中文題目:一位頭頸癌病人接受免疫檢查點抑制劑治療發生結核菌的再活化

英文題目：Reactivation of pulmonary tuberculosis during anti-programmed death-1 treatment in a patient with head and neck malignancy

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Introduction:

Programmed cell death protein 1 (PD-1) is an immune checkpoint protein located on T cells providing negative inhibitory signals to T cells.[1] Antibody PD-1 has been discovered to activate the immune system to attack the tumor cells and been approved to be effective in treating melanoma, lymphoma, non-small cell lung cancer, as well as head and neck cancers.

While immune checkpoint inhibitors are novel therapeutic agents, they may induce several unusual immune-related adverse events involving cardiovascular, neurological, pulmonary, gastrointestinal, renal, and cutaneous systems. Besides, these agents may cause varies of infections, such as oral candidiasis, herpes zoster infection, and tuberculosis. Until present, there have been five cases of tuberculosis reactivation in patients receiving PD-1 checkpoint inhibitor treatment reported.[2] Among them, three cases were non-small cell carcinoma of lung, one was Hodgkin lymphoma, and the other was melanoma.

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Case report:

A 49-year-old man had stage IV squamous cell carcinoma of hard palate and underwent concurrent chemo-radiotherapy with 8-courses of weekly cisplatin in 2016. He also received cetuximab, paclitaxel, and carboplatin for the disease later. While the disease progressed, he received PD-1 checkpoint inhibitor treatment (nivolumb, 3mg/kg every two-weeks) five months after the diagnosis of the disease. Three months after the initiation of the PD-1 checkpoint inhibitor treatment, he was admitted for fever and productive cough of two-week duration. On examination, rhonchi breathing sound was heard on bilateral lung fields. A chest radiography showed patchy opacities of the left upper lobe lung. A computed tomography of the chest revealed patchy consolidations and a mass lesion with cavitation in the left upper lobe lung. Both the acid-fast staining and *Mycobacterium tuberculosis* culture of sputum specimens yielded positive results. The polymerase chain reaction for *M. tuberculosis* also disclosed positive result. A diagnosis of pulmonary tuberculosis was confirmed. We discontinued the nivolumb and initiated anti-tubercular therapy for him. The patient expired five months after the diagnosis of tuberculosis because of bacterial pneumonia with acute respiratory failure.

Discussion:

PD-1 has a crucial regulatory role during the immune response of the host to the *M. tuberculosis*. In animal experiments, PD-1 pathway was found to play a key role in controlling excessive inflammatory responses and regulating antimicrobial immunity after *M. tuberculosis* infection in the lungs.[3] Recently, the PD-1/PD-L1 pathway was pointed out to be involved in the pathophysiology of *M. tuberculosis* infection by inhibiting the effector T cell functions and suppressing the accumulation of parenchymal CD4 T cells and their IFN-γ production.[4] However, the exact mechanism about the tuberculosis reactivation during PD-1 checkpoint inhibitor treatment remains inconclusive.

Those with head and neck cancers are eligible for tuberculosis infection because of their immunocompromised status. Conventional chemotherapy and radiotherapy for head and neck cancers would augment the risk of several kinds of pathogens infection, including tuberculosis infection. Nivolumab, as an innovative therapeutic option, has been proposed to cause a better prognosis than standard therapy in patients with platinum-refractory, recurrent squamous-cell carcinoma of the head and neck cancers[5] and is expected to be used increasingly in the future. However, the possible adverse events of this treatment should also be noticed carefully. More intense screening for tuberculosis infection before and during the PD-1 checkpoint inhibitor treatment for head and neck cancers may be needed.

References:

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