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Severe Acute Respiratory Syndrome–Coronavirus-2 Infection and Patients With Lung Cancer: The Potential Role of Interleukin-17 Target Therapy

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ABSTRACT

The coronavirus disease 2019 outbreak is evolving rapidly worldwide. The lungs are the target of the primary infection and patients with lung cancer seem to have a poor prognosis. To our knowledge, this is the first reported investigation of a possible role of interleukin-17 target therapy in patients with lung cancer and concomitant severe acute respiratory syndrome–coronavirus-2 infection.

Keywords: COVID-19; Lung cancer; IL-17 target therapy; Monoclonal antibody

Possible Role of interleukin-17 in Severe Acute Respiratory Syndrome-Coronavirus-2 Infection

In the lungs, the interleukin-17 (IL-17) cytokine is produced by T helper-17 cells in response to viral infection.[1] IL-17 activates several signaling pathways, which in turn lead to the induction of chemokines. Chemokines recruit immune system cells to the inflammation site. The persistence of the pathogen generates hyperactivity of the immune system, which can lead to a cytokine storm.[1]

Furthermore, IL-17, in synergy with IL-6, promotes viral persistence by inhibiting apoptosis.[2] As per the same study, it is possible to determine the biologic mechanisms related to organ damage mediated by viruses through the IL-17 pathway.[2] The role of IL-17 does not seem to be confined to these mechanisms. In fact, in addition to mediating the cytokine storm (resulting in lung damage) and inhibiting the apoptosis of infected cells (resulting in viral persistence), it also seems to have the ability to increase the replication of some viruses by actually increasing their virulence.[3] It has also been found in an experimental model that viral persistence, caused by generating a continuous increase in IL-17, produces acute respiratory distress syndrome,[4] which is what happens in severe acute respiratory syndrome–coronavirus-2 (SARS–CoV-2) infection. The increasing level of IL-17 could also be related to the hypercoagulation status in patients with coronavirus disease 2019 (COVID-19).[5]

Adverse Outcome of COVID-19 Related to Previous Comorbidity

On investigation of the risk factors related to the poor prognosis of COVID-19, it was revealed that the IL-17 pathway was always altered in these cases. In fact, with advancing age, inflammatory response to viruses is altered with an excessive increase in the production of IL-17.[6] The same effect is noted in patients with asthma,[7] among smokers,[8] diabetics,[9] patients with heart conditions,[10,11] and men.[12]

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Specific IL-17 and SARS-CoV-2 Evidence

There is emerging evidence supporting the role of IL-17 in SARS–CoV-2 pathogenesis, including a report on the first anatomopathologic lung analysis (with a high number of T helper-17 lymphocytes in the alveolar space)[13] and two recent publications,[14,15] which reviewed the immune response in a patient with SARS–CoV-2 infection.

Protumor Effect of IL-17 in Lung Cancer

The role of IL-17 in lung cancer is well-recognized[16] and it has been known to induce VEGF secretion in cancer cell lines.[17] This effect was dependent on the STAT3-GIV–associated protein pathway, which was abolished when the cells were exposed to a small interfering RNA.[18] It was observed that those patients who had increased levels of serum IL-17 had poorer survival and enhanced angiogenesis compared with healthy controls.[19] Furthermore, exposure of three different NSCLC cell lines to IL-17 has also been reported to increase neoangiogenesis and promote in vivo tumor growth in severe combined immunodeficient mice through a CXCR-2-dependent mechanism. IL-17 up-regulated several proangiogenic CXC chemokines, including CXCL1, CXCL5, CXCL6, and CXCL8. Inhibition of IL-17 with monoclonal antibodies abolished this up-regulation and could be potentially useful in patients with COVID-19 when other systemic therapies have been excluded.

Potential Role of IL-17 Antibody in the Treatment of Patients With Lung Cancer and COVID-19

The use of IL-17 antibody is well-recognized; it is currently approved in the treatment of psoriatic arthritis. Moreover, the therapeutic role of IL-17 antibodies has already been established not only in different cancer types[16] but also in the treatment of lung infection with H1N1 virus,[19] in acute respiratory distress syndrome,[4,20] and pulmonary fibrosis.[21] From this analysis, and in the context of the global pandemic, there seem to be some theoretical elements to testing the potential utility of IL-17 antibodies in patients with lung cancer and COVID-19 in a clinical trial setting, with its potentially high social impact and given the lack of specific validated treatments.

Potential Future Applications

If a clinical trial is performed and it is found that the IL-17 target therapy can determine both the control of the tumor and resolution of SARS–CoV-2 infection, it can also be applied to other tumors in which IL-17 plays a role.[15] A clinical trial in patients without cancer could also provide opportune data specific to COVID-19 treatment.

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