storm [9] and thereby promote severe pneumonitis. Notably, treatment with ICIs was found to be a predictor of severe respiratory compromise, independent of age, type of cancer, and presence of other comorbidities [10]. We need prospective studies of treatment options and additional patient characteristics to further understand the variables associated with COVID-19-associated death in patients with Ewing's Sarcoma.

Conclusion

Mounting evidence suggests that immunocompromised cancer patients have a higher risk of developing severe symptoms upon SARS-CoV-2 infection compared with the general population. Although cancer treatments often cause immunosuppression, current evidence suggests that immunosuppressive therapies do not affect the COVID-19 fatality rate. Clinicians and cancer patients should take preventive measures to minimize the risk of exposure to SARS-CoV-2. Additionally, cancer patients diagnosed with COVID-19 should be closely monitored, regardless of the severity of their symptoms. Additional studies are required to better understand the impact of SARS-CoV-2 infection on the already compromised health of cancer patients, as well as the effects of cancer treatments on the course of COVID-19.

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