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Successful treatment of advanced prostate cancer patient with moderate to severe COVID-19 infection: A case report and review of the literature

Zeinab Mehrabi[1]; Shirin Haghighat[2]*; Seyed Alireza Zomorodian[3]

[1]Assistant Professor of Infectious Diseases, Internal Medicine Ward, Shiraz University of Medical Sciences, Shiraz, Iran.

[2]Department of Hematology and Medical Oncology, Shiraz University of Medical Sciences, Shiraz, Iran.

[3]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran.

***Corresponding Author: Shirin Haghighat**
Shiraz University of Medical Science Zand Avenue, Namazi Hospital, Hematology and Medical Oncology Department, Iran.
Tel: 0098 9173088977;
Email: sh.haghighat2010@yahoo.com

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Keywords: Coronavirus; Prostate cancer; ADT.

Abbreviations: LDH: Lactate Dehydrogenase; ADT: Androgen Deprivation Therapy; PSA: Prostate Specific Antigen; CT scan: Computerized Omography Scan; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; rRT-PCR: Real-Time Reverse-Transcription Polymerase Chain reaction; ACE-2: Angiotensin-Converting Enzyme 2; TMPRSS2: Type II Transmembrane Serine Protease; ETS: E-Twenty-Six.

Abstract

Background: A novel coronavirus known as severe acute respiratory syndrome coronavirus2 (SARS-CoV2) discovered in late December 2019 in China and spread across the world rapidly. Cancer patients are among the more vulnerable population to severe COVID-19 infection. Immunosuppression caused by cytotoxic agents, comorbidities and aging may be the reason of their susceptibility to COVID-19. However, some studies showed that prostate cancer patients receiving androgen-deprivation therapy seem to have lower risk of covid-19 infection and better prognosis of this infection. TMPRSS2 is a member of family of serine protease which is not only expressed on pneumocytes and facilitates coronavirus entry but also on normal and malignant prostate tissue and is involved in prostate cancer progression. Based of these findings, the hypothesis of possible effectiveness of anti-androgen therapy (ADT) in the treatment of COVID-19 has been proposed.

Case presentation: A 83 years old man, known case of castration resistant metastatic prostate cancer and diabetes mellitus, presented with diagnosis of COVID-19 infection confirmed by RT-PCR and chest CT-scan. He was on androgen deprivation therapy (ADT) and docetaxel as a chemotherapeutic agent for treatment of prostate cancer before his recent COVID-19 presentation. Laboratory findings and chest CT-scan showed moderate to severe presentation of COVID-19. Fortunately, he responded well to our treatment including remdesivir and corticosteroid and discharged from the hospital on 8th days of admission without any major sequela.

Conclusion: The protective effect of ADT on SARS-CoV-2 infection in prostate cancer patients was reported by some studies. Also putative role of TMPRSS2 in both prostate cancer development and SARS-CoV-2 infection suggest the hypothesis of targeting TMPRSS2 and androgen receptor as a novel treatment of COVID-19 which needs more investigation.

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Background

In late December 2019, the novel coronavirus (COVID19) discovered in Wuhan, China that spread worldwide rapidly [1]. Clinical spectrum of COVID19 varies from asymptomatic or mildly symptomatic, including fever, cough and myalgia, to severely respiratory compromised [2,3]. Although most patients have mild symptoms and favourable outcome, mortality among hospitalized patients was reported as high as 4.3% to 16.7% [4-7]. Potential risk factors for severe disease include higher age, higher lactate dehydrogenase (LDH), higher D-dimer level, and comorbidities such as hypertension, diabetes, cardiovascular disease, respiratory disease and malignancy [6,8,9]. Although most authors identified cancer as a risk factor for severe COVID-19 and poor outcome, the effect of recent chemotherapy on COVID19 outcome is not clear [10]. In an analysis of the data extracted from electronic medical records from New York city, 6% of COVID-19 infected patients had cancer. The most common primary sites of cancer were breast, prostate and lung respectively [11]. A systematic review showed the higher mortality among patients with hematologic malignancies followed by lung cancer compared to other subtypes of cancers. In that study no association was found between the type of oncologic treatment and mortality [12]. An Italian study showed that androgen deprivation therapy (ADT) in prostate cancer was associated not only with lower risk of COVID-19 infection but also better outcome of this infection [13]. Here we report an 83 years old man with prostate cancer who survived a severe COVID-19 infection.

Case presentation

A 83 years old Asian man, known case of diabetes mellitus, hypertension and metastatic prostate cancer, was admitted in our hospital with 4 days history of dry cough, generalized body pain and dyspnea. He did not have fever but had history of chills, anorexia and diarrhea. Past medical history of patient was positive for diabetes mellitus and prostate cancer. His prostate cancer was diagnosed 4 years ago which presented by bone metastases at the beginning. ADT was initiated subsequently and maintained until now. Approximately 7 months ago PSA started to raise followed by increase in the patient's symptoms including pelvic bone pain. Chemotherapeutic agent (docetaxel) was added to ADT due to the disease progression. The last chemotherapy cycle was two weeks before his recent hospital admission. On arrival at the hospital, he had a respiratory rate of 30/min, pulse rate of 110/min, blood pressure of 110/80 mmHg, temperature 36.8, and O_2 saturation of 82% on room air. Chest Computerized Tomography (CT) scan (Figure 1) showed round patches of bilateral multifocal ground glass opacities and crazy paving that was typical for COVID-19 infection with moderate to severe lung involvement. The patient was transferred to COVID-19 isolation ward for treatment and closed observation. Laboratory tests on first day of admission revealed the following: white blood cell count 16700/µl with lymphocyte count 1280/µl, haemoglobin 10.1 g/dl, platelet count 169000/µl, ESR 40 mm/hour, ferritin>1000 ng/ml, CRP 96 mg/l, creatinine 1.6 mg/dl, LDH 754 U/L, troponin negative and fasting blood glucose 98 mg/dl. Liver function test was normal. Nasopharyngeal and oropharyngeal swabs, tested by real-time reverse-transcription polymerase chain reaction (rRT-PCR) assay, were positive for COVID-19. He was treated with antiviral agent remdesivir, and dexamethasone. During hospital course meropenem and linezolide was added to his medications because of suspicion of superimposed bacterial infection. He also received antithrombotic prophylaxis with enoxaparin and stress ulcer prophylaxis with proton pump inhibitor (pantoprazole). During hospitalization he was managed with oxygen therapy via nasal cannula or facial mask at 3 L/min, resulting acceptable oxygen saturation (94%). On 4th days of admission, he showed improvement in his symptoms and was discharged on 8th days of hospitalization with almost complete clinical recovery.

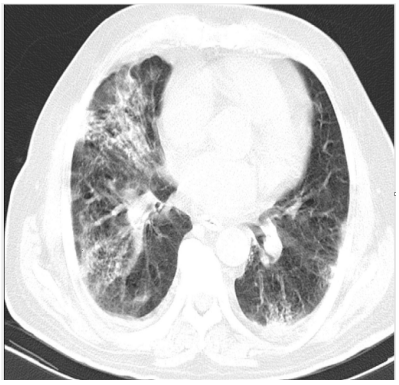

Figure 1: High-Resolution Computed Tomography (HRCT) scan of the chest showed bilateral and multifocal ground glass opacities and crazy paving, typical of COVID-19 pneumonia.

Discussion and conclusion

Although some reports from different COVID-19 centres did not represented malignancy as a risk factor for severe COVID-19 infection, there are many retrospective and nonrandomized studies showed the vulnerability of cancer patients to more severe forms of this viral infection [14]. Recently, Montopoli demonstrated that prostate cancer patients receiving androgen deprivation therapy (ADT) had significantly lower risk of SARS-CoV2 infection compared to prostate cancer patients not received ADT and patients with any other types of cancers [13]. Several studies have reported that men are more susceptible to COVID-19 compared to the women. Also, the incidence of more severe cases, the possibility of ICU admission and COVID-19-related mortality are higher among men than women [7,15]. Viral pathogenicity seems to be the reason of this difference between male and female. The role of Angiotensin Converting Enzyme 2 (ACE2) receptor and Type II Transmembrane Serine Protease (TMPRSS2) were discussed by several studies [16,17]. Coronavirus gets to entry host cells via binding of its spike protein to the ACE2 receptor located on the surface of pulmonary epithelial cells. TMPRSS2, expressed on the surface of type II pneumocytes, facilitates viral entry by cleaving the viral S glycoprotein which is considered the key mechanism of viral pathogenicity [17,18]. The TMPRSS2 gene is located on the human chromosome 21q22.3 which shows a fundamental role in the prostate cancer development and its progression. TMPRSS2 is also expressed on normal prostatic epithelium that is upregulated in malignant prostatic cells [17-19]. ERG is another gene located on chromosome 21q22 which belongs to the E-Twenty-Six family (ETS) members that shows an important role in differentiation, apoptosis, cell proliferation, and inflammation [18]. TMPRSS2: ERG fusion which occurs in about half of prostate cancers has a key role in prostate carcinogenesis [18,19]. In addition, TMPRSS2 gene expression is regulated by androgen

in prostate cells which could explain the possible susceptibility to COVID-19 in men compared to women [16]. As regards the modulation of TMPRSS2 expression by androgen and some reports of lower rate of OCVID-19 infection in patients with prostate cancer receiving ADT, further studies are needed to evaluate the role of antiandrogenic agents in the treatment and prevention of COVID-19 infection.

During the COVID-19 pandemic, the management of cancer patients is a challenging issue. Concerning the increased mortality of cancer patients affected by covid-19, some guidelines have been prepared for the treatment of cancer patients during COVID-19 pandemic. According to these guidelines, chemotherapy has recommended only for advanced prostate cancer progressing rapidly without response to ADT. For these patients, prophylactic growth factors are recommended following the chemotherapy [20]. ADT is the preferred treatment for advanced metastatic prostate cancer and can continue safely during COVID-19 pandemic. As possible, androgen receptor targeted therapy will be a preferred choice over the chemotherapy in the treatment of patients with metastatic hormone-sensitive and castration-resistant prostate cancer [20].

In conclusion, these data need to investigate more by further study to confirm the role of targeting the TMPRSS2 and androgen receptor in the treatment and prevention of COVID-19 specially in the high-risk groups.

Declarations

Ethics approval and consent to participate: Not applicable

Consent of publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Availability of data and material: No datasets were generated or analysed during this study.

Competing interest: The authors declare that they have no competing interest.

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Authors contributions: ZM was responsible for patient care during hospital admission, SH was responsible for treatment of patient's cancer and wrote the paper. AZ collected data and review the literatures.

All authors read and approved the final manuscript.

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