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Synchronous Colon Cancer and ALK Positive Lung Cancer

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Abstract

We present a case of synchronous ALK positive lung cancer and colon cancer. Patient presented to the hospital for routine health checkup and was incidentally detected with both the cancers. Initially it was thought to be colon cancer with lung metastasis. IHC was done on the lung biopsy specimen which was positive for TTF1 and ALK mutation and negative for SATB2. Colon specimen was also reported as mucinous adenocarcinoma histopathologically but IHC was negative for ALK mutation. Hence the diagnosis of synchronous double malignancy was made. Both the cancers were locally advanced without any distant metastasis. Curative resection is done for both the lesions along with targeted therapy for the lung cancer and adjuvant chemotherapy for the colon cancer

Keywords: Synchronous cancers, ALK positive Lung Cancer, Targeted Therapy, Adjuvant Chemotherapy, Synchronous Colon Cancer

Introduction

Colon cancers often present with metastasis to various organs, liver being the most common site for metastasis [1]. Lung is the second most common organ to get metastasis from a primary colon cancer [2]. Whenever a patient presents with both colon growth as well as lung mass, it is very easy to misinterpret as a primary colon cancer with lung metastasis [1]. In such cases it becomes crucial to differentiate between metastasis and a second primary based on radiological and histopathological features. Synchronous colon cancer and lung cancer cases are reported but there is still very little information available to simultaneously manage both the cancers [3-5]. A fusion gene comprising portions of the echinoderm microtubule-associated protein-like 4 (EML4) gene and

the anaplastic lymphoma kinase (ALK) gene in NSCLC is found in 3 to 5 percent of NSCLC and is almost mutually exclusive with EGFR and KRAS mutations [6]. This frequency is higher in those who develop lung cancer as never smokers. Curative resection is the treatment of choice for both lung and colon cancer [1] but the real challenge is to decide on the systemic therapy.

Case Presentation

A 54 year old male, asymptomatic at presentation went for a master health checkup. CECT abdomen revealed asymmetric wall thickening in the ascending colon and hepatic flexure along with pericolic and ileocolic lymph nodes. CECT Thorax showed a 3.3 x 2.9 cm lesion in right upper lobe along with right hilar, paratracheal and subcarinal lymph nodes. Serum CEA was 28.81. Colonoscopy showed ulcer oproliferative growth in the ascending colon. Colonic biopsy was reported as nonspecific colitis. CT guided biopsy was done from right upper lobe of lung which was reported as mucinous adenocarcinoma.

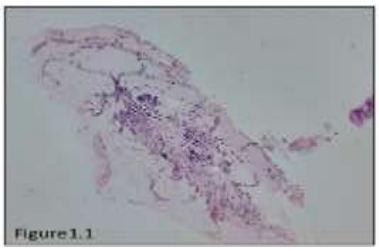


Figure 1.1: (40x power) Linear cores of lung parenchyma infiltrated by tumour cells arranged in lepidic pattern.

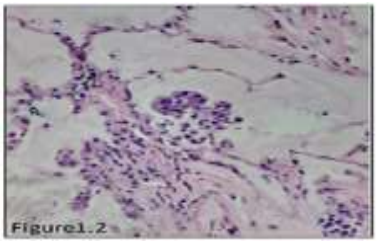


Figure 1.2: (400x power) Nests of tumour cells in alveolar spaces. Individual cells with moderate cytoplasm and hyperchromatic nucleus.

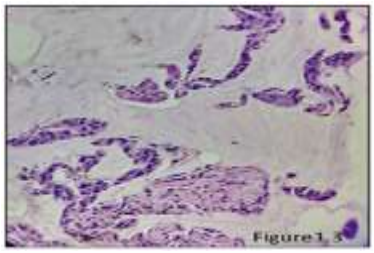


Figure 1.3: (400x) Tumour cells floating in pools of mucin

IHC was done for the lung biopsy which showed TTF1 positivity and SATB2 was negative.

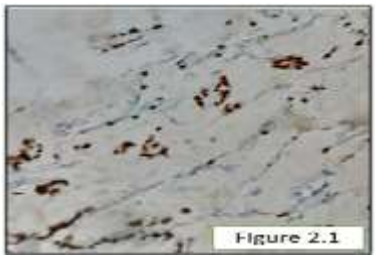


Figure 2.1: (400x) Tumour cells show Positive nuclear staining for TTF1.

Figure 2.2: (400x) Tumour cells are Negative for SATB2

Whole body PET CT was ordered which confirmed the findings of CECT abdomen, pelvis and thorax. There were no distant metastasis elsewhere. Thus diagnosis of primary right lung adenocarcinoma was made which was staged as cT2N2M0 according to AJCC 8th edition.

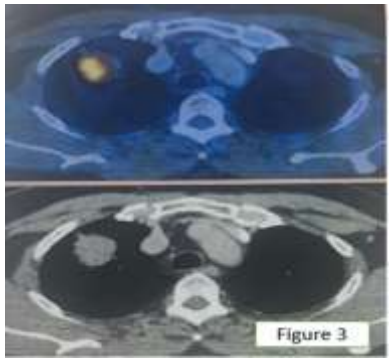


Figure 3: PET CT showing right upper lobe mass

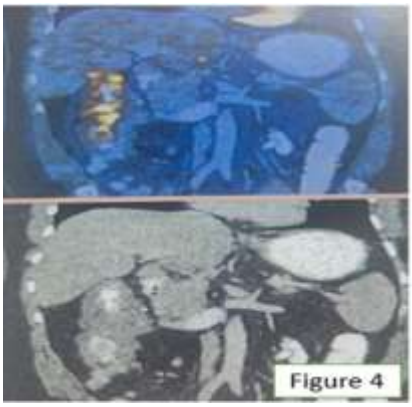


Figure 4: PET CT showing colonic growth

Later, Next generation sequencing(NGS) was also requested on the lung biopsy which revealed a clinically relevant pathogenic mutation in KRAS gene and EML4:ALK fusion was also identified. Case was discussed in multispecialty tumor board and patient was started on Tablet Lorlatinib because of ALK fusion positivity. Monthly chest X ray was done which showed partial response to the therapy.

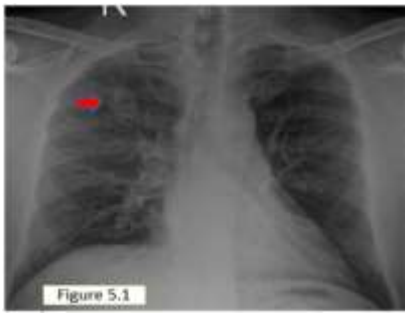


Figure 5.1: Chest X Ray before Lorlatinib.

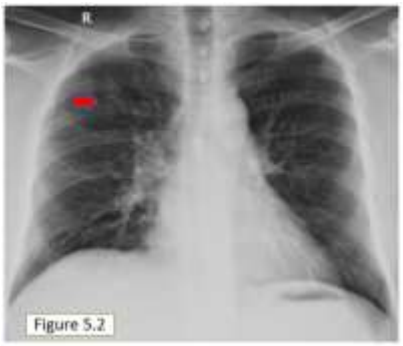
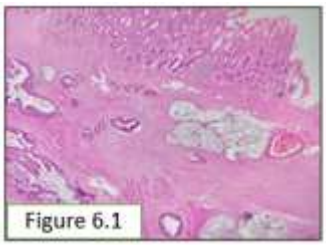


Figure 5.2: Chest X Ray after 2 months of Lorlatinib

Meanwhile patient had 2 episodes of bleeding P/R. Colonoscopy and biopsy was repeated which was reported as high grade dysplasia with tiny foci of invasion. Patient was taken up for Extended Right hemicolectomy in view of high clinical suspicion for colonic malignancy. On histopathological examination of the surgical specimen, it was reported as Moderately differentiated mucinous adenocarcinoma of the ascending colon.

All margins were free of tumor. Lymphovascular invasion was not identified and 3 out of 18 lymph nodes dissected were positive for malignancy. Thus, diagnosis of carcinoma ascending colon stage pT3N1bM0 was made. IHC for MLH1, MSH2, MSH6 and PMS2 was done which showed intact nuclear expression



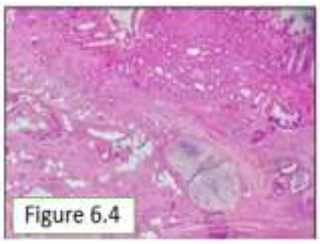


Figure 6.1: (40x) and Figure6.4(40x): Colonic mucosa infiltrated by tumour cells.

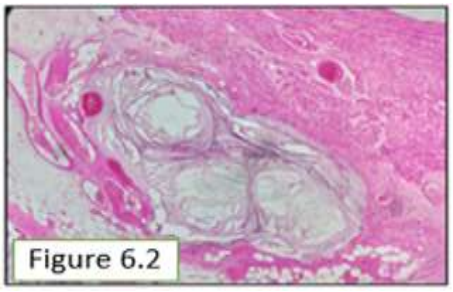


Figure 6.2: (200x) Tumour cells extending into the pericolonic fat.

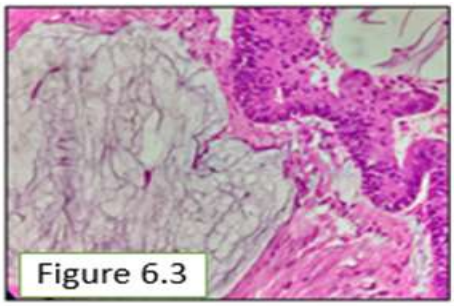


Figure 6.3: (400x) Mucinous pools with tumour cells.

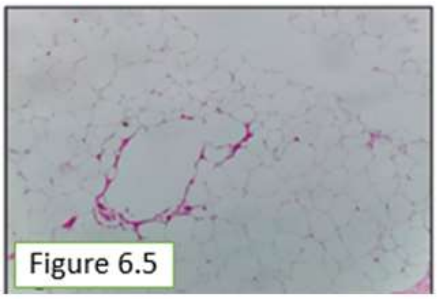


Figure 6.5: (200x) Fibrofatty tissue (Sent from nodule over Transverse mesocolon)

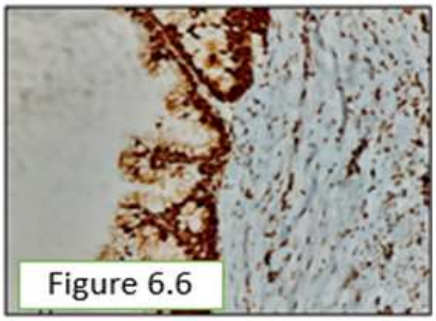


Figure 6.6: (400x) Shows Intact DNA Mismatch repair.

Impression: Mucinous Adenocarcinoma – Ascending colon

Since, colon histopathologic features were similar to the lung biopsy, NGS was requested on the colon biopsy also to confirm whether it is synchronous primaries or metastasis. ALK fusion came out to be negative on the colon specimen hence it was concluded that patient has synchronous double malignancy. Patient was started on adjuvant therapy with CAPOX regimen along with Tab Lorlatinib. Whole body PET CT was repeated after 4 months of Lorlatinib which showed complete resolution of the lung mass, paratracheal and subcarinal lymph nodes. There was reduction in size of right hilar lymph node from 20x15 mm to 11x7 mm which was non FDG avid. Patient was taken up for right upper lobectomy along with mediastinal lymph node dissection which was staged as ypT1b N0 M0. Only 5% residual viable tumor cells were seen in the surgical specimen. Thus patient completed 6 cycles of Adjuvant CAPOX and is currently on Tab Lorlatinib planned for 2 years.

Discussion

Colon cancers often present with metastatic disease with liver being the most common site of metastasis [1]. Since lung is the second most common site of metastasis from the colon cancer, it is very easy to make the diagnosis of carcinoma colon with lung metastasis whenever a patient present with colon growth and a lung nodule simultaneously. It is very important to differentiate between a metastasis and a second primary since the intent and treatment protocol may vary depending on it. In our case, patient presented with colon growth as well as the lung nodule. Histologically both the lesions were mucinous adenocarcinoma.

Thyroid transcription factor 1(TTF-1) is used to differentiate between primary lung adenocarcinoma and lung metastasis from other sites. TTF-1 shows strong positivity in over 75% of lung adenocarcinomas and is negative in carcinomas from other sites except thyroid [1]. Special AT-rich sequence-binding protein 2(SATB2) is usually positive in colon cancers [7] and negative in lung cancers hence both of these markers were done which helped in making the diagnosis of synchronous double primary. NGS also revealed ALK fusion positivity in the lung specimen which was not present in the hemicolectomy specimen.

Since there are very few cases reported with synchronous colon and lung cancers, there is a dilemma associated with the choice and sequencing of systemic therapy. First line chemotherapy for colon cancer is either 5FU/Leucovorin/Oxaliplatin (FOLFOX regimen) or Capecitabine/Oxaliplatin (Capox Regimen). For primary lung adenocarcinoma a combination of pemetrexed with cisplatin or carboplatin is usually preferred.

ALK fusion is positive in about 3-5% of lung adenocarcinomas [6]. There are different generations of ALK inhibitors available for the treatment. Lorlatinib, a

third generation ALK inhibitor is preferred for the front line treatment of metastatic ALK positive lung adenocarcinoma [8]. The lung lesion was not amenable for resection upfront thus patient was planned for neoadjuvant Lorlatinib so that it can be continued with CAPOX in order to target both the cancers simultaneously. ALK fusion positivity turned out to be a boon for the patient since it provided the option of targeted therapy instead of chemotherapy. Lung cancer responded very well to Lorlatinib which is still not the standard of care in the neoadjuvant setting.

Conclusion

We hereby present a case of Synchronous colon cancer and ALK positive lung cancer which was managed with curative resection for both the cancers. Since the chemotherapy regimen varies widely for both the cancers, lung cancer was managed with targeted therapy and colon cancer was managed with adjuvant chemotherapy. Patient responded to the treatment well and is on targeted therapy currently.

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