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Journal of Oral Medicine, Oral Surgery, Oral Pathology and Oral Radiology

Journal homepage: www.jo000.org

Editorial

Oral squamous cell carcinoma, a potential risk factor for SARS-CoV-2 infection and COVID-19 associated complications

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ARTICLE INFO

Article history:

Received 27-10-2020

Accepted 29-10-2020

Available online 02-11-2020

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The recent outbreak of the COVID 19 pandemic has caused untold anxiety and a threat to human life. It is caused by the SARS-CoV-2 Virus belonging to the coronaviridae family.¹ The disease spreads by droplet transmission from person to person. As at present there are no specific drug or vaccine available, social distancing along with good hygiene practices are the need of the hour to prevent the disease spread. It has been reported that the prognosis of the disease is poor in the case of associated comorbidity such as diabetes,² hypertension,³ and malignancy.⁴

Oral squamous cell carcinoma (OSCC) is ranked as the 6th most common malignant worldwide.⁵ Although the disease is multifactorial in etiology, tobacco and alcohol have been proposed as the major risk factors.⁶ It is a well-known fact that several molecular pathways are altered in oral carcinogenesis causing overexpression of various proteins such as EMMPRIN,⁷ TMRSS,⁸ Furin,⁹ and Cathepsin L.¹⁰ It has been hypothesized that these molecules could facilitate SARS Cov- 2 entry into the host.¹¹ Hence oral squamous cell carcinoma could be considered a predisposing factor for SARS Cov- 2 infections. In addition to the plethora of molecules overexpressed in OSCC/oral cancer, the role of

inflammasomes in the pathobiology and progression of oral cancer deserve mention at this juncture. Danger signals of endogenous origins elicit an immune response in form of inflammasomes, which are a large complex of multiple proteins capable of signaling. These inflammasomes are located in the cell's cytosol and are capable of caspase-1 (inflammatory protease) upregulation. They can also cleave the interleukin (IL)-1 β and pro-IL-18 (pro-inflammatory cytokines) to their respective active forms, thereby initiating pyroptosis.¹² Nod-like receptor (NLR), the adapter apoptosis-associated speck-like (ASC) protein, and Caspase-1 constitute the inflammasome complex. Nod-like receptor protein 3 (NLRP3), is an NLR protein family member and is in turn comprised of 22 members.^{13,14} NLRP3 responds to several infectious and endogenous ligands. Thus, NLRP3 dysregulation is a vital part of the molecular biology of numerous pathologies both inflammatory and tumorigenic nature. Inflammation is a strength linked to genetic and epigenetic changes capable of inducing OSCC.¹⁵ Upregulated NLRP3 inflammasome has been reported in both animal OSCC model and human OSCC cases. Hence it is anticipated that patients with OSCC could have higher levels of circulating pro-inflammatory cytokines such as IL 1 beta and IL 6 as a consequence of NLRP3 activation. Further evidence for the

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same is obtained from clinical studies that have assessed circulating proinflammatory cytokines in OSCC patients.¹⁶

It is also noteworthy that the NLRP3 inflammasome is activated in SARS-Cov 2 infection.¹⁷ In sequela of SARS-Cov 2 infection such as acute respiratory distress syndrome and acute lung injury, NLRP3 activation has been implicated as a major source of aberrant cytokine production which finally culminates in multi-organ injury and morbidity.¹⁸ It has been postulated that the injury of cells bearing the Angiotensin-converting enzyme 2 (ACE 2) leads to dysregulated NLRP3 activation.¹⁹ Interestingly, the ACE 2 enzyme is a receptor for binding and entry of SARS Cov 2 into the human host.²⁰ In this scenario, it could be hypothesized that a patient having OSCC and SARS Cov 2 infection is at high risk for SARS Cov 2 complications due to increased NLRP3 activation as this phenomenon occurs in both the above conditions. Hence it is expected that a patient with OSCC and SARS Cov 2 will have very high levels of circulating cytokines and is hence vulnerable to multi-organ failure. It is hence suggested that patients with OSCC should be utmost careful considering the vital complications they could suffer if they contract SARS Cov2. This situation is also a red flag alert to dental surgeons, oral pathologists, and oral surgeons who regularly screen and treat OSCC patients.

1. Conflict of Interest

None.

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Cite this article: Balaji TM, Varadarajan S, Patil S, Raj AT. Oral squamous cell carcinoma, a potential risk factor for SARS-CoV-2 infection and COVID-19 associated complications. *J Oral Med, Oral Surg, Oral Pathol, Oral Radiol* 2020;6(4):166–167.