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Tracheoesophageal Fistula as ARare Complication of Diffuse Large B Cell Lymphoma: A Case Report

Mikolaj Dulaj*, Joanna Lipińska and Dariusz Kosatka

Department of Thoracic Surgery at Wojskowa Akademia Medyczna (WAM) Medical University of Lodz, Poland

***Corresponding author:**

Mikolaj Dulaj

Department of Thoracic Surgery at Wojskowa Akademia Medyczna (WAM) Medical University of Lodz, Poland

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1. Abstract

We report a rare case of DLBCL complicated with tracheoesophageal fistula in an 88 year old male patient. He was initially diagnosed with pneumonia and treated with antibiotics as an outpatient. Patient was admitted to the hospital andendoscopic biopsy provided final diagnosis of lung DLBCL.Secondary finding in contrast esophageal X-ray was TEF. Patient had self- expanding tracheal and esophageal stent placement with good results and then was referred to oncologist.

2. Introduction

Diffuse large B cel lymphoma is the most common type of non-Hodgkin lymphoma. It evolves from large B- cells in lymph nodes. This type of lymphomas have high index of proliferation and are described as highly malignant. Histopathological features include basophilic cytoplasm with increased nucleus/cytoplasm index. Some of them are connected with genetic rearrangements such as: t(14;18) with BCL2 overexpression, t(8;14) with MYC overexpression. This mutation is unique, because it leads to extralymphoidal location of the tumor. However the most common genetic mutation related to DLBCL is BCL6 gene anomaly with 30-40 % prevalence. Considering etiology, environmental factors such as: chemicals, occupational hazard, viruses (HHV-8, HCV, HTLV-1), H.pylori infection, previous chemo-/ radiotherapy playcrucial role. It is believed that autoimmune diseases and immunodeficiencies are also vital in development of all type lymphomas. As far as clinical manifestation is concerned we would like to emphasize that symptoms are non-specific. Usually general malaise with fever, night sweats and losing weight are noted. Symptoms depend on primary location and metastases of the tumor. They develop frequently in GI tract, skin, bone marrow, nasal sinuses. Chemotherapy is the treatment of choice due to the best outcomes.

3. Case Report

88 year old male patient was treated by his general practitioner for pneumonia. At first he was having fever, cough with purulent sputum and two episodes of hemoptysis. He had suffered these symptoms four weeks with only slight improvement despite antibiotics. His treatment included cefuroxime and clarithromycin per os. Then he was referred medical ward. While episodes of hemoptysis were thought- provoking, Past Medical Records didn't include nicotinism, however included aphasia due to stroke instead. On admission (31.10.2023) his condition was moderate and he presented with rhonchi sounds at the right lung base. Chest X- ray revealed 3 cm oval- shaped opacification in the upper portion of the left hilum. On CT scan [03.11.2023] radiologist reported a 36x33x41 mm tumor in the left lung hilum and another metastatic lesion in 5th left segment (20x19 mm). This imaging revealed mediastinal lymphadenopathy with multiple calcifications and thickening of the esophagus was at the level of 4 left lung segment. Primary lesion of the esophagus couldn't have been excluded Subsequently, upper GI endoscopy (06.11.2023) showed fistula 25 cm from incisors. No other pathologies. Patient was consulted by thoracic surgeon as tracheoesophageal fistula (TEF) was suspected. On 07.11.2023 patient was transferred to surgical ward, where he had bronchofiberoscopy with tumor biopsy. Inflitration of the trachea 3-4 cm under vocal folds from rear- left side was noted. No opening of tracheoesophageal fistula was observed. On 08.11.2023 contrast X-ray revealed leakage at the level of Th7 from esophagus to main bronchi. So, Evolution 12,5 cm stent was implanted to the esophagus the same day. X-

ray follow-up on 11.11.2023 showed up no leakage and two days later the patient was discharged and referred to oncologist.Biopsy confirmed Diffuse large B- cel lymphoma. High proliferation index at the level of 90% was described (KI- 67=90%). Lymphoma's immunophenotype was: BCL6(+), CD20(+), c-myc(+), CD45(+), PAX-8(+).Readmission to the ward took place on 05.12.2023 with suspected recurrent tracheoesophageal fistula. Patient reported dysphagia, dyspnea, hoarseness and productive cough. At that time the patient had his first cycle of chemotherapy without any other serious complications. X- ray with contrast revealed TEF.On the second day bronchofiberoscopy revealed two outlets of TEF in the membranous part of the trachea. This problem was treated with one tracheal stent and complete cover of the fistula. The same day gastroscopy showed ingrown previous prosthesis. Our patient was discharged home well with recommended follow-up and stents replacement in 4 weeks. He didn't show up anymore.

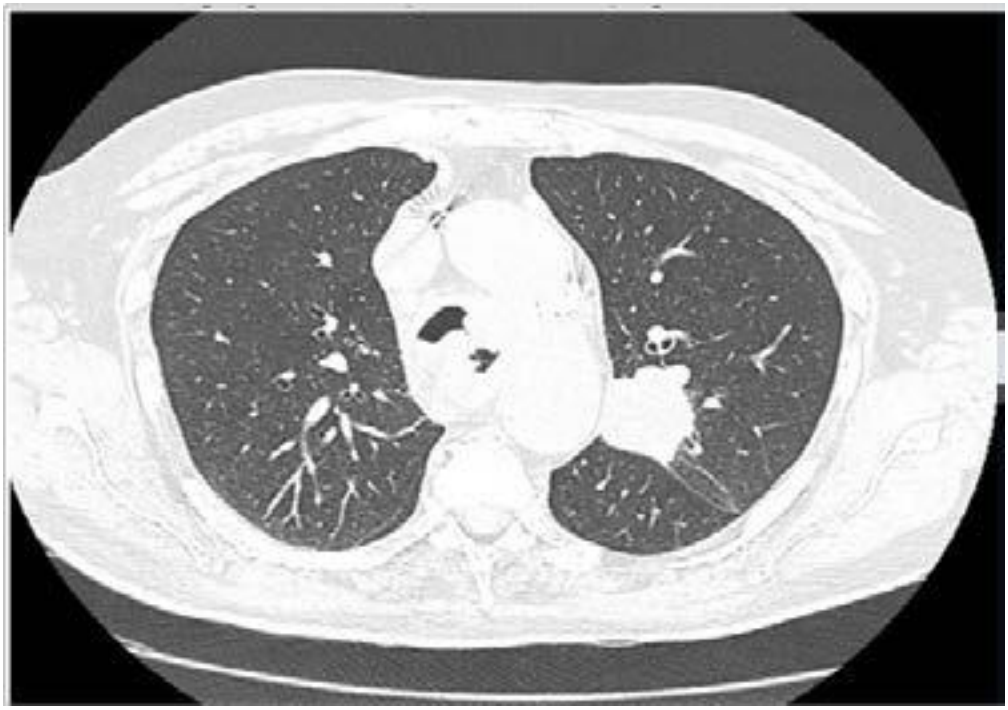

Figure 1: Subsequently, upper GI endoscopy (06.11.2023) showed fistula 25 cm from incisors. No other pathologies. Patient was consulted by thoracic surgeon as tracheoesophageal fistula (TEF) was suspected. On 07.11.2023 patient was transferred to surgical ward, where he had bronchofiberoscopy with tumor biopsy. Inflitration of the trachea 3-4 cm under vocal folds from rear- left side was noted. No opening of tracheoesophageal fistula was observed. On 08.11.2023 contrast X-ray revealed leakage at the level of Th7 from esophagus to main bronchi. So, Evolution 12,5 cm stent was implanted to the esophagus the same day.

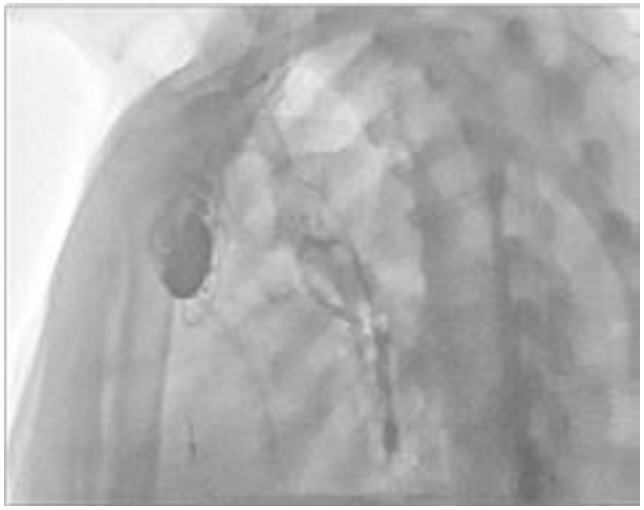

Figure 2: On the second day bronchofiberoscopy revealed two outlets of TEF in the membranous part of the trachea.

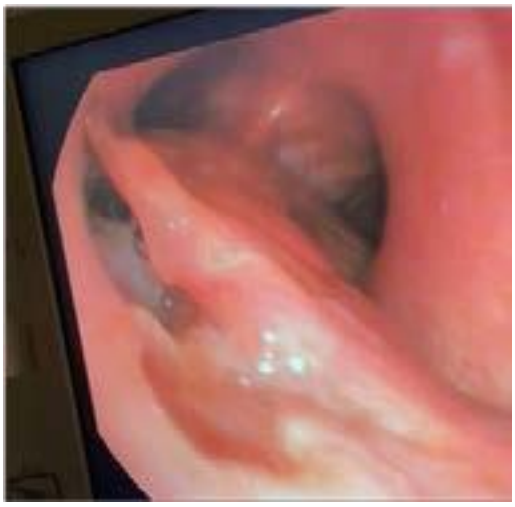

Figure 3: This problem was treated with one tracheal stent and complete cover of the fistula. The same day gastroscopy showed ingrown previous prosthesis. Our patient was discharged home well with recommended follow-up and stents replacement in 4 weeks. He didn't show up anymore.

4. Discussion

Tracheoesophageal fistula is a very rare complication of lymphoma. In this case primary location was in left hilum and metastasing to the mediastinum. We suspect that lympoma cells surpassed lymph node capsule and invaded mediastinal structures such as: trachea and esophagus.Our patient had „double hit" genetic changes- c-Myc(+), BCL6(+), which were indicators for highly aggressive lymphoma. Most concerning, the patient had c- Myc mutation, which commonly gives extranodular manifestations. C-myc overexpression leads to extensive proliferation and resistance to apoptosis. On top of that, it has direct influence on prognosis. These patients have significantly lower overall survival (OS) as well as progression free survival (PFS) rates. They exhibit weaker response to standard chemotherapy. By saying standard we mean R-CHOP (rytuxymab, cyclophosphamide, doxorubicin, vincristine, prednisone). They require more intense protocols like DA-EPOCH-R (dose-adjusted- CHOP + etoposide, rituximab). On CT 20x19 mm suspected metastasis was reported in 5L segment. We may only speculate if it was primary lesion instead. In terms of patient management we would like to emphasize the role of primary care physicians. Access to blood and imaging tests in Poland is limited.However in this particular case we believe that chest X-ray should have been done primarily by general practitioner- just before course of antibiotics keeping in mind hemoptysis symptoms. Another factor for prior X-ray is aphasia, which could potentially led to aspiration pneumonia. It involves anaerobic bacteria like Peptostreptococcus for which treatment is different and affects posterior parts of both lungs. Secondly, blood smear could have been useful for lymphoma diagnosis. We mention these simple tests which can be time- and life- saving.

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