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Lung: Case Report

Salvage Surgery for Thoracic SMARCA4-Deficient Undifferentiated Tumor

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Thoracic SMARCA4-deficient undifferentiated tumors (SMARCA4-UT) may be effectively managed with immune checkpoint inhibitors; however, the management of posttreatment exacerbations remains uncertain. A 48-year-old man underwent chemotherapy (cisplatin and pemetrexed) along with PD-L1 and CTLA-4 inhibitors, resulting in significant improvement. Subsequently, maintenance therapy was initiated but discontinued because of drug-induced pneumonia. Although prednisone treatment resolved the pneumonia, salvage surgery was performed for exacerbation of an enlarged chest tumor and lymph nodes. No additional postoperative treatment was administered, and the patient has completed 2.5 years of treatment. This case highlights the potential efficacy of salvage surgery in the management of SMARCA4-UT exacerbations.

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Thoracic SMARCA4-deficient undifferentiated tumors (SMARCA4-UT) are a newly recognized entity in the 2021 World Health Organization lung tumor classification.[1] SMARCA4-UT is a highly aggressive tumor commonly observed in young heavy smokers, predominantly in men, with a median survival rate of approximately 5 to 7 months.[2,3] Even in patients who undergo complete resection, the prognosis remains unsatisfactory, and conventional cytotoxic chemotherapy is only marginally effective.[4] Whereas recent studies have underscored the benefits of immunotherapy and treatment strategies have increasingly focused on it, the management of SMARCA4-UT after exacerbation has been little reported. Herein, we report SMARCA4-UT successfully managed with salvage surgery for a lesion that worsened after combined immunotherapy and chemotherapy. This report suggests the efficacy of incorporating surgical resection into the treatment strategies for post-therapy exacerbations.

The patient, a 48-year-old man, presented with left shoulder pain. A tumorous lesion in the left pleura was identified on contrast-enhanced computed tomography, and positron emission tomography/computed tomography revealed significantly increased fluorodeoxyglucose uptake at the same site as well as in multiple lymph nodes in the bilateral lung hilum and mediastinum (Figure 1). SMARCA4-UT was diagnosed (cT4 N3 M1a stage IVa; driver mutation negative; anti-programmed cell death ligand 1 [PD-L1] tumor proportion score, 1%-24%) after pleural biopsy (Supplemental Figure 1). Treatment with 2 cycles of cisplatin and pemetrexed combined with an anti-PD-1 blocker, nivolumab, and an anti-cytotoxic T-lymphocyte protein 4 (CTLA-4) blocker, ipilimumab, resulted in a significant reduction (RECIST: partial response, 86% reduction). Ipilimumab was discontinued because of joint pain, and maintenance therapy (nivolumab plus ipilimumab, 1 course; nivolumab, 6 courses) was administered. During maintenance therapy, bilateral ground-glass opacities and nodular shadows were observed (Supplemental Figure 2) along with elevated KL-6 levels (874 IU/mL). Bronchoalveolar lavage revealed a predominance of lymphocytes, leading to discontinuation of maintenance therapy and initiation of prednisone (0.5 mg/kg) for drug-induced pneumonia.

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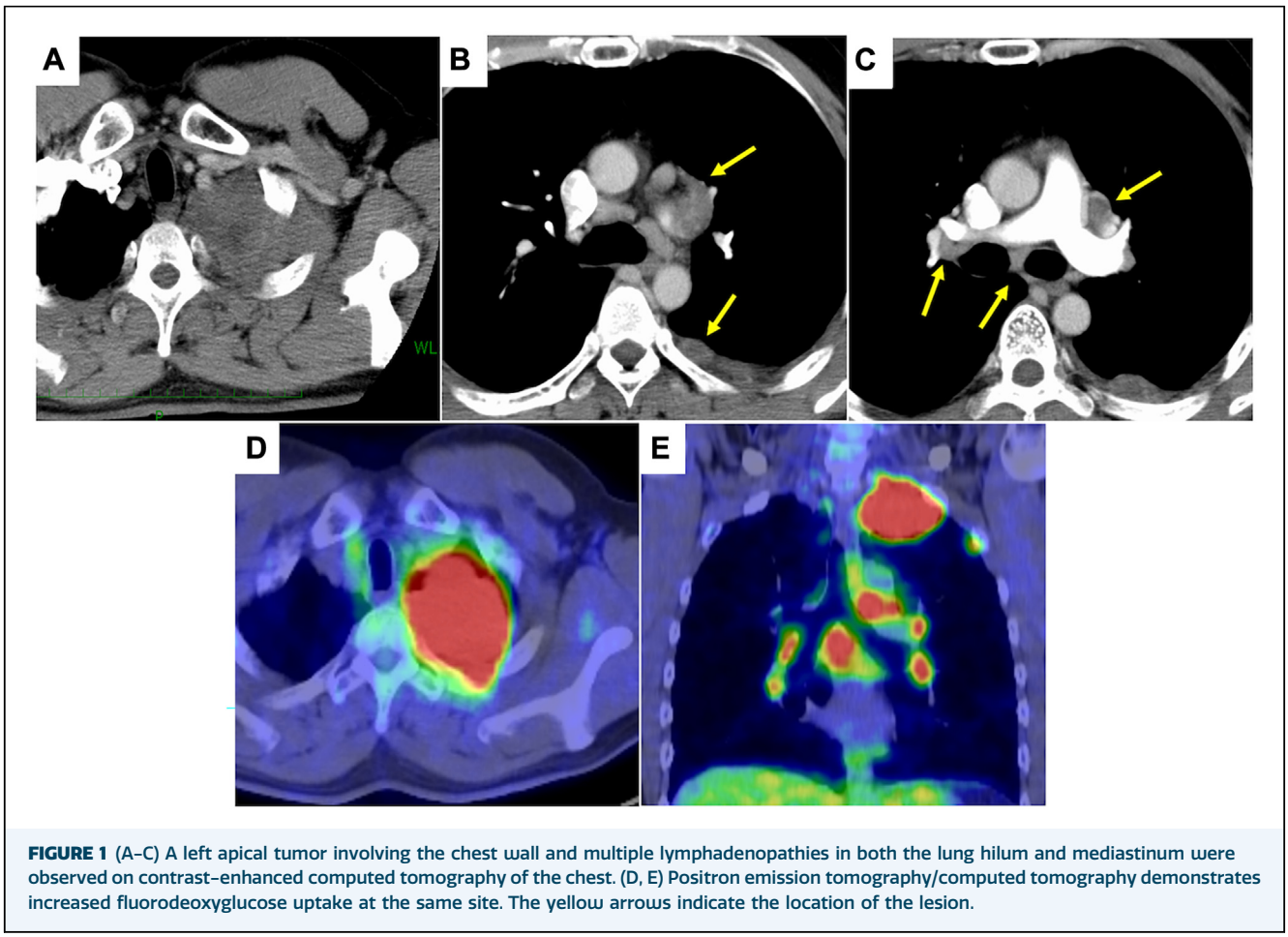

FIGURE 1 (A–C) A left apical tumor involving the chest wall and multiple lymphadenopathies in both the lung hilum and mediastinum were observed on contrast-enhanced computed tomography of the chest. (D, E) Positron emission tomography/computed tomography demonstrates increased fluorodeoxyglucose uptake at the same site. The yellow arrows indicate the location of the lesion.

The pneumonia improved with prednisone treatment but recurred 3 months after discontinuation of maintenance therapy, with enlargement of the chest wall lesions and lymph nodes at the same site (Figure 2). Resuming immunotherapy was challenging because of concerns about drug-induced pneumonia, prompting the decision to proceed with salvage surgery for the same site. The operation involved excision of the chest wall tumor and lymph node dissection through a posterior lateral incision, with a surgical duration of 4 hours 4 minutes and blood loss of 460 mL. The tumor in the chest wall did not invade the ribs, and no complications involving the ribs were resected. Pathologic diagnosis revealed that all 3 lesions exhibited tissue morphology identical to that of SMARCA4-UT. The chest drain was removed on postoperative day 7, and the patient was discharged without complications on postoperative day 21. Additional postsurgical treatment was not administered, and the patient is currently 2.5 years into treatment (1.5 years after surgery), with no evidence of disease progression.

COMMENT

This case is significant as it describes salvage surgery performed on a SMARCA4-UT that deteriorated after systemic therapy. Remarkably, this intervention resulted in medium-term recurrence-free survival without the need for additional treatment. It underscores the potential of surgical intervention after systemic therapy for SMARCA4-UT.

Salvage surgery, defined as surgical intervention for residual or recurrent lesions after prior treatment, has shown curative potential in select cases of lung cancer.[5] In this case, salvage surgery was chosen because of factors such as drug-induced pneumonia and the localized nature of thoracic lesions. The outcome revealed no recurrence or metastasis without additional postoperative treatment, suggesting the sustained therapeutic efficacy of immunotherapy.

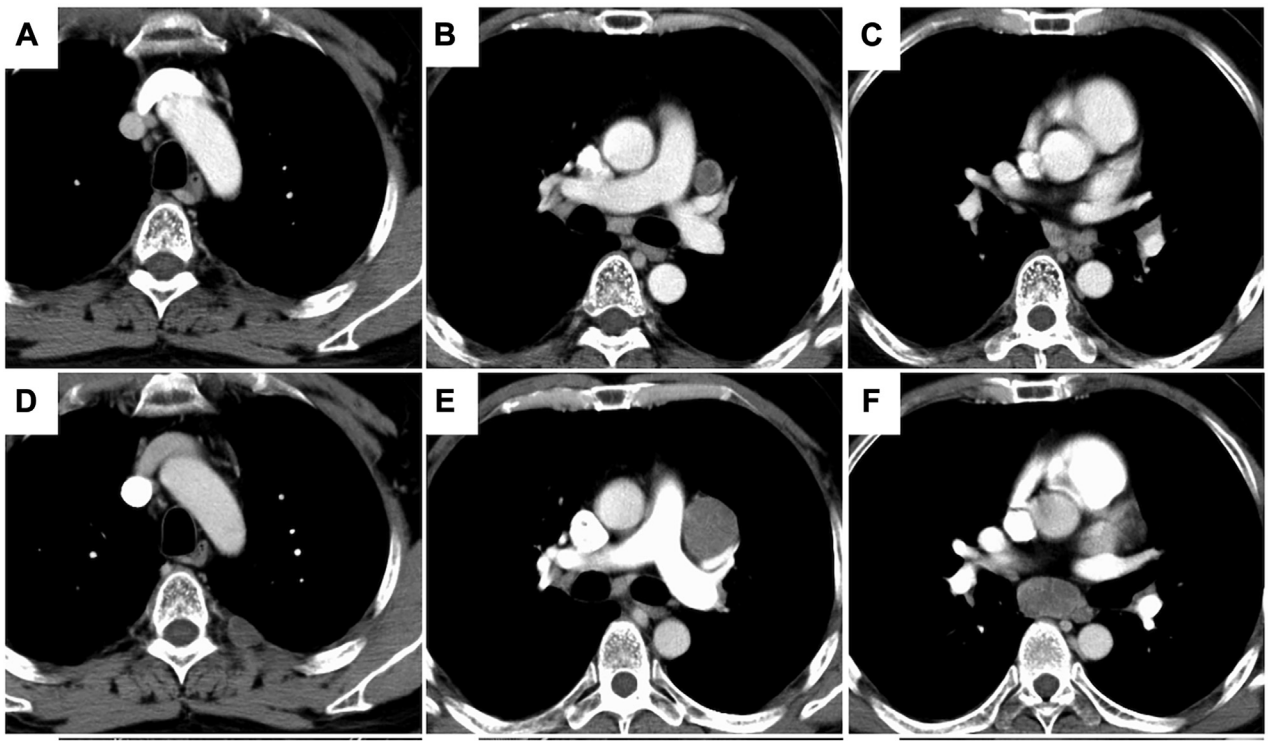

FIGURE 2 Contrast-enhanced computed tomography of the chest (A–C) before and (D–F) after prednisone initiation. Recurrence in the chest wall and mediastinal lymph nodes is noted.

Although chemotherapy has limited effectiveness against SMARCA4-UT, these tumors exhibit a high tumor mutational burden, indicating potential responsiveness to immune checkpoint inhibitors.[6] Previous reports have demonstrated the efficacy of PD-L1 inhibitors alone or in combination with chemotherapy.[6,7] Although data on PD-L1 and CTLA-4 combination therapy for SMARCA4-UT are limited,[8] this report presents an example of combining PD-L1 and CTLA-4 inhibitors with chemotherapy, which resulted in remarkable therapeutic outcomes. This combination therapy holds promise for future treatments, especially given the association of SMARCA4-UT with impaired regulatory T-cell activation, potentially enhancing susceptibility to CTLA-4 inhibitor therapy. In addition, ongoing drug development aims to improve prognosis,[4] offering hope for more effective treatments.

However, the effective management of lesions that worsen after treatment remains critical. This report provides valuable insights into the effectiveness of salvage surgery for SMARCA4-UT.

In conclusion, this report demonstrates the successful management of SMARCA4-UT by salvage surgery for posttreatment exacerbated lesions. This highlights the potential efficacy of incorporating surgical resection into treatment strategies for posttreatment exacerbations and provides a valuable approach for managing SMARCA4-UT.

The Supplemental Figures can be viewed in the online version of this article [https://doi.org/10.1016//j.atssr.2024.08.008] on http://www.annalsthoracicsurgery.org.

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REFERENCES

1. Nicholson AG, Tsao MS, Beasley MB, et al. The 2021 WHO classification of lung tumors: impact of advances since 2015. *J Thorac Oncol*. 2022;17:362–387.

2. Rekhtman N, Montecalvo J, Chang JC, et al. SMARCA4-deficient thoracic sarcomatoid tumors represent primarily smoking-related undifferentiated carcinomas rather than primary thoracic sarcomas. *J Thorac Oncol*. 2020;15:231–247.

3. Yoshida A, Kobayashi E, Kubo T, et al. Clinicopathological and molecular characterization of SMARCA4-deficient thoracic sarcomas with comparison to potentially related entities. *Mod Pathol*. 2017;30:797–809.

4. Shinno Y, Ohe Y, Lung Cancer Study Group of the Japan Clinical Oncology Group (JCOG). Thoracic SMARCA4-deficient undifferentiated tumor: current knowledge and future perspectives. *Jpn J Clin Oncol*. 2024;54:265–270.

5. Shimizu K, Ohtaki Y, Suzuki K, et al. Salvage surgery for non-small cell lung cancer after definitive radiotherapy. *Ann Thorac Surg*. 2021;112:862–873.

6. Shinno Y, Yoshida A, Masuda K, et al. Efficacy of immune checkpoint inhibitors in SMARCA4-deficient thoracic tumor. *Clin Lung Cancer*. 2022;23:386–392.

7. Lin Y, Yu B, Sun H, et al. Promising efficacy of immune checkpoint inhibitor plus chemotherapy for thoracic SMARCA4-deficient undifferentiated tumor. *J Cancer Res Clin Oncol*. 2023;149:8663–8671.

8. Nakano Y, Sekinada D, Kuze Y, Okamoto N, Gohma I, Yasuhara Y. A case of thoracic SMARCA4-deficient undifferentiated tumor successfully treated with combination ipilimumab-nivolumab. *Clin Case Rep*. 2022;10:e6745.