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Case report

Severe interstitial pneumonia associated with anti-PD-1 immune checkpoint antibody after talc slurry pleurodesis

Shinya Sakata[a,1,*], *Yuichiro Matsuoka*[b,1], *Kenta Kawahara*[b], *Yosuke Kakiuchi*[a], *Akira Takaki*[a], *Akiyuki Hirosue*[b], *Ryoji Yoshida*[b], *Sho Saeki*[a], *Kazuhiko Fujii*[a], *Hideki Nakayama*[b]

[a]*Department of Respiratory Medicine, Kumamoto University Hospital, 1-1-1 Honjo, Chuo-ku, Kumamoto 860-8556, Japan*
[b]*Department of Oral and Maxillofacial Surgery, Faculty of Life Sciences, Kumamoto University, 1-1-1 Honjo, Chuo-ku, Kumamoto 860-8556, Japan*

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ABSTRACT

A 70-year-old Japanese man with recurrent squamous cell carcinoma of the head and neck presented with severe interstitial pneumonia associated with nivolumab, after talc slurry pleurodesis. Following the development of malignant pleural effusion, he underwent chest drainage and was administered intrathoracic talc as a pleurodesis. Two weeks later, we administered nivolumab (3 mg/kg) to be repeated every 2 weeks. However, on day 12, chest computed tomography scan demonstrated diffuse non-segmental ground-glass opacity and mild bronchiectasis. We diagnosed interstitial pneumonia associated with nivolumab. Although corticosteroid pulse therapy was initiated, the patient died of respiratory failure on day 14.

Abbreviations: SqCC, squamous cell carcinoma; anti-PD-1, anti-programmed death-1; irAE, immune-related adverse event; PS, Eastern Cooperative Oncology Group performance status; CRP, C-reactive protein; LDH, lactate dehydrogenase; CT computed tomography; VC, vital capacity; $FEV_{1.}$, forced expiratory volume in one second; SP-D, surfactant protein-D; KL-6 Krebs von den Lungen-6; GGO, ground-glass opacity; COP, cryptogenic organizing pneumonia; AIP, acute interstitial pneumonia; ARDS, acute respiratory distress syndrome; OK-432, heat-killed *Streptococcus pyogenes*

*Corresponding author. Fax: +81 96 373 5328.
E-mail address: sakata-1027@hotmail.co.jp (S. Sakata).
[1]These authors contributed equally to this work.

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1. Introduction

Patients with metastatic squamous cell carcinoma (SqCC) of the head and neck have a poor prognosis. While patients demonstrating recurrence after platinum-based chemotherapy have limited therapeutic options, anti-programmed death-1 (PD-1) antibody has recently been approved in Japan for treating metastatic SqCC of the head and neck.

Nivolumab, a fully human IgG4 anti-PD-1 monoclonal antibody, has shown antitumor efficacy in various tumors [1,2]. Patients with platinum-refractory, recurrent SqCC of the head and neck who were treated with nivolumab showed significant survival benefit [3]. However, nivolumab is associated with immune-related adverse events (irAEs). Among the irAEs, pneumonitis is a clinically serious toxicity. In a randomized trial examining >350 patients with recurrent SqCC of the head and neck, pneumonitis was observed in 2.1% of the nivolumab-treated patients [3]. However, the risk factors in nivolumab-induced pneumonitis have not yet been established. To our knowledge, a case of severe pneumonitis after talc slurry pleurodesis has not been reported yet.

Here, we report the case of an adult male with recurrent SqCC of the head and neck who showed severe interstitial pneumonia associated with nivolumab treatment after talc slurry pleurodesis.

2. Case report

A 70-year-old Japanese male with a 2-year history of SqCC of the tongue was admitted to our hospital with dyspnea. Two years earlier, he underwent concurrent chemoradiotherapy: 60 Gy (total dose) and intra-arterial infusion chemotherapy with cisplatin. When a recurrence of tongue cancer was later diagnosed, the patient underwent chemotherapy with cisplatin, 5-fluorouracil, and cetuximab.

The patient had a 24 pack/year smoking history and his Eastern Cooperative Oncology Group performance status (PS) was 2. The results of the laboratory examinations showed elevated C-reactive protein level (CRP) (6.70 mg/dL; normal range < 0.3 mg/dL) and white blood cell (WBC) count (11,200 /μL). The serum lactate dehydrogenase (LDH) level was 191 U/L (normal range < 220 U/L). Chest computed tomography (CT) scan revealed right pleural effusion and multiple pleural disseminations without any findings of interstitial pneumonia (Fig. 1 A, B). Before the right pleural effusion appeared, chest CT showed no findings of interstitial pneumonia (Fig. 1 C, D). The data from the pulmonary function test were as follows: vital capacity (VC) 3.94 L, forced VC 4.02 L, %VC 108%, forced expiratory volume in one second (FEV_1) 2.90 L, and % FEV_1 100%.

We performed chest drainage and the patient subsequently received a single intrathoracic administration of sterile graded talc (Unitalc®; Nobelpharma, Tokyo) slurry at a dose of 4 g, as pleurodesis. Two weeks later, we administered nivolumab (3 mg/kg, day 1) to be repeated every 2 weeks. Laboratory examinations performed just before this nivolumab treatment showed elevated CRP level (7.10 mg/dL) and WBC count (10,600 /μL). The serum LDH level was 180 (U/L) and the serum surfactant protein-D (SP-D) level was 16.5 ng/mL (normal range < 110 ng/mL). The serum Krebs von den Lungen-6 (KL-6) level was 233 U/mL (normal range < 500 U/mL).

The clinical course is illustrated in Fig. 2. Eight days after the first administration of nivolumab, we initiated antibiotics (ampicillin/sulbactam, 3 g repeated every 6 h) as empiric therapy because the patient presented with fever and

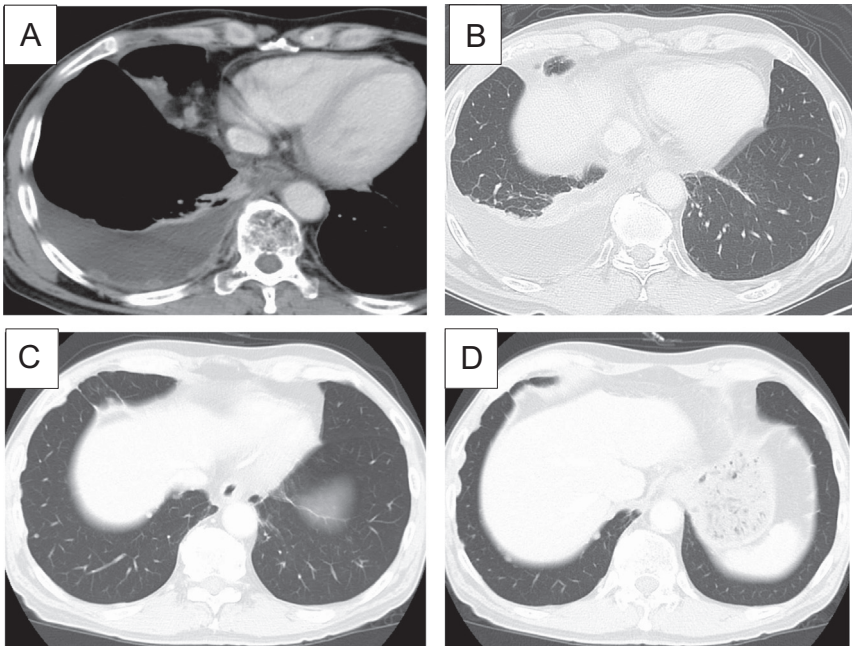

Fig. 1 – A, B: Chest computed tomography (CT) scan demonstrating right pleural effusion and multiple pleural disseminations without any findings of interstitial pneumonia. C, D: Chest CT scan demonstrating multiple right pleural disseminations and no findings of interstitial pneumonia, before the appearance of right pleural effusion.

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