Case Report

Malignant Tracheoparenchymal Fistula in Primary Mediastinal B-Cell lymphoma detected on Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography

Abstract

Acquired tracheobronchial fistulas are a relatively uncommon complication. Among them, tracheo-mediastinal-parenchymal fistulas are particularly rare. Most of the reported cases are associated with concurrent chemoradiotherapy in lung cancer. It has not been reported in lymphomas. These fistulas are associated with high mortality due to infection and bleeding, and there is no consensus on a definitive optimal therapy. Here, we present a case of tracheoparenchymal fistula in a follow-up primary mediastinal B-cell lymphoma case. This case highlights the utility of fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) in the initial diagnosis and follow-up of lymphoma. The PET/CT could show demonstrate the residual disease and differentiate it from other therapy-related benign changes.

Keywords: *Diffuse Large b-cell Lymphoma, Rituximab-Etoposide-Prednisolone-Vincristine-Cyclophosphamide-Hydroxydanorubicin chemotherapy, primary mediastinal B-cell lymphoma, Tracheoparenchymal fistula*

Vijay Singh, Manish Ora, Sanjay Gambhir

Department of Nuclear Medicine, SGPGIMS, Lucknow, Uttar Pradesh, India

Introduction

Primary mediastinal B-cell lymphoma (PMBCL) is a rare lymphoma that arises from thymic B-cells and has distinct clinicopathological aggressive features.[1] It constitutes approximately 2%–4% of non-Hodgkin's lymphomas (around 6% of diffuse large B-cell lymphoma [DLBCL]).[1] PMBCL resembles nodular sclerosing Hodgkin's lymphoma more than DLBCL. Both arise from thymic B-cells, affect a young patient, and have similar clinicopathological and genetic characteristics.[2] This disease primarily affects young adults (median age of 35), with a female/male ratio of 1.7–2/1.[3] Patients often present with signs and symptoms of a rapidly growing bulky mediastinal mass and superior vena cava obstruction. Sometimes, they demonstrate intrathoracic extension into the lung, pleura, chest wall, and pericardium. Disseminated disease, especially extranodal involvement, is frequently seen at relapse.[4] Nearly one-third of patients present B symptoms (fever, weight loss, and night sweats). Approximately a quarter of patients present with advanced disease.[5] A Dose Adjusted, Rituximab-Etoposide-Prednisolone-Vincristine-Cyclophosphamide-Hydroxydanorubicin (DA-REPOCH) and Rituximab-Cyclophosphamide-Vincristine-Prednisolone (R-CHOP) chemotherapy regimen may lead to high survival rate.[6] The survival rate of PMBCL is significantly higher than DLBCL.[4] Despite highly curative immunochemotherapy regimens, 10%–30% of PMBCL patients develop relapsed/refractory disease and require salvage therapies, with unsatisfactory outcomes.[6]

Case Report

A 22-year-old male presented with left-sided chest pain, cough, and supraclavicular swelling 2 years back. The thorax's computed tomography (CT) revealed a large soft tissue mass in the anterior mediastinum. Laboratory parameters showed high serum lactate dehydrogenase values (8123 U/l). The rest of the biochemical parameters were unremarkable. CT-guided biopsy from mediastinal mass reported PMBCL. On immunohistochemistry, it exhibited diffuse, strong B-cell markers (CD20, PAX-5) and CD30. TdT, CK, and CD117 were negative. Ki67 index was ~80%–85%. Pretreatment fluorodeoxyglucose positron emission

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Address for correspondence:
Dr. Manish Ora, Department of Nuclear Medicine, SGPGIMS, Lucknow - 226 014, Uttar Pradesh, India.
E-mail: drmanishora@yahoo.com

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tomography/CT (FDG PET/CT) revealed metabolically active conglomerated lymph nodal mass in the anterior mediastinum (not shown). Lymphadenopathy was noted on both sides of the diaphragm with liver involvement. The patient was started on R-CHOP-based chemotherapy regimen. After three-cycle interim, FDG PET/CT revealed partial response to therapy (not shown). End of cycle CT thorax revealed a residual mass lesion in the anterior mediastinum. A repeat biopsy revealed PMBCL, and a dose-adjusted REPOCH regimen was started. Follow-up FDG PET/CT after three cycles of DA-REPOCH revealed a residual mass lesion in the mediastinum. The patient received three more cycles of DA-REPOCH (not shown). After that, he had chest pain and cough for 20 days. FDG PET/CT revealed a large cavitary lesion in the anterior mediastinum and adjacent lung parenchyma. A tracheoparenchymal fistula (TPF) was seen communicating the trachea and upper lobe of the left lung. There was a direct communication of the left upper lobe bronchus with the cavity [Figures 1 and 2]. The patient has been advised surgical treatment for this fistula. The patient was lost to follow-up during the COVID-19 pandemic.

Discussion

Tracheomediastinal fistula is a broad term that represents fistulous communication between the trachea and mediastinal structures. It includes tracheoesophageal fistula (TEF), tracheobronchial fistula, and TPF. These may be congenital or acquired (tumor, infection, local trauma, but chiefly following tracheostomy or artificial ventilation). TEF is a rare complication of tumors, found mainly in the lung or esophageal cancer, and occurs mainly after radiotherapy or chemotherapy. Few cases of TEF in mediastinal lymphoma have been reported.[7] However, no tracheobronchial fistula and TPF have been reported as per the literature to the best of our knowledge.

Tracheomediastinal or bronchial-mediastinal fistulas represent a rare entity associated with high morbidity and mortality. The reported literature is limited to case reports or series. Iatrogenic benign fistulas are the most common type. Lymphoma, squamous cell carcinoma,[8] and lung adenocarcinoma[9] are common malignancies associated with it. The pathophysiology of a malignant airway-mediastinal fistula formation is unknown. However, various risk factors have been postulated. It includes radiotherapy, histopathological examination of squamous cell carcinoma, superimposed infections, and treatment with antiangiogenic factors (e.g., bevacizumab).[8,9] Airway necrosis and perforation after chemotherapy and radiation have been reported.[10] The respiratory tract is sensitive to radiation, and adverse effects on the airway epithelium occur within 2 months of treatment. These changes include transient inflammatory reaction with ciliary paralysis, localized necrosis, architectural distortion, deterioration of airway wall integrity, and mediastinitis.[11] Chemotherapy may play a role as well. A high incidence of TEF has been noted in lung cancer treated with chemoradiation combined with angiogenesis inhibitor.[9,12]

Mediastinal lymphoma complicated by TPF has not been reported previously. In our case, associated risk factor may be the chemotherapeutic regimen. Few sporadic cases of gastrosplenic fistulas have been reported with the REPOCH regimen.[13] The treatment of airway-mediastinal fistulas is difficult. Management of malignant fistulas is primarily palliative. Extensive surgical repair is usually not performed, and a less invasive approach is preferred. Recently, a local application of an autologous

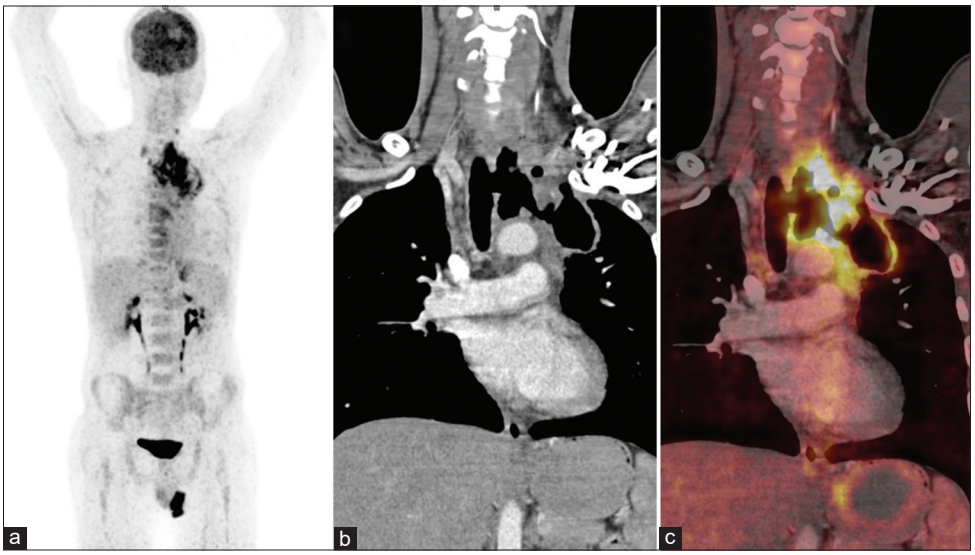

Figure 1: Maximum intensity projection image of positron emission tomography/computed tomography (a) increased uptake in the mediastinum and the left thoracic region. Coronal computed tomography of the thoracic region (b) shows a fistulous communication between the trachea and lung parenchyma (tracheoparenchymal fistula). Fused coronal positron emission tomography/computed tomography (c) reveals fistulous communication between the trachea and lung parenchyma (tracheoparenchymal fistula)

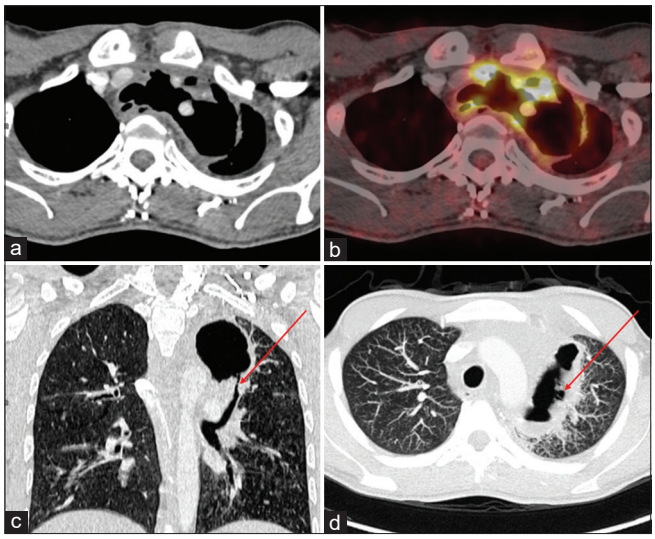

Figure 2: Computed Tomography Axial view (a) reveals a tracheoparenchymal fistula between the trachea and upper lobe of the left lung. A fused Positron emission tomography/computed tomography axial view (b) shows a metabolically active thick-walled tracheoparenchymal fistula in the upper lobe of the left lung communicating with the left lateral wall of the trachea. Computed tomography coronal and axial view in lung window (c, d) reveal direct communication of tracheoparenchymal fistula with the left upper lobar bronchus (red arrow)

adipose-derived stem cell suspended in fibrin glue is being used to treat a malignant tracheomediastinal fistula.

Conclusion

TPF is a rare complication of malignancy and has not been commonly reported in lymphomas. Physicians should be vigilant of airway disruption in patients with thoracic malignancies infiltrating or eroding the tracheobronchial tree, even those responding well to treatment. The prognosis of patients with such complications remains dismal due to the limitations of the currently available therapies. FDG PET/CT is a valuable modality in detecting recurrence or residual disease. It could unveil therapy-related complications as well.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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