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Extensively Metastaticlung Carcinoma without Any Actionable Mutation in a 20 year Old Nonsmoker Adolescent Male - A Case Report

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Abstract: ***Lung cancer is the second most common cancer in world and it is one of the leading causes of cancer death worldwide[1]. It is the most common cancer among male. Adenocarcinoma is the commonest type of lung cancer[2]. Median age of lung cancer diagnosis 65 years or more. Incidence of lung cancer below 40 years is less common[3]. Here we report a case of extensively metastatic adenocarcinoma of lung in a 20 years old non smoker male. This 20 years non smoker male without any comorbidity and significant family history, presented to Neurosurgery Department with complaint of headache and vomiting for 4 - 5 days. He was evaluated with plain and contrast enhanced MRI Brain which revealed well circumscribed soft tissue lesion in right occipital region and few small well defined heterogeneously enhancing lesion involving left temporal lobe, right cerebellum, vermis and left parietal lobe. He underwent craniotomy and excision of right occipital lesion. . Histopathology showed poorly differentiated malignant tumour, possibility of either metastatic carcinoma or malignant meningioma, grade 3. Immunohistochemistry was suggestive of metastatic adenocarcinoma, primary from lung. Whole body FDG PET CT scan showed FDG avid well to ill defined extensive soft tissue density lesion involving bilateral lung fields, largest in left infra hilar region associated with FDG avid mediastinal lymphadenopathy and metabolically active periportal, peripancreatic and pelvic lymphadenopathy, FDG avid hypodense lesion measuring in segment V and VI of liver and multiple FDG avid bony lytic lesion. He received whole brain radiation. Then patient was referred department of Medical Oncology for systemic therapy. Next generation sequencing (NGS) on tissue block did not show any actionable mutation. PDL1 testing by immuno histochemistry done by SP263 showed Tumour Proportion Score (TPS) score 28 - 30%. As patient could not afford immunotherapy, he was treated with Platinum based combination chemotherapy with Zoledronic Acid. After 4 cycles of chemotherapy CECT Brain, thorax, abdomen and pelvis was done. It showed significant regression of primary lesions and metastases. In view of very good response and good tolerance two more cycles of same chemotherapy then Pemetrexed based maintenance therapy was planned for him. Incidence of lung cancer in young adults is quite rare. Most of the patients are asymptomatic initially and because of low suspicion of lung cancer in this age group, diagnosis often gets delayed and patients may present in advanced stage. Genetic factors may have role in development of lung cancer in this patient population. In this case patient was non smoker and did not have any significant family history and history of pre existingpulmonaryaetiology. Because of the rarity of lung cancer in young population, underlying risk factors could not be studied. International multi institution based studies are needed to identify risk factors of young lung cancer.***

Keywords: lung cancer, adolescent male, 20 years, adenocarcinoma, chemotherapy

1. Introduction

Carcinoma lung is the second most common cancer in world and it is one of the leading causes of cancer death worldwide[1]. It is the most common cancer among male[1]. Adenocarcinoma is the commonest type of lung cancer[2]. Median age of lung cancer diagnosis 65 years or more. Incidence of lung cancer below 40 years is less common[3]. NSCLC is extremely rare in patients under age of 25 years, having an incidence rate of 0.3 per 100, 000 during 2002 - 2006[4]. Though most of lung cancer is associated with smoking, non small cell lung carcinoma (NSCLC) like adenocarcinoma are common among non smoker Asian female population. Here we report a case of extensively metastatic adenocarcinoma lung in a 20 years old non smoker male.

2. Case Summary

This 20 years non smoker male without any comorbidity and significant family history, presented to Department of Neurosurgery with complaint of headache and vomiting for 4 - 5 days. He was evaluated withplain and contrast enhanced Magnetic Resonance Imaging (MRI) Brain showed well circumscribed soft tissue lesion measuring 2.7 ×2.4 ×3.4 cm in right occipital region and few small well defined heterogeneously enhancing lesion involving left temporal lobe, right cerebellum, vermis and left parietal lobe.

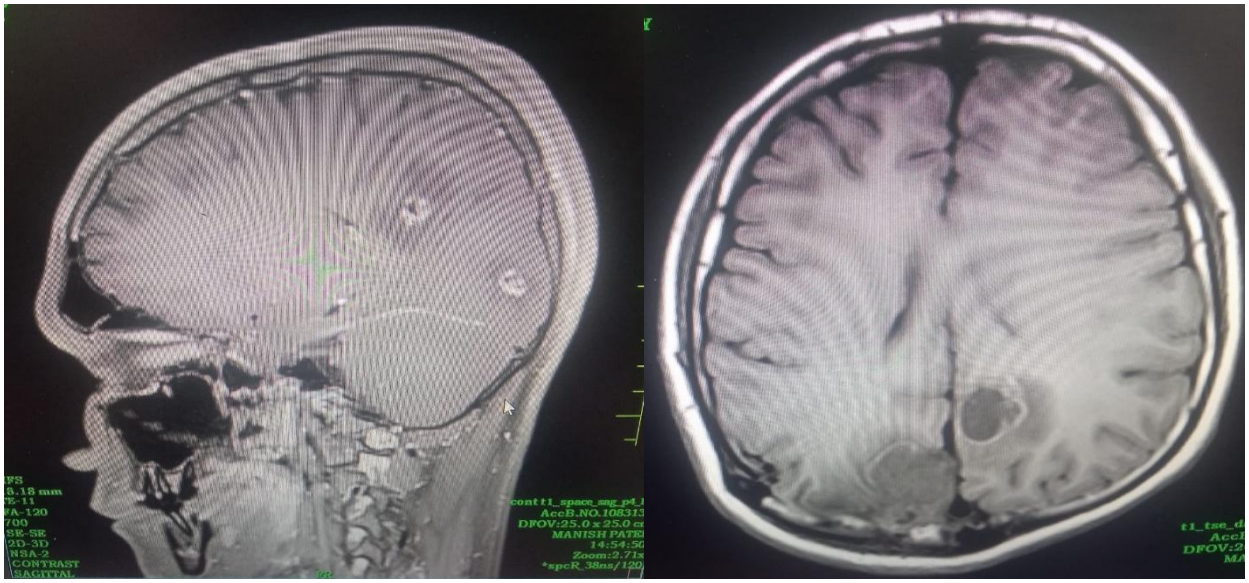

Figure 1 & 2: T1 contrast and T1 non contrast MRI images

He underwent craniotomy and excision of right occipital lesion. Frozen biopsy was suggestive of malignant high grade tumour showing rhabdoid morphology, possibility of Rhabdoid meningioma, WHO Grade 3. Histopathology showed poorly differentiated malignant tumour, possibility of either metastatic carcinoma or malignant meningioma, grade 3. Immunohistochemistry showed marker positivity of AE1, EMA, CK7, TTF1 and Napsin A. SALL4, HMB45, PR, Vimentin, P40, P63, CK20, PAX8, Thyroglobulin all markers were negative. Final diagnosis was metastatic adenocarcinoma, primary from lung.

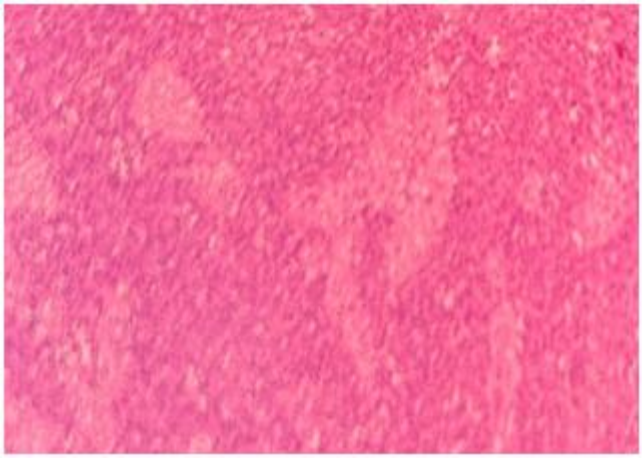

Figure 3: H & E stain, 200 x magnification

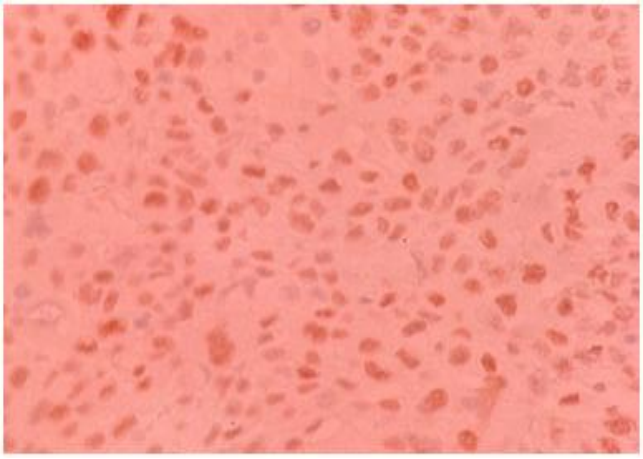

Figure 4: Immunohistochemistry; TTFstain

Whole body 18 F FDG PET CT scan showed FDG avid well to ill defined extensive soft tissue density lesion involving bilateral lung fields, largest in left infra hilar region measuring 6.2×4.7 cm (SUV max 11.8) associated with mediastinal lymphadenopathy largest 1.5×1.1 cm, SUV max 7 and metabolically active periportal, peripancreatic and pelvic lymphadenopathy, FDG avid hypodense lesion measuring 3×2.5 cm, SUV max 10.5 in segment V and VI of liver and multiple bony lytic lesion, SUVmax 7.9. So final Diagnosis was Adenocarcinoma left lung (T4N2M1b), stage group – IVB.

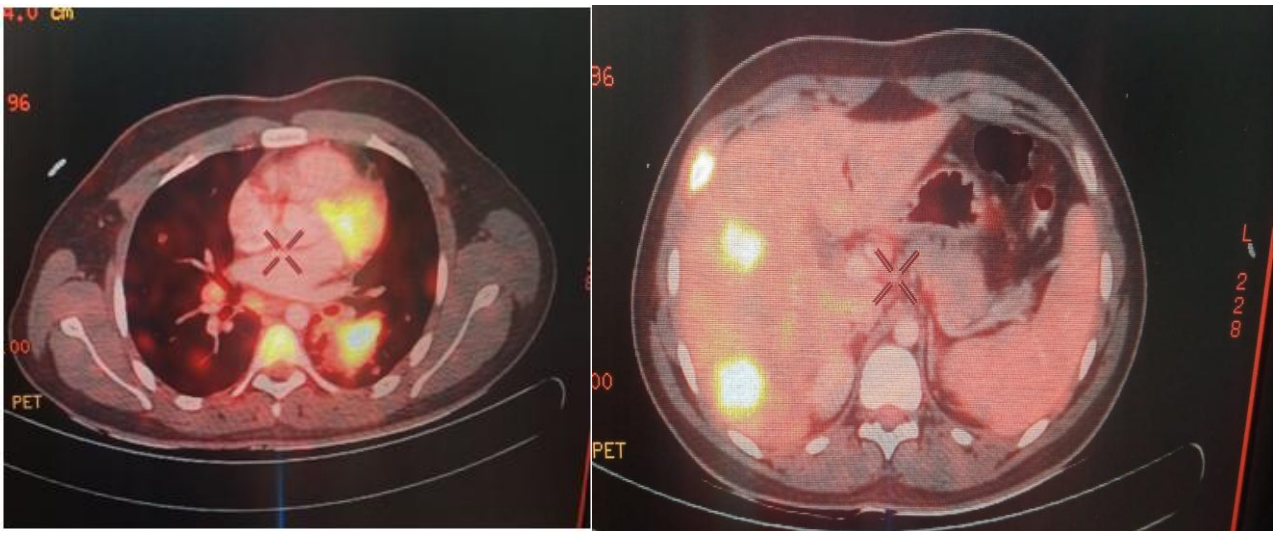

Figure 5 and 6: FDG PET Image

He received whole brain radiation with 30 Grey in 10 fractions. Then patient was referred to us for systemic therapy. Patient was ECOG Performance score 1 and his neurological examination did not show any abnormality. Complete blood count, renal function test and liver function test were within normal limit. Next generation sequencing (NGS) on tissue block did not show any mutation like EGFR, ALK, BRAF, ERBB2, RET, ROS1, KRAS, MET, NTRK1/2/3, P53etc. PDL1immunohistochemistry done by SP263 showed Tumour Proportion Sore (TPS) score 28 - 30%. As patient could not afford immunotherapy, we started combination chemotherapy with Pemetrexed and Carboplatin along with 3 monthly Zoledronic Acid. Patient tolerated chemotherapy well and improved subjectively. After 4 cycles of chemotherapy CECT Brain, thorax, abdomen and pelviswas done. It showed significant good response - few hyperdense lesion in left temporal lobe, cerebellum, largest in left temporal lobe measuring 6×5 mm, likely residual metastases. Multiple well defined soft tissue opacities in both lung fields, largest in mediobasal segment of left lower lobe measuring 2.2×1.8 cm and 2 hypodense lesion in segment VI and VII of liver, largest 1.6×1.4cm and few ill defined sclerotic bony lesions. In view of verygood response and tolerance planned two more cycles of Pemetrexed and Carboplatin combination chemotherapy then Pemetrexed maintenance therapy was planned. He received 5th cycle ofchemotherapy. Chemotherapy was tolerated well. There is no grade 3/4 toxicities.

3. Discussion

Incidence of lung cancer in young adults is quite rare. . Risk factors for lung cancer in young population is unknown. Most of the patients are asymptomatic initially and because of low suspicion of lung cancer in this age group, diagnosis gets delayed and patients may present in advanced stage[4]. In one study lung cancer patients of age more than 45 years were compared to patients aged less than 45 years[5]. That study revealed lung cancer staging was the most determinant for survival in patients below 45 years of age[5]. Genetic factors may have role in development of lung cancer in this patient population[6] Common gene mutation like EGFR, KRAS, TP53 are associated with a higher risk of development of lung adenocarcinoma. EGFR and EML4 - ALK mutation are common among young lung cancer patients[7]. In our patient all these mutations were absent. In our case patient was a non smoker male without any significant family history and history of any pre existing benign lung lesion[8]. IHC was negative for P40, P63 ruling out squamous cell carcinoma. IHC negativity of HMB45, SALL4, Thyroglobulin ruled out metastases from malignant melanoma, germ cell tumour and thyroid malignancy respectively.

4. Conclusions

Because of the rarity of lung cancer in young population, underlying risk factors could not be studied. International multi institution based studies are needed to identify risk factors of young lung cancer. There is lack of different guideline for young adolescent lung cancer due to very less number of cases. As per NCCN guideline this patient should be treated with combination of chemotherapy and immune checkpoint inhibitor[9], however because of affordability issues this patient was treated with chemotherapy only.

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