

Case Report

Running Title: Triple Malignancies in a Patient-Case Report

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Synchronous Hodgkin's Lymphoma and Adenocarcinoma Lung with Metachronous

Squamous Cell Carcinoma of Esophagus – A Rare Case Report

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Abstract

The patients with multiple malignancies are difficult to diagnose as one malignancy may be indolent and usually diagnosed as an incidental finding, while proceeding with staging workup for the other malignancy. Treating such patients is even more difficult due to the issues related to sequencing the treatment for each of them. We report a case study where a patient was diagnosed with dual malignancies (Hodgkin's lymphoma and adenocarcinoma lung) and was treated for both malignancies sequentially. The patient had five years of disease-free survival and was kept under follow-up. He was diagnosed with metachronous malignancy, squamous cell carcinoma of esophagus, and underwent treatment for the same condition.

Keywords: Hodgkin's lymphoma, Adenocarcinoma, Squamous cell carcinoma, Disease-free survival, Case report

Introduction

The improvement in the survival rates of cancer patients is attributed to effective treatment and enhanced diagnostic methodology; in this regard, the number of synchronous and metachronous malignancies has increased, ranging from 0.734 to 11.3%.¹ Synchronous cancers are defined as malignant tumors that present either simultaneously or within a six-month period of identifying the original tumor,

each of which must be distinct with no possibility of one being the metastasis of the other.² Cancers diagnosed beyond the six-month interval are referred to as metachronous. The possible reasons for their incidence are genetic predisposition, environmental factors, or the treatment associated with other malignancies.³ National Cancer Institute's Surveillance, Epidemiology and End Results Program (SEER) reported that about one in six cancer

patients would develop second malignant neoplasm in their future life.⁴ The patient whom we are reporting had synchronous primary (Hodgkin's lymphoma and adenocarcinoma lung) and was initially treated for lymphoma first since the lung malignancy was thought as a part of lymphoma metastasis (Stage IV). He was then diagnosed as synchronous lung primary and was treated accordingly. The patient was kept under follow-up and after a disease-free survival of 5 years, he developed metachronous esophageal cancer and underwent treatment for esophageal cancer. The importance of this patient's case report is the usage of appropriate diagnostic tools, sequencing of treatment, constant follow-up and multidisciplinary approach to improving the diagnostic ability, and delivering appropriate treatment which ultimately resulted in improved survival and quality of life.

Case Presentation

A 70-year-old male with no known comorbidity and an ex-smoker for 10 years was assessed for swelling in the neck for eight months duration and loss of weight for a year. The patient presented to us after cervical lymph node biopsy which was reported as Hodgkin's lymphoma (mixed cellularity) in 2010.

On examination at the time of presentation, the patient was hemodynamically stable with right cervical adenopathy. PET CT imaging (Figure 1) revealed a small 2.2 X 1.8 cm spiculated mass (Figure 2) in the left upper lobe with a small mediastinal adenopathy. Abdominal imaging revealed only mild splenomegaly with hypodense nodule. Few small peripancreatic and para aortic nodes were detected with increased SUV of 4.0. The patient was staged as Hodgkin's Lymphoma Stage III AS/? IV (Lung).

He was reassessed with Interim PET after three cycles of ABVD which showed complete response of cervical and retroperitoneal nodes and splenic nodule. However, the left upper lobe nodule showed a significant uptake of 7.5 SUV with small residual mediastinal nodes.

Following the completion of six chemotherapy cycles, the patient underwent Chamberlain's procedure and Wedge resection of left upper lobe lung mass. Postoperative histopathology revealed adenocarcinoma Grade II. The subject underwent radical radiotherapy and received 60Gy to primary and 50Gy to mediastinal nodes using rapid arc technique (Figure 3). He was started on Tablet Gefitinib in view of EGFR exon 19 mutation.

Patient was kept on a regular follow-up and he presented after two years in May 2014 with the complaints of dysphagia. Upper GI endoscopy revealed growth in the lower thoracic esophagus and the biopsy was suggestive of squamous cell carcinoma. Figure 4 shows the microscopic appearance of all the three malignancies of the patient. PET imaging at that time (Figures 5 and 6) revealed growth in the distal thoracic esophagus short of OG junction with periesophageal nodes and luminal compromise (SUV 11.8). Post radiation changes with bronchiectasis and irregular consolidatory changes were also observed in the left lung field.

As the patient was not keen on surgical management, he received palliative radiotherapy using conventional technique and showed symptomatic improvement. On follow-up after six months, the patient presented back with dysphagia. Upper GI endoscopy showed circumferential growth in the mid/lower thoracic esophagus 28 to 32cm. Biopsy suggested squamous cell carcinoma. The patient underwent palliative stenting in January 2015 and his last follow-up was in April 2015.

Discussion

Although synchronous malignancies are rare, it is mandatory to diagnose them at a proper time in order to sequence the treatment. Patients should be advised for a constant follow-up for identifying the side effects as well as diagnosing the occurrence of new primaries as was evident in our case. The incidence of second malignancy, especially esophageal malignancy, was 1% after ABVD chemotherapy and 4% after chemo radiotherapy.⁵ The maximum dose received by oesophagus during the treatment of lung cancer is 54 Gy. The esophageal malignancy occurs just at the lower end of radiation field. It fits the Cahan's criteria⁶ for radiation-induced second malignancies. The metachronous malignancy in our case might have been induced by chemotherapy, radiation, or chemoradiation, or might have arisen as *de novo*.⁷ Surgery was not contemplated for esophageal malignancy due to the patient's unwillingness. Chemotherapy was not considered given the patient's age and his poor performance status. Radiotherapy beyond 40Gy was not contemplated for oesophagus due to re-irradiation complications. The patient had clinical complete response following radiotherapy as is evident from the follow-up of upper GI endoscopy finding. However, in due course, the patient developed recurrence and underwent palliative stenting and had a reasonably good QOL.⁸

The secondary malignancies which develop after Hodgkin's lymphoma can be classified into either solid (lung, skin, breast, and gastrointestinal) or hematological (leukemia, myelodysplastic syndromes, non-Hodgkin's lymphoma).⁹ The chemotherapy associated secondary malignancies are mostly leukemia and lymphoma, whereas radiotherapy induced malignancies are mostly solid organ malignancies.¹⁰

In female patients, the most prevalent malignancy associated with

mediastinal irradiation and extended field radiotherapy (EFRT) is breast cancer.¹¹ Alkylating agents of chemotherapy are associated with increased risk of second malignancies, but the risk of ABVD regimen is negligible. Although BEACOPP regimen was associated with a small increase in the risk of acute myeloid leukemia and myelodysplasia, the overall rate of secondary malignant disease did not increase compared with other chemotherapy regimens.¹²

Although patients with Hodgkin's lymphoma run a risk of developing other conditions, such as cardiac failure, coronary disease, stroke, endocrine dysfunction, and peripheral neuropathy, secondary malignancies should always be heeded, particularly in patients who are long-time survivors. Although our patient did not develop treatment associated major morbidity (non-oncological), he developed secondary malignancies. Hence it is recommended to look for all types of morbidity, including secondary malignancy at follow-up.

Conclusion

With advancements in Science and Technology, we are able to detect synchronous malignancies and able to treat them effectively.¹³ Patient should be insisted on constant follow-up to identify metachronous malignancies. Our Case report is one of the examples for both the above. With proper treatment sequencing, and constant follow-up, patient was able to live for 5 years. This shows that appropriate investigations, proper treatment sequencing and constant follow-up are mandatory for all patients diagnosed with malignancy. These kinds of malignancies should be treated with the joint effort of medical, surgical and radiation oncologists, radiotherapists, medical physicists, psycho oncologists, nurses, dieticians, and other paramedical

staff in order to make the treatment more effective.

Conflict of Interest

None declared.

Informed Consent

Informed consent was obtained from the patient.

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Figure 1. PET – CT done in May 2011 showing generalized adenopathy with increased uptake in the nodes.

PET – CT: Positron Emission Tomography - Computerised Tomography

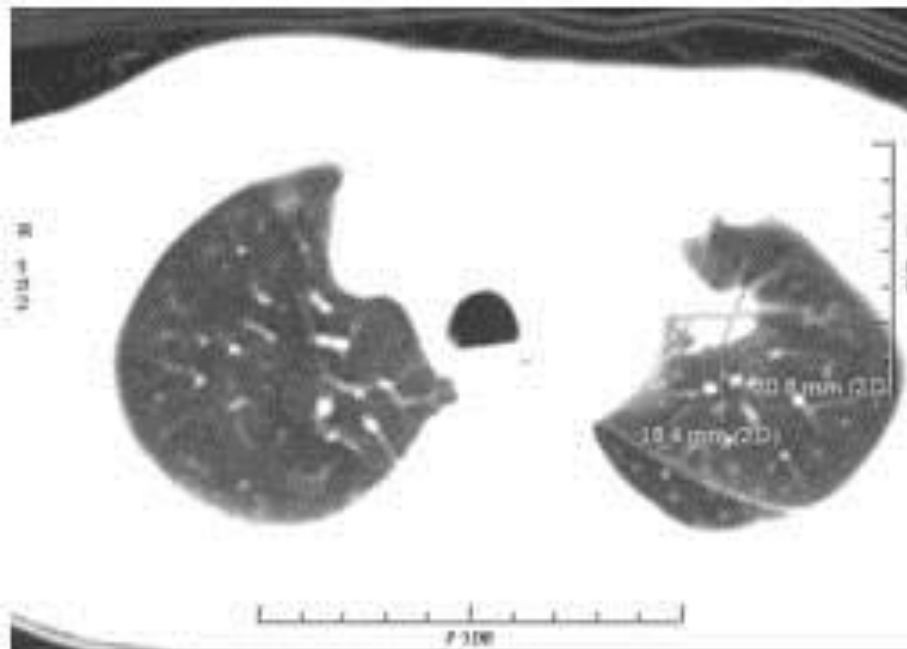


Figure 2. CT Image shows spiculated mass in the left lung-upper lobe.

CT: Computerised tomography

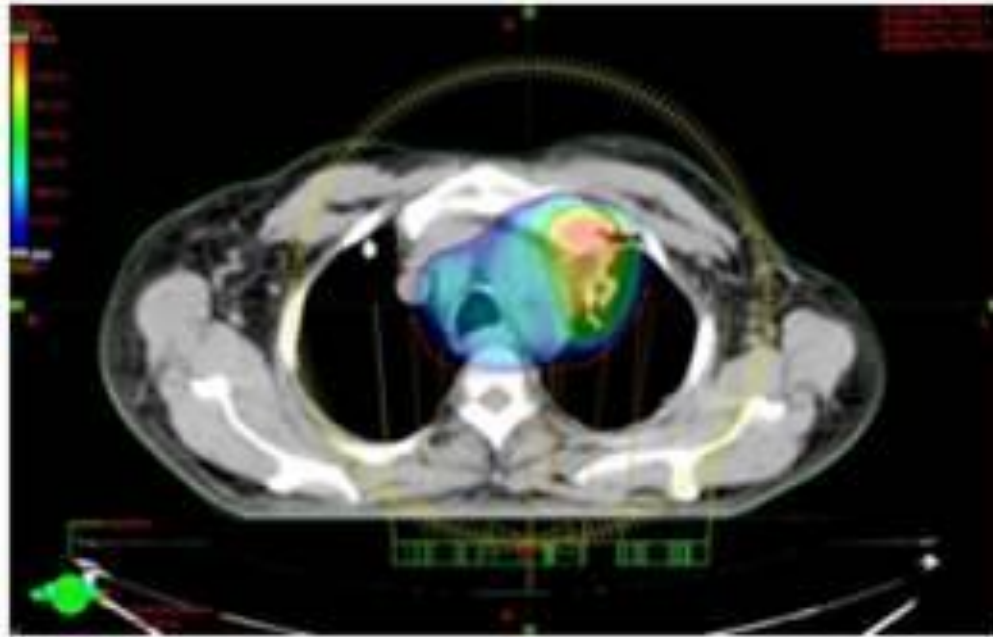


Figure 3. This image shows radiotherapy plan using rapid arc technique to mass in the left upper lobe and the mediastinum.

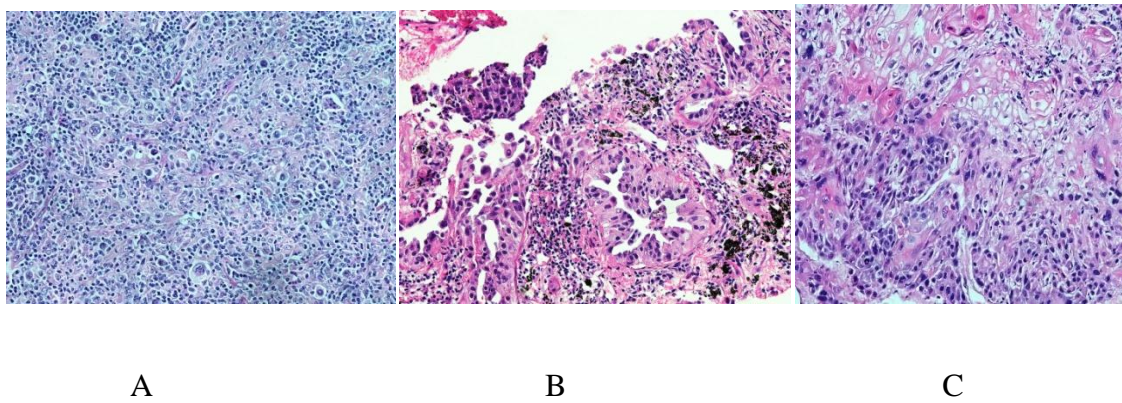


Figure 4. This figure shows the microscopic appearance of non-Hodgkin's lymphoma (A), adenocarcinoma lung (B), and squamous cell carcinoma esophagus (C).



Figure 5. CT shows growth in the distal esophagus with increased uptake.
CT: Computerised tomography



Figure 6. Positron Emission Tomography (PET) shows growth in the distal esophagus with increased uptake.
PET: Positron emission tomography