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Case Report

The Never-Ending Dilemma with Lung Cancer; It Never Gives Up!

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ARTICLE INFO

Article history:
Received: 21 September, 2019
Accepted: 8 October, 2019
Published: 30 December, 2019

Keywords:
Multiple primary lung cancer

ABSTRACT

Lung cancer remains the leading cause of cancer related deaths worldwide. Unfortunately, up to 20% of these patients go on to develop multiple primary lesions in the lung. This phenomenon, termed as multiple primary lung cancers, is currently on the rise. Approach to MPLC is unique as they require meticulous assessment by a multi-disciplinary team. However, literature and guidelines on MPLC remain limited. Our case sheds light over few important aspects of MPLC and calls for lung cancer committees to address the grey areas in their diagnosis and management.

Introduction

Multiple primary lung cancers (MPLC) are defined as more than two distinct malignant lung tumors with similar or differing histological composition, arising from one or both lungs. If they occur concurrently at the same time they are referred to as synchronous MPLCs. It can often be difficult to differentiate synchronous MPLC from metastatic lesions, especially if there are histological similarities between the two tumors. On the other hand, metachronous MPLC are cancers which do not occur concurrently, and even if they have a similar histological composition there is at least a 4-year interval (some consider 2 years) between the two primary cancers [1]. The epidemiology of MPLC is currently on the rise [2]. MPLC are hypothesized to have a prevalence of 0.2 – 20 percent in the population [3]. Herein, we report a male patient who was initially diagnosed and treated as squamous cell lung carcinoma and then went on to develop second and third primary/recurrent cancers 10 and 12 years subsequently.

Case Presentation

A 46-year-old male with a 30-pack year smoking history, presented to our hospital with symptoms and signs of a malignant lung mass. Workup at the time confirmed the diagnosis of squamous cell carcinoma of the left lower lobe; stage IIIB. The patient was started on radical chemotherapy (Cisplatin and Vinblastine) with concurrent radiotherapy (a total dose of 56 gray in 28 fractions). Follow up computerized tomography (CT) scan showed complete resolution of the mass and the patient was discharged in a healthy condition. Following that the patient remained cancer free until 10 years from initial diagnosis, when he was noticed to have supraclavicular lymphadenopathy. A complete cancer work-up at the time showed additional mediastinal lymphadenopathy along with moderate SUV uptake in the left lower lobe, SUV of 2.3 (Figure 1); this was the same region as the previous presentation. Interestingly the Fine Needle Aspiration biopsy from the supraclavicular lymph node showed adenocarcinoma, unlike the histological diagnosis 10 years back (Figure 3A).

Due to a very high radiotherapy dose last time around, this time the patient was started on lone chemotherapy (Carboplatin & Pemetrexed); after 6 cycles of which there was complete resolution of the supraclavicular and mediastinal lymph nodes. Additionally, the FDG-avid lesion in the left lower lobe also showed interval regression with the uptake coming down to 1.4 SUV. From there on the patient was doing

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http://dx.doi.org/10.31487/j.SCR.2019.05.07

well on his regular follow-up appointments until 2 years later when a PET-CT scan showed a SUV uptake of 6.1, again in the same left lower region (Figure 2). A complete workup on this admission showed no other areas of FDG uptake. This led us to the dilemma as whether to consider this as progression, recurrence or a new primary tumor. Based on a majority opinion in the multi-disciplinary meeting, the patient was restaged; this time as 1A. The patient underwent a left lower lobe lobectomy with lymph node dissection. Post-operative histology came back as adenocarcinoma (Figure 3B); similar histology to the cancer 2 years back. Post-op the patient was doing fine with no complaints. Pet CT during his latest follow-up 4 years' post-surgery (16 years from his first diagnosis) revealed no new lung lesions.

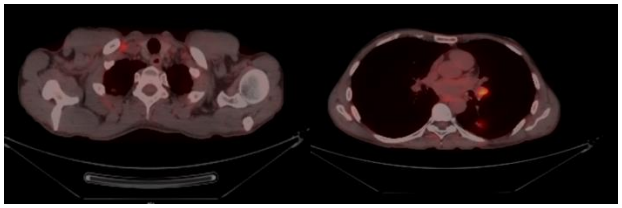

Figure 1: 2nd presentation: Pet-CT showing right supraclavicular, left hilar lymphadenopathy, and left lower lobe nodule, all having positive uptake.

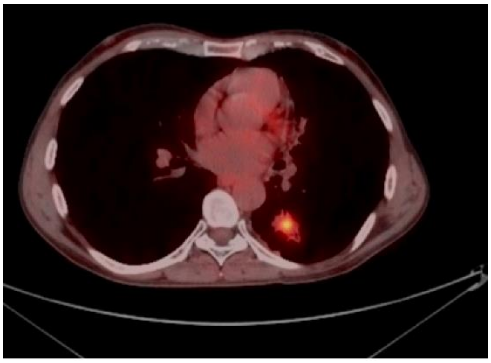

Figure 2: 3rd presentation: Pet-CT showing hyper-metabolic activity within the spiculated mass lesion in the left lower lobe.

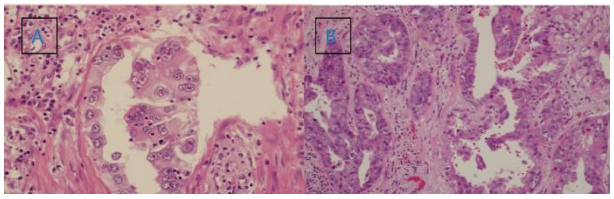

Figure 3: (A) Histopathology from supraclavicular biopsy at 2nd presentation: adenocarcinoma, **(B)** Post-op histopathology at 3rd presentation: adenocarcinoma.

Discussion

Over the past decade or two, the incidence of metachronous multiple primary lung cancers (M-MPLC) is rising. This rise can be attributed to two major factors; first, advances in diagnostic radiological studies and second, more rigorous post-surgical follow-ups and screening [4]. In light of this, our case fittingly discusses several important aspects of M-MPLC and disease free intervals (DFI) in lung cancer. First and foremost, our case questions the definition of M-MPLC. The most widely accepted criterion for labeling M-MPLC depends on the histology of the patient's primary cancer. If both, first and second lung cancers are of the same histological variant then there should be at least a 4-year interval for the second cancer to be labeled as M-MPLC. If the period between two cancers is less than 2 years then most likely the second one is not a distinct cancer but a metastasis from the initial lung cancer, unless of course it is histologically different from the initial cancer [5].

Based on this definition there exists a grey area between the 2 to 4-year period. What would the second cancer be termed as if it occurs in this period & has a similar histological composition; would it be a second primary cancer or a recurrence? Furthermore, regardless of the time period between two cancers, what if the second cancer occurs in the exact same area as the first cancer and also has the same histological composition; would that shake our conviction with which we label it as a new primary cancer?

Second, our case brings to light the challenging approach to MPLC. Diagnosing these requires meticulous work-up where numerous investigations need be performed. This is because it is of utmost importance to rule out other secondary causes for the second lesion before labeling it as another primary cancer [6].

Third, our case raises the subject of ideal management route in MPLC? Based on the current literature, surgical resection is currently the standard approach to M-MPLC, with the choice of surgery chiefly being influenced by stage, tumor size, extent and lung reserve post op [7]. Lastly, our case questions the reliability of disease free intervals as a prognostic factor in lung cancer. The fact that our patient had a new cancer after a 10 year long DFI, despite previous chemo-radiation supports the previous suggestions by Benjamin E Lee: DFI, long or short, does not have a significant impact on lung cancer prognosis and accurate clinical staging seems to be the gold standard in determining long term prognosis [7].

In conclusion, despite worldwide advances in healthcare and disease management, MPLC remain an understudied topic in literature. Several grey areas still exist which need addressing to in upcoming lung cancer guidelines.

Acknowledgements

None.

Disclosure

None.

Funding

None.

Conflicts of Interest

None.

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