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Transvertebral Cryoablation of a Paraesophageal Mass in a Patient with Metastatic Malignant Pleural Mesothelioma

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Abstract: Malignant pleural mesothelioma is a rare but aggressive cancer with limited treatment options. Percutaneous cryoablation is emerging as a promising treatment option for control of local recurrence and for palliative management of the disease-related symptoms. At times, recurrent malignant pleural mesothelioma is difficult to target as it can recur within the mediastinum and can be surrounded by vital organs and large vessels. This case report describes a challenging yet safe and successful transvertebral approach for percutaneous cryoablation of a paraesophageal mass for palliative treatment of a patient with single-site recurrent metastatic malignant pleural mesothelioma within the mediastinum.

Keywords: *cryoablation, transvertebral, transosseous, mesothelioma*

Key Points

- Percutaneous cryoablation is an effective treatment modality for recurrent malignant mesothelioma.
- A transvertebral approach for percutaneous ablation can be a safe and advantageous method for difficult to reach mediastinal tumors.

Case Presentation

A 65-year-old man presented for follow-up fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) seven months after left radical pleurectomy and decortication for pleural mesothelioma (MPM). The examination revealed evidence of a new FDG-avid paraesophageal mass measuring 30 mm x 27 mm and located close to the inferior vena cava (IVC) and the left atrium (Figure 1A and 1B). Approximately 14 months prior to this encounter, the patient had presented with a two-week history of back pain radiating to the abdomen. The baseline CT of the chest revealed a left-sided pleural effusion, pleural plaques throughout the left hemithorax, pleural nodularity, beading and nodularity along the left fissure, mediastinal adenopathy, and an enlarged paraesophageal lymph node. The patient underwent left-sided thoracoscopy with pleural biopsy and placement of a pleural catheter. Histopathologic examination revealed epithelioid malignant mesothelioma. The patient received multiple courses of neoadjuvant chemotherapy with cisplatin, pemetrexed disodium, and bevacizumab.

Seven months after initial presentation, the patient had left radical pleurectomy and decortication. Histopathologic examination of the surgical specimen revealed mixed epithelioid type and sarcomatoid type of mesothelioma. Then the

Figure 1. Computed Tomography (CT) and Fused FDG-PET/CT of a Paraesophageal Mass in a 65-year-old Man with Recurring Malignant Pleural Mesothelioma.

A CT of the chest, axial view

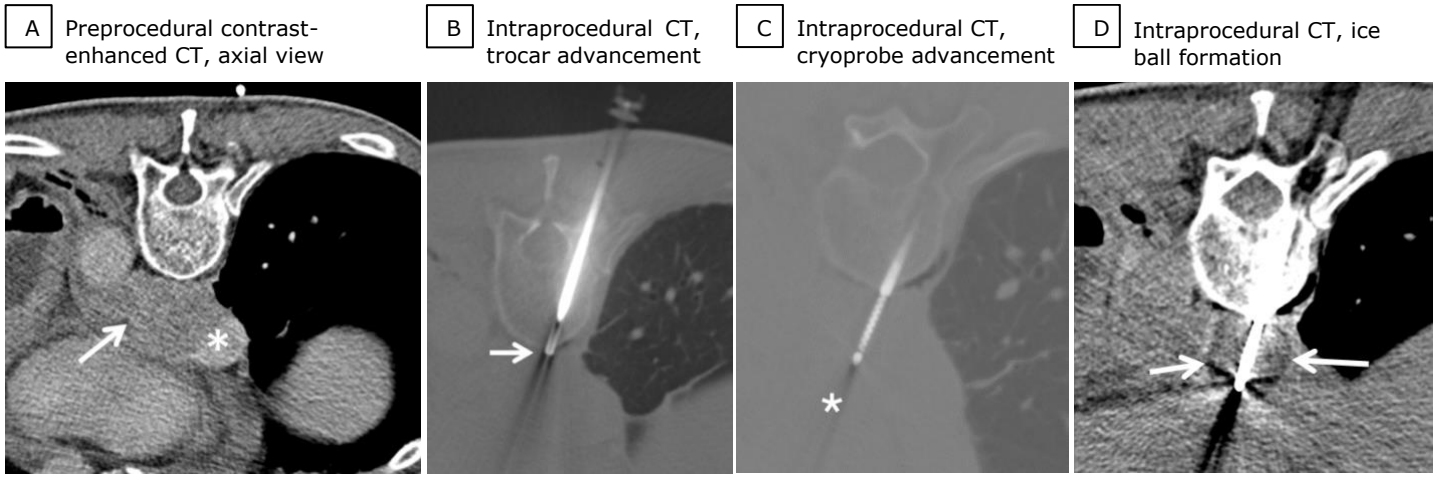
B FDG-PET/CT of the chest, axial view

(A and B) CT of the chest and fused FDG-PET/CT images show an enhancing left paraesophageal mass (A, arrow) with intense metabolic activity (B, arrow). The mass is situated close to the esophagus, the aorta, the inferior vena cava, and the left atrial pericardium.

patient received stereotactic radiation therapy with delivery of 45 Gy in 25 fractions to the left pleura and a boost of additional 9 Gy in 5 fractions to the inferior pleura and the left paravertebral area. Thereafter, the patient was prescribed three cycles of gemcitabine and carboplatin followed by a maintenance regimen of pembrolizumab. During a 5-month postoperative follow-up, FDG-PET/CT showed residual hypermetabolic activity of the left paravertebral mass at the T12 vertebral level. At this point, cryoablation of the mass was performed followed by FDG-PET/CT that showed reduction of FDG uptake consistent with treatment response. The patient had follow-up FDG-PET/CT at three-month intervals.

The finding of a new, FDG-avid paraesophageal mass during a 7-month postoperative follow-up was discussed at a tumor board, and the treatment team agreed to proceed with the mass cryoablation as a palliative treatment to avoid extension of the mass into the surrounding vital structures. A transvertebral approach to target the paraesophageal mass was chosen. At the time of the procedure, general anesthesia was administered with total anesthesia time of two hours. Under CT guidance, a 19-gauge coaxial needle was advanced to the level of the right side of the T12 vertebral body. Local anesthetic was administered along the tract of the needle. The coaxial needle was exchanged for a 10-gauge drill Kyphon Express II Osteo Introducer (Medtronic). The drill was advanced through the pedicle and then through the vertebral body and placed just beyond the vertebral cortex (Figure 2A and 2B). The stylet was removed, and the cryoablation needle IceFORCE® 2.1 CX 90° (BTG plc) was

Figure 2. Cryoablation-planning and Intraprocedural Imaging of Transvertebral Cryoablation of a Paraesophageal Mass in a 65-year-old Man with Recurrent Malignant Pleural Mesothelioma.



(A) Cryoablation-planning contrast-enhanced computed tomography (CT) of the patient in prone position shows heterogeneous enhancement of the mass (A, arrow) situated close to the inferior vena cava (A, asterisk), the esophagus, and left atrial pericardium. (B) The tip of the trocar is seen just beyond the edge of the vertebral cortex (B, arrow). (C) The cryoprobe is advanced incrementally and placed at the edge of the tumor, close to the left atrial margin (C, asterisk). (D) Ice ball (D, arrows) is seen as a low-density area surrounding the cryoprobe.

advanced through the coaxial needle into the tumor to its border and to the edge of the pericardium (Figure 2C). Cryoablation was then performed, including a ten-minute freeze followed by three minutes of passive thaw and an additional ten-minute freeze, with a resultant ice ball size of 28 mm x 27 mm (Figure 2D). The patient was discharged home on the same day after a period of observation. Subsequently, the patient received a maintenance regimen of pembrolizumab. Follow-up FDG-PET/CT, one month after the procedure, showed reduction in both FDG uptake and the size of the tumor. Three months after cryoablation, FDG-PET/CT showed complete resolution of metabolic activity with continued decrease in size of both the tumor and the residual postablation zone (Figure 3). However, the patient developed multiple, resistant-to-systemic-treatment metastases at different sites along the thoracic and the lumbar spine and died 12 months after the cryoablation.

Discussion

Malignant pleural mesothelioma (MPM) is an aggressive malignant tumor that is typically associated with exposure to asbestos; it carries a poor prognosis, "with median survival 9-12 months after diagnosis," and has an upward trend in incidence.[1] The management of MPM is based on its stage and includes various combinations of surgical therapy, radiation therapy, and chemotherapy.[1,2] Surgical options include extrapulmonary pneumonectomy (EPP) or lung-sparing pleurectomy/decortication, with no survival benefit demonstrated by existing published randomized controlled trials.[1] A standard chemotherapy regimen includes a platinum-based agent and pemetrexed with or without bevacizumab.[1] Immunotherapy is emerging as a promising new treatment modality, with the Checkmate 743 study demonstrating an increase in overall survival in patients who received dual immunotherapy of nivolumab and ipilimumab compared to those patients who received the standard chemotherapy with platinum compounds combined with pemetrexed.[1] The so-called "trimodal therapy" (TMT) involves neoadjuvant or adjuvant chemotherapy, EPP, and adjuvant radiotherapy.[3] Inconsistencies between studies evaluating the efficacy of TMT limit the aggregation of data, while local and distant recurrence of the disease are reported in ranges 4%-41% and 5%-65%, respectively.[3]

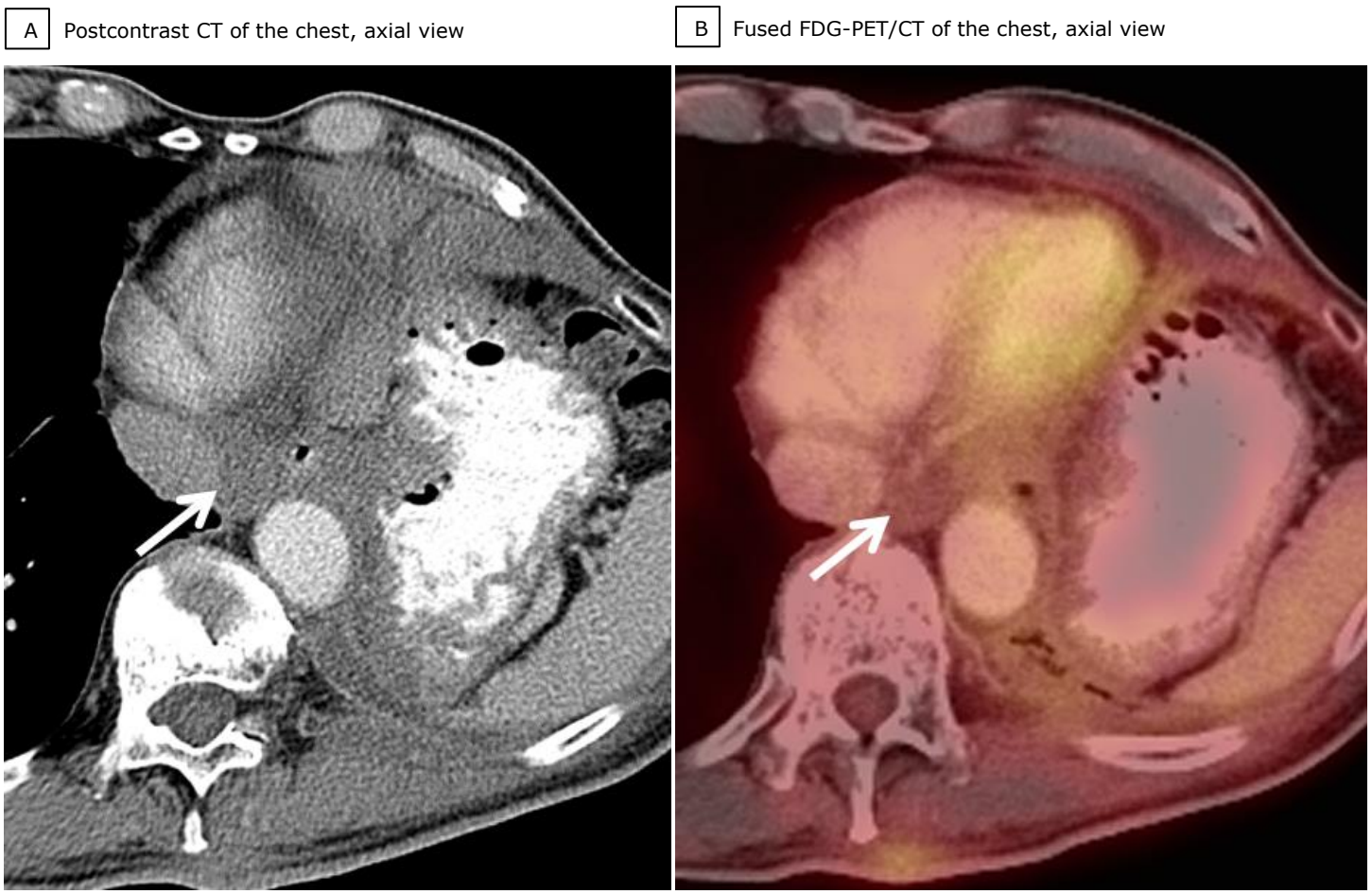
Second-line therapy options, namely surgery, chemotherapy, or radiation therapy may increase time of postrecurrence survival.[4] Because of initial

high-dose radiation treatment, some patients may not be candidates for additional radiotherapy in the setting of recurrent disease.[5] A second surgery is particularly beneficial for relief of symptoms and prevention of local dissemination of a recurring tumor.[5] However, the second surgery is not recommended in cases when the disease recurs contralaterally and in patients in a poor state of health.[4] A second-line chemotherapy is associated with a shorter overall survival compared to other modalities and should be considered in patients who previously responded to chemotherapy.[4]

Percutaneous cryoablation has been shown to be a safe and effective treatment option for controlling local recurrence of malignant pleural mesothelioma, with relapse-free survival 90.8% at 1 year and 73.7% at 3 years.[6] The cryoablation technology implemented in our case utilized argon gas channeled through probes to create an ice ball at the tip of the probe. Cryoablation causes cellular damage, death, and necrosis of tissue by directly inducing cold injury to cells and by affecting the cellular microenvironment.[7] One of the advantages of cryoablation is that it allows clear visualization of the ablation margins on intraprocedural CT.[6]

Because in our case the targeted tumor was surrounded by the left atrium anteriorly, the liver to the right, and the aorta and the esophagus to the left, our operative approach was limited. In addition, given the patient's limited pulmonary reserve, a transpulmonary approach was unacceptable as it would have posed risk of tumor seeding into and possible damage of the

Figure 3. Three-month-postprocedural Computed Tomography (CT) and Fused FDG-PET/CT of the Ablated Paraesophageal Mass in a 65 year-old Man with Recurrent Malignant Pleural Mesothelioma.



(A and B) Postcontrast CT and fused FDG-PET/CT images of the ablated tumor show decrease in size of the tumor (A, arrow) and complete metabolic response (B, arrow).

unaffected right lung. Further, the length of the available probes would not have been enough to accommodate a transpulmonary approach. Given these considerations, a unique transvertebral path to reach the paraesophageal mass was chosen (Figures 2B and 2C). Transosseous routes, including routes taken through the rib and the scapula, have been used for radiofrequency ablation of thoracic lesions when no other path was available or when the transosseous route was the safest.[8,9] The transvertebral approach, specifically, has been used for biopsy or ablation of both paraesophageal lesions and lung lesions.[10] Advantages of the transvertebral approach, as discussed by Chehab et al,[10] include the possibility of using a shorter needle and accessing lesions in parallel to great vessels, while risks include the "potential injury to the epidural space or paraspinal musculature."[10] During ablation procedures, a transosseous route can be limiting because it precludes repositioning of the ablation probe to perform overlapping ablations that allow for adequate treatment margins.[9]

The cryoablation in our case was initially planned for palliative care because of the location of the tumor and concern for possible invasion of vital structures. Considering the tumor's contact with the aorta, the esophagus, and the left atrium, complete tumor ablation was impossible. As described by Abtin et al,[6] cryoablation of recurrent MPM can be achieved by a cytotoxic temperature of -20 °C and an ablative margin of 5 mm. In our case, for the tumor to be completely eradicated, the ice ball would need to extend to surrounding structures, which would cause catastrophic injury to the esophagus. In addition, the presence of the large vessels and the heart limits the cooling effect of ice, the so-called cold-sink effect, and keeps the ice from reaching lethal temperatures at the periphery.[11] In our case, the ice ball size (28 x 27 mm) was ultimately smaller than the target mass (30 x 27 mm); therefore, at least a 7 mm margin of tumor was located outside the -20 °C cytotoxic ice. Despite the presumed palliative intent of the procedure, the results were much more favorable, and the one- and three-month postprocedure FDG-PET/CT revealed gradual resolution of metabolic activity (Figure 3). The exact cause of this complete metabolic response to the treatment is not clear, but likely it resulted from a synergistic effect of cryoablation combined with immune therapy. Hypothetically, following cryoablation and tumor necrosis, intracellular content and antigen remain intact and are released, affecting tumor cells outside the ablated field.[12] Therefore, when combining cryoablation with a *PD-1* (OMIM 600244) inhibitor, such as pembrolizumab, the release of cryoablation-induced antigen along with inhibition of *PD-L1* (OMIM 605402) on tumor cells results in an effective antitumor T-cell response.[12] As cryoablation increasingly becomes a staple in the treatment of patients with recurrent malignant pleural mesothelioma as well as other intrathoracic malignant tumors, the transvertebral approach, as described in this case report, could be considered a safe but demanding option for treating posteriorly located intrathoracic mediastinal masses.

Author Contributions

Conceptualization, F.A., K.F.S. and R.B.C; Acquisition, analysis, and interpretation of data, F.A., K.F.S., R.B.C. and S.F.; Writing – original draft preparation, S.F. and F.A.; Review and editing, S.F. and F.A.; Supervision, F.A. and R.B.C. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Disclosures

None to report.

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