



First line PD-1 inhibitor, Serplulimab Plus Chemoradiotherapy for Extensive Stage Thymic Carcinoma: A Case Report

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SUMMARY

Thymic carcinoma originated from epithelial cell thymus within the anterior mediastinum. Limited treatment options available for unresectable and metastatic disease. The emergence of immunotherapies for solid tumors has generated significant interest and PD-1 inhibitor have shown to be a promising alternative choice. We reported a case of a 47 year old male with presternal chest pain and dyspnoe underwent a chest CT in January 2024 in which showed anterior mediastinal mass 8.2×4.3×8.7 cm obliterating superior vena cava, supra azygos and brachiocephalic bilateral. In addition bilateral pleural and pericardial effusion were described. After core needle biopsy pathology result thymic carcinoma then a next generation sequencing study with no gene alteration was found. Patient received 20 times radiotherapy followed by chemotherapy based on ADOC regimen for 6 cycles accompanied with 3 cycles 200 mg Serplulimab three weekly. Final RECIST ver 1.1 reveal 13% tumor shrinking and disappearance of pleural effusion. The immune related adverse event only grade 1. Management of thymic epithelial neoplasm is a paradigm of multidisciplinary approach. Complete surgical resection is the only potentially curative option. For metastatic disease, palliative chemotherapy based on platinum is the first line standard therapy. A few prospective studies have investigated multiple novel agents such as immune check point inhibitors. To our knowledge this is the first case report use of serplulimab in extensive thymic carcinoma with encouraging results. However, given the high incidence of autoimmunity, irAEs should be carefully monitored.

Keywords: PD1 inhibitor; serplulimab; thymic carcinoma.

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INTRODUCTION

Thymic carcinoma (TC) originated from the epithelial cells of the thymus within the anterior mediastinum. Compared to thymoma, it usually presents at more advanced stages and carries a poorer prognosis. First-line therapy typically includes platinum-based chemotherapy with or without radiotherapy; however, durable responses remain infrequent. The

emergence of immunotherapies for solid tumors have shown promising efficacy in limited studies involving thymic epithelial tumors (TETs), though with a recognized risk of immune-related adverse events (irAEs). Serplulimab, a humanized IgG4 anti PD-1 monoclonal antibody initially approved for first line treatment of extensive stage small cell lung cancer (ES-SCLC) in combination with chemotherapy and now with expanding indications for solid tumors.

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CASE REPORT

A 47-year-old male in January 2024 presented with pre-sternal chest pain accompanied by progressive dyspnea. He reported no weight loss, fever or cough. Physical examination revealed upper chest wall veins dilation and mediastinal compression. His body mass index (BMI) was 25.3, never smoker, has no family history of malignancy. He works daily as entrepreneur most activities from home. He currently on antiviral for chronic hepatitis C with complication of grade 1–2 esophageal varices controlled with medication. Viral load during treatment was undetected and liver function was stable. The primary concern is immune-mediated liver injury, which can be difficult to distinguish from a viral flare, therefore we monitor transaminase enzymes vigilantly. Some researchs indicate that blocking PD-1/PD-L1 pathway may actually help the immune system suppress the hepatitis C virus by restoring exhausted T-cell function. [1] Axial view (Fig. 1a) contrast- enhanced thoracic computed tomography (CT) revealed heterogenous

solid-cystic superior-anterior mediastinal mass size $8.2 \times 4.3 \times 8.7$ cm obliterating superior vena cava, supra azygos and brachiocephalic bilateral with collateral veins at para-aortic level. In addition, bilateral pleural and pericardial effusion indicating extensive disease was described (Fig. 1b). Spirometry showed mild restrictive pattern with Forced Vital Capacity (FVC) 75.8% and normal Forced Expiratory Volume in one second (FEV-1).

Bronchoscopy found no endo-bronchial mass and negative cytology. Trans thoracic needle aspiration cytology (Fig. 2a) and CT guided core-biopsy revealed a squamous cell carcinoma (Fig. 2b) originated from thymus gland. Multiple discipline team discussion consists of pulmonology, pathology and radiology decided thymic carcinoma is the most appropriate diagnosis then a next generation sequencing (NGS) study with no gene alteration found but unfortunately PDL-1 expression was unavailable due to limited sample size. Brain Magnetic Resonance Imaging (MRI) and bone scan showed no evidence of metastasis. Signs of superior vena cava (SVC) syndromes observed in-

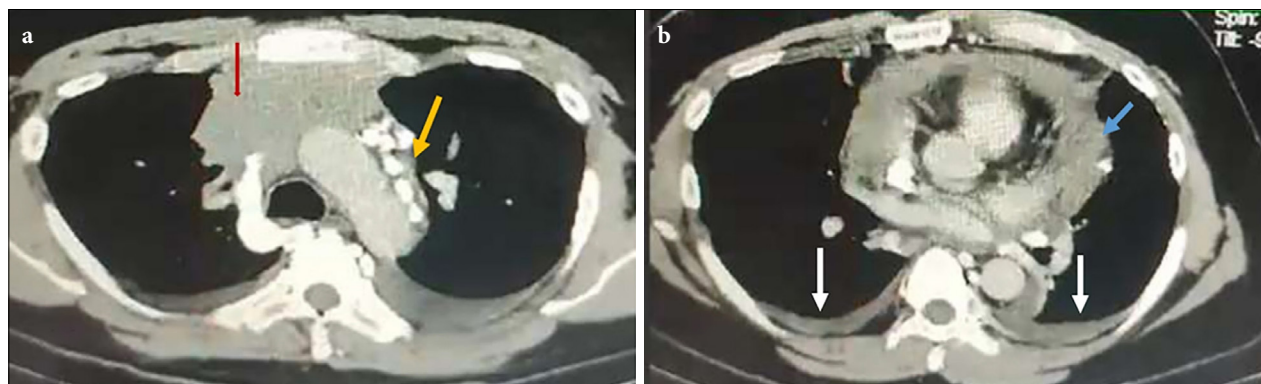


Fig. 1. (a) Anterior mediastinal mass obliterate superior vena cava and brachiocephalic vein (red arrow), collateral veins at para-arcus aorta (yellow arrow). (b) Bilateral pleural effusion (white arrow) and pericardial effusion (blue arrow).

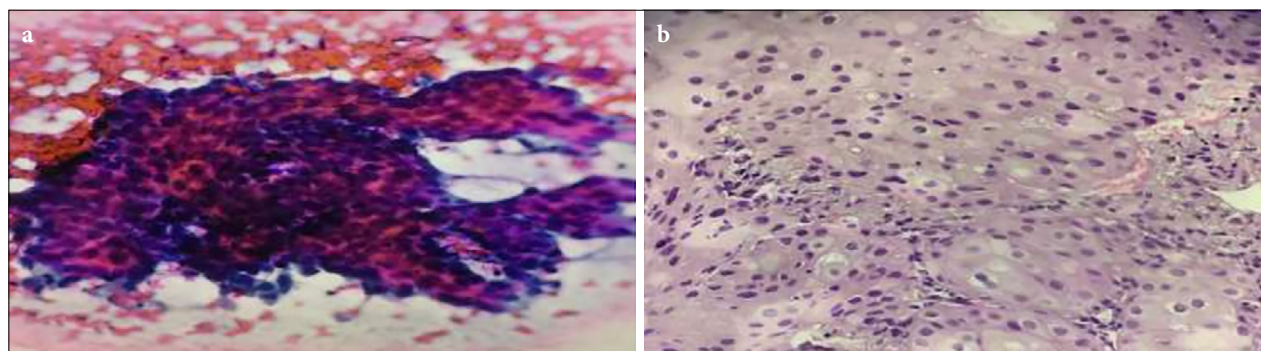


Fig. 2. (a) Cytology slide showed cluster tumor cells, round/oval nuclei and rough cromatin. (b) Histology slide reveal solid cluster tumor cells, infiltrative. Round/oval nuclei, phleormorphic, rough chromatin and wide cytoplasm.

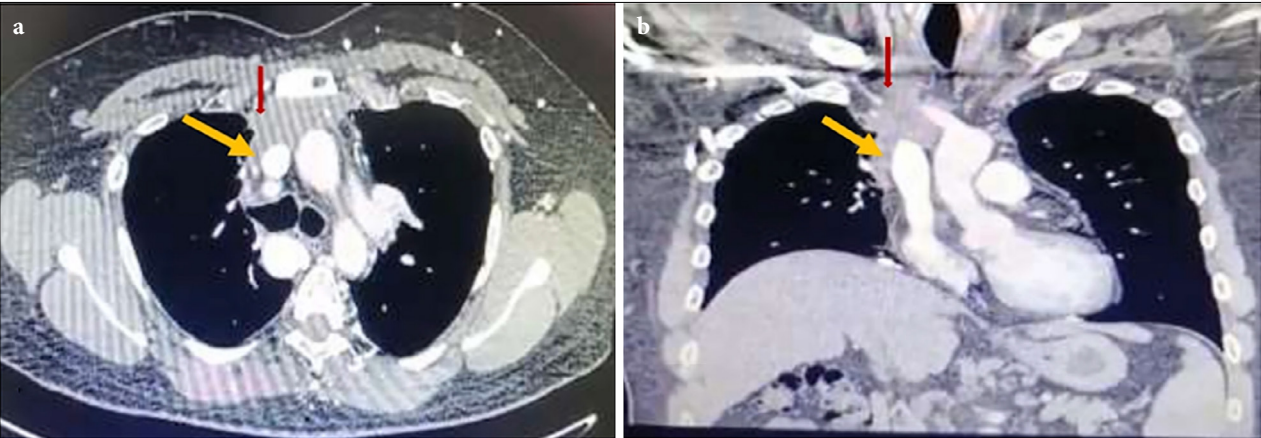


Fig. 3. (a, b) Decrease size of anterior mediastinal mass (red arrow), restore patency of superior vena cava (yellow arrow), disappearance of pleural and pericardial effusion.

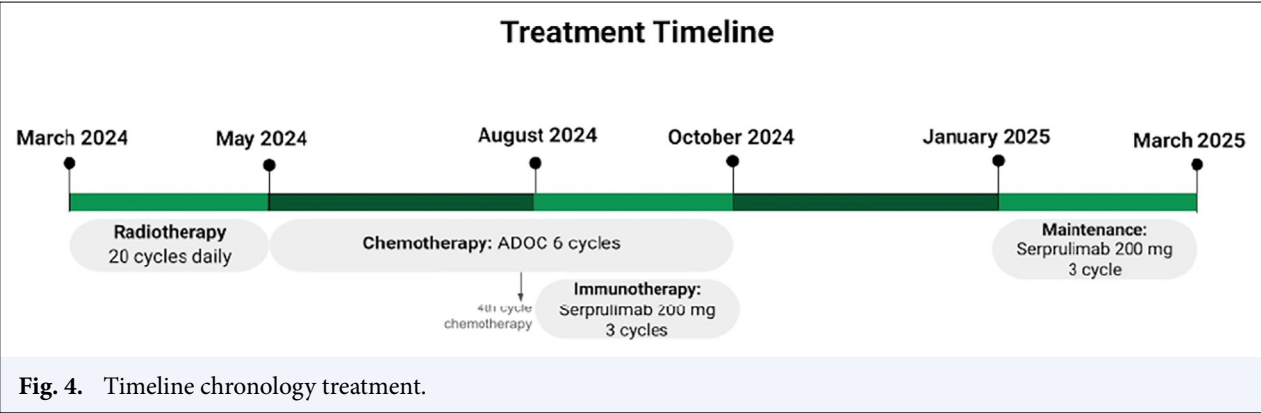


Fig. 4. Timeline chronology treatment.

cluding dilated superficial veins, distended jugular venous vein, neck and upper limb oedema, therefore twenty courses of palliative radiotherapy weekday daily dose 200 cGy (total 4000 cGy) using 3D conformal radiation therapy (3D-CRT) were commenced on March to April 2024. Planning target volume (PTV) was used to ensure the prescribed dose is actually delivered to the clinical target volume despite variations in patient positioning or beam alignment. Primary organs at risk such as heart, lungs, spinal cord and oesophagus are prioritized for dose monitoring to minimize toxicity. Chemotherapy started two weeks after radiotherapy completion based on adriamycin, carboplatin, vincristine and cyclophosphamide (ADOC) regimen three weekly for 6 cycles started from May 2024. Concurrently 200 mg of serprulimab three weekly were administered within chemotherapy cycle 4 to 6 (three cycles) followed by three cycles of serprulimab maintenance therapy. CT evaluation at October 2025 revealed tumour size shrink to 7.6×2.2×5.2 cm

or approximately 13% by response evaluation criteria in solid tumors (RECIST) 1.1 in other words stable disease control with minimal calcification (Fig. 3a). Under the RECIST 1.1 guidelines, target lesions in this case were anterior mediastinal mass measured by their longest diameter (LD) performed on axial planes. Baseline LD was 8.7 cm and follow up after treatment was 7.6 cm. Other findings also showed restored patency of superior vena cava, disappearance of non-target lesions (pleural and pericardial effusion) and no lymph nodes enlargements (≥ 15 mm) without any new lesions were found. (Fig. 3b). The immune related adverse event was limited only grade I (fatigue, dry skin). Patient regains his activity and came back to work without any notable complaints. Evaluation and monitoring were scheduled monthly for subjective response and three monthly for radiological measurement. Timeline chronology treatment presented in figure (Fig. 4). Written informed consent was obtained from the patient.

DISCUSSION

TC is associated with a poor prognosis due to its aggressive biology and limited response to conventional therapies.[2] Platinum based chemotherapy offers modest benefit and radiotherapy contributes to local control in selected patients. Recent interest has focused on immune checkpoint inhibitors (ICIs) particularly PD-1/PDL-1 inhibitors.[3] This case highlights the potential benefit of PD-1 blockade in TC, an area with limited treatment options.[4]

The present case is notable for a measurable radiological response, disappearance of pleural and pericardial effusion with minimal toxicity of ICIs despite the known higher risk of irAEs in TETs compared with other solid tumours. This is primarily due to the thymus's role in central immune tolerance; tumors in this organ often lead to the release of autoreactive T cells.[5] Incidence of irAEs in thymoma up to 71% of patients experience grade ≥ 3 toxicities, while incidence in TC are generally lower with grade ≥ 3 events occurring in approximately 10–20% patients.[6] Other anti PD-1 such as pembrolizumab shown an objective response rate (ORR) of approximately 19.2 to 23% in TC patients, while nivolumab in some studies reported no objective responses but disease stabilization was achieved in about 73.3% patients in the PRIMER study.[7,8] Serplulimab has a higher affinity (2.42nM) to human PD-1 compared with pembrolizumab (8.04nM) and nivolumab (11.9nM). High-affinity antibody binding to antigens results in greater internalization and degradation. It induced a significantly more robust PD-1 internalization than nivolumab, with approximately 20% of the internalization persisting at 6 and 14 hours, while pembrolizumab exhibited limited internalization.[9] Serplulimab utilizes its heavy and light chains differently than other inhibitors, leading to unique spatial interaction and robust induction of PD-1 receptor endocytosis. Though it less widely reported in this disease still produced a meaningful tumour reduction and symptomatic improvement with only mild toxicity. Clinical studies for serplulimab have demonstrated antitumor activity in oesophageal, lung and MSI-H tumors.[10] Management of TETs is a paradigm of multidisciplinary approach while complete surgical resection remains the only potential curative options. The patient's improvement and achievement of disease control following chemotherapy, radiation and subsequent PD-1 inhibition support the rationale for multimodal therapy in aggressive TC. This case aligns with emerging literature suggesting that selected patients may derive benefit from ICIs.[11]

Limitations

TC often has high expression of PD-L1 which is positively correlated with better response rates to PD-1/PD-L1 inhibitors. The lack of this marker made us unable to explain biologic and therapeutic implications for the treatment.

CONCLUSION

To our knowledge, utilization of exact combination between serplulimab and chemo-radiotherapy in advanced TC is rare but the broader therapeutic context indicates that PD-1/PD-L1-based strategies are already being actively investigated in TETs, thus demonstrates a favourable radiological and clinical response. This report contributes to growing evidence supporting PD-1 inhibition in achieving durable disease control as a therapeutic option in advanced TC cases.

Ethics Committee Approval: This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Conflict of Interest Statement: All authors declare that they have no conflict of interest.

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