

## Rare Presentation of Miliary Brain Metastasis in Absence of Typically Associated Mutation

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### Abstract

Lung cancer frequently presents with metastasis to the brain. Previously multiple metastases to the brain, described as miliary metastasis, have been reported with lung cancer and more commonly adenocarcinoma subtype. Various gene mutations involving exon 19, exon 20 and exon 21 have been reported with such metastasis. Though the prognosis is poor it is useful to identify such spread in order to tailor the treatment plan for a patient. We present a case of miliary metastasis to the brain in a patient with Grade IVa lung cancer presenting with confusion and speech difficulties.

**Keywords:** Miliary; Brain metastasis; Adenocarcinoma; Carcinomatosis

### Introduction

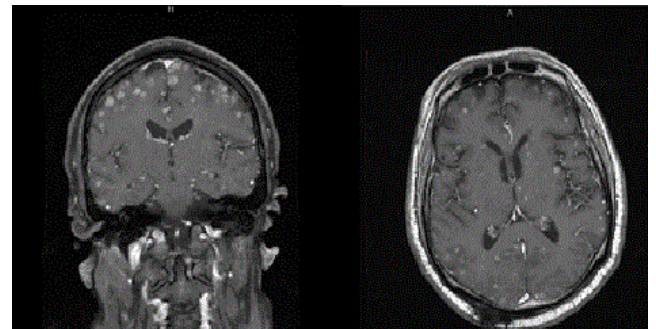
Adenocarcinoma of the lung is the most common type of lung cancer associated with brain metastasis. Modern diagnostic and therapeutic approaches including surgical resection, chemotherapy and radiation therapy have been tried with advanced cancer. However, prognosis continues to remain poor. A pattern of miliary metastasis to the brain has been depicted in various case reports across literature. Gene mutations involving exon 19, exon 20 and exon 21 have also been associated with such miliary pattern. Certain benefits from tyrosine kinase inhibitors have been reported in cases with mutation of the EGFR gene [1]. Our case is a rare presentation of brain metastasis in patients with lung adenocarcinoma.

### Case Report

A 60 year old African American man presented to our institution with confusion for 2 weeks. He had trouble with word finding and had perseverating speech. There was progressive weakness in his lower extremities to the extent of hampering his ambulation. There was also loss of bowel control. He had shortness of breath with minimal activity. He was being treated for stage IVa adenocarcinoma (acinar type) of the lung (EGFR wild and ALK translocation negative) which was diagnosed about a year ago and had a 12 year history of smoking. He received six cycles of therapy with Carboplatin, Pemetrexed and Pembrolizumab as part of a clinical trial and later received Docetaxel and Ramcirumab therapy. Previously he was treated for prostate cancer (Gleason 7) 10 years ago with prostatectomy and external beam radiation without evidence of recurrence. Prostate specific antigen was <0.1 ng/mL.

On exam he was awake and oriented to self and the city but not time. He was able to identify objects and repeat phrases, though at times he would perseverate. He was slow to respond and could calculate normally. His right hip flexion and knee extension was 4/5 in

strength. Magnetic Resonance Imaging of his brain, cervical and thoracic spine revealed numerous hyper-intensities which were suspicious for metastatic lesions in brain. They were present in both supratentorial and infratentorial brain parenchyma with the largest lesion in the right frontal lobe measuring at 9 × 7 mm in size. The picture was peculiar for miliary appearance in the brain. He was also started on Levetiracetam 500 mg twice a day dose for seizure prevention. He was tried on whole brain radiation therapy and continued with chemotherapy (Docetaxel and Ramcirumab) (Figure 1).



**Figure 1:** Left to right coronal section and transverse section show multiple contrast enhancing lesions.

### Discussion

Rarely cases associated with metastasis to the brain have a miliary appearance. Previously described as carcinomatosis encephalitis, it is now frequently described with advanced imaging techniques and has been reported in 17 cases across literature in conjunction with lung adenocarcinoma [2]. A retrospective analysis of these cases has depicted an association of miliary pattern with exon 19 deletion (EGFR mutation) [1]. However earlier cases described in the meta-

analysis lacked information about genetic mutations. Further, the cases described lacked history of smoking which lead to the thought that miliary metastasis was associated more with non-smokers [2]. Dziadziuszko et al. [3] also demonstrated a ROS1 gene mutation in a lung cancer patient with miliary metastasis and history of smoking. Tyrosine kinase inhibitors and whole brain radiation therapy have shown benefit in patients with NSCLC that have EGFR mutations in a setting of brain metastasis [1,2,4]. Our case is unique in its absence of mutation to the EGFR or ALK gene and having a history of smoking. Unfortunately, our patient did not respond to chemotherapy or whole brain radiation therapy and was eventually transferred to hospice center for end of life care.

## Conclusion

Most miliary lesions as seen in our patient do not have significant edema or mass effect until it involves eloquent cortex. Possibility of miliary metastasis with a relatively benign clinical presentation should be considered in the setting of adenocarcinoma of lung, as further management and the extent of therapy may depend on the spread of

the tumor. Further, novel associations or causes for such presentations need to be explored to help with clinical prognosis at the time of presentation and likely gene therapy in future.

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