

A Rare Case: Adenocarcinoma Bronchogenic Dextra Std IVB on Gefitinib (15 months) accompanied by decreased visual acuity, Bilateral Sensorineural Deafness and Psychiatric Disorders with No Radiological Evidence of Brain Metastasis

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Abstract

Background: Leptomeningeal disease occurs in 3-5% of patients with lung cancer, mainly adenocarcinoma subtype. Adenocarcinoma is the most common histological finding in Asian women.

Case: A 51-year-old woman with right-sided bronchogenic adenocarcinoma T4N3M1c Std IVB mutation(+) developed decreased vision, severe bilateral sensorineural deafness and psychiatric disorders after receiving Gefitinib 15 months. There was no evidence of brain metastasis from brain MRI. From evaluation of chest CT-scan, we found the disease was progressive and no Mutation Detected from ctDNA, so Gefitinib was discontinued.

Conclusion: We found some difficulties in evaluating side effects of therapy and disease progression due to patient's condition in the form of decreased total vision, severe sensorineural deafness, and psychiatric disorders. However, because no radiological evidence of brain metastases was found, we suspect this patient suffered from leptomeningeal disease.

Keywords: Lung Cancer, Adenocarcinoma, Gefitinib, Leptomeningeal Disease

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1. Introduction

Adenocarcinoma is the most common histological finding in lung cancer in Asian women. EGFR mutation is the most common DNA mutation found in Adenocarcinoma. Leptomeningeal disease occurs in 3-5% of

patients with lung cancer, mainly adenocarcinoma subtype

2. Case

A 51-year-old woman with right-sided bronchogenic adenocarcinoma T4N3M1c

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Std IVB mutation(+) developed decreased vision, severe bilateral sensorineural deafness and psychiatric disorders after receiving Gefitinib for 15 months.

From evaluation of MRI and Head CT-Scan we didn't found imaging proof of brain metastases. From Oto Acoustic Emission and Brainstem Evoke Response Audiometry by Otorhinolaryngologist we found both side sensorineural hearing loss on right side and Severe sensorineural hearing loss on left side.

From Perimeter Examination by Ophthalmologist we found total blindness in right

side and scosentral visual field defect in left side. From examination of psychiatry, we found Organic mental disorders and bipolar disorder with episode of depression. There was no evidence of brain metastasis from brain MRI, thus we suspected a leptomeningeal metastases in the patient. To diagnose leptomeningeal metastases, CSF analysis is required. This was not done on the patient because when the patient was being treated, CSF fluid analysis could not be performed at our hospital.



Figure 1. CT- Scan Thorax + Contras: Right lung mass, ipsilateral and contralateral nodules, multiple bilateral mediastinal lymphadenopathy, liver nodules according to T4N3M1b

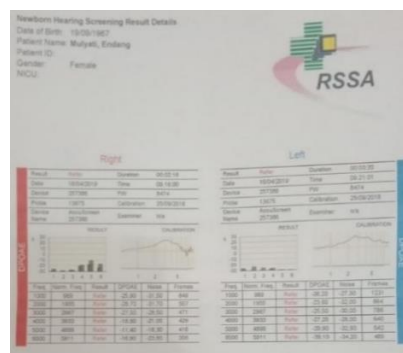


Figure 2. Oto Acoustic Emission: Acoustic D/S: Refer/Refer

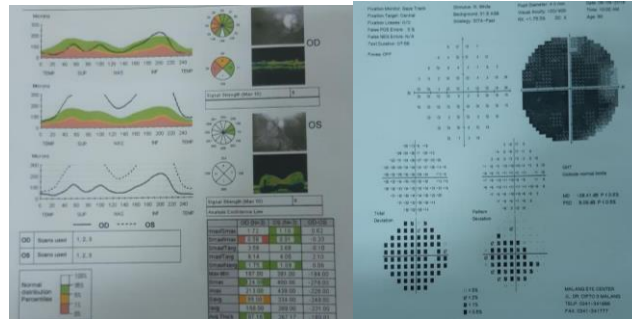


Figure 3. Perimeter Examination: total blindness in right side and scotomatous visual field defect in left side

3. Discussion

We report our patient with adenocarcinoma bronchogenic dextra EGFR Mutation (+) and get gefitinib therapy for 15 months developed decreased vision, severe bilateral sensorineural deafness and psychiatric disorders after receiving Gefitinib 15 months. There was no evidence of brain metastasis from brain MRI.

The patient was consulted to Ophthalmologist, Otorhinolaryngologist, neurology and psychiatry. From Psychiatry, she was suspected with organic mental disorder and schizophrenia, optic nerve damage was found by Ophthalmologist, and sensorineural deafness was found by Otorhinolaryngologist, and from neurology it was suspected to be brain metastases, but brain metastases could not be proven from Head MRI, this is probably due to leptomeningeal metastases.

Brain metastases are the most common metastases in patients with lung cancer. That

was found due to symptoms of increased intracranial pressure, such as headache and nausea, or due to seizures or focal neurological deficits usually cause substantial morbidity and affect the patient's physical and mental function and performance status ¹. Leptomeningeal metastases are late-stage complications of systemic cancer caused by multifocal metastases to leptomeninges.²

The first generation of TKI EGFR has a low capability to penetrate blood-brain barrier. This causes the brain to become a sanctuary site where the blood-brain barrier provides cancer cell protection against TKIs and leads to increased metastasis to the central nervous system, including leptomeningeal disease.^{3,4,5}

Patients with cancer can experience psychiatric disorders among during initial detection, diagnosis and during therapy. In addition to experiencing psychosocial problems, patients can also experience psychiatric

disorders such as adjustment disorders, depression, delirium, bipolar disorder and suicide tentaments.^{6,7}

Sensorineural hearing loss was suspected because of the ototoxic effects of targeted therapy. This is not in accordance with literature because side effects of gefitinib are diarrhoea and skin rash. Cochlear sensorineural hearing loss is caused by drug intoxication with streptomycin, kanamycin, saline, neomycin, quinine and chemotherapeutic agents.^{3,8,9}

Platinum-based chemotherapy is widely used and particularly effective against solid tumors. The main side effect of cisplatin is irreversible sensorineural hearing loss. Carboplatin is generally less ototoxic than cisplatin.^{8,9}

A gradual decrease in vision during gefitinib therapy and then progressively worsened. This happens because the optic nerve can be infiltrated by tumour and by various inflammatory processes, it can be infiltrated in systemic malignancies such as lymphoma, leukaemia, multiple myeloma, and carcinoma.¹⁰

4. Conclusion

This case is interesting to report because the patient with bronchogenic adenocarcinoma EGFR mutation (+) after receiving the first generation EGFR-TKI, the patient

experienced various symptoms suggestive of leptomeningeal metastases but no radiological evidence was found to support it.

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