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Case Report

Gefitinib induced convulsions: a rare case report

Atul J. Rajpara*, Neeta J. Kanani

Department of Pharmacology, Medical College, Baroda, Gujarat, India

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***Correspondence to:**
Dr. Atul J. Rajpara,
Email: atulrajpara@gmail.com

ABSTRACT

Gefitinib, an epidermal growth factor receptor (EGFR) inhibitor is used as first-line therapy for non-small cell lung cancer and sometimes also used to treat the other metastatic carcinomas. Diarrhoea and pustular/papular rash occur in ~50% of patients taking gefitinib. Other side effects include dry skin, nausea, vomiting, pruritus, anorexia, and fatigue, but central side effects, especially convulsions are very rare. Here, we report a rare case of 60 years old female patient, a known case of carcinoma uterus with local metastasis and on high dose gefitinib (500 mg/day) treatment for 3 months, who developed generalized tonic-clonic seizure with frothing in mouth and postictal confusion. The dose of suspected medication was reduced to 250 mg/day and patient was given standard care for this adverse drug reaction.

Keywords: Drug induced convulsions, Gefitinib, Rare adverse drug reaction

INTRODUCTION

Gefitinib ('Iressa') is an orally active, selective EGFR tyrosine kinase inhibitor that blocks signal transduction pathways implicated in proliferation and survival of cancer cells and other host-dependent processes promoting cancer cell growth.[1] It is used as first-line therapy for non-small cell lung cancer and sometimes also used to treat the other metastatic carcinomas. Diarrhoea and pustular/papular rash occur in ~50% of patients taking gefitinib. Other side effects include dry skin, nausea; vomiting, pruritus, anorexia, and fatigue.[2] According to the data from VigiAccess™, pharmacovigilance Program of India, convulsions caused by gefitinib are very rare and till only 7 cases reported including ours all over the world.[3]

CASE REPORT

We reported a case of adverse drug reaction of Gefitinib in 60 years old, female patient, a known case of carcinoma of uterus with metastasis on 06/10/2015, who was on chemotherapy, in form of tablet gefitinib (250 mg) twice a day from last 3 months. Patient was not taking any other concomitant medications. She was presented with complaint of a single and first onset episode of generalised tonic clonic seizures (GTCS) associated with frothing coming out of mouth and postictal confusion for a period of about an hour. The only other complain was low grade fever of one-day duration. There wasn't any a sign or symptoms that could have contributed to this GTCS. Also, there is no past history of any epileptic disorder.

On general examination, patient's pulse and respiration were normal, with low grade fever. Blood pressure was 160/90 mm Hg. Random blood sugar was 99 mg/dl and Urine ketone bodies were absent. Electrolytes were also in normal limits, ruling out all the organic causes for convulsion. Central nervous examination was grossly normal, except higher functions were altered to some extent because of postictal confusion.

Patient was admitted in medicine ward same day and advised to go for MRI brain. She was started Tablet Sodium Valproate (200 mg) twice a day for the convulsion and tablet paracetamol and tablet amlodipine ware given for fever and high blood pressure respectively. Tablet gefitinib was continued in the same dose of 500 mg/day.

The report of MRI brain suggested some abnormal hyper intense areas in the bilateral parieto-occipital lobe: suggesting differential diagnosis of subacute infarct/toxic/metabolic lesions and further clinico-pathological correlation was advised (Figure 1, 2).

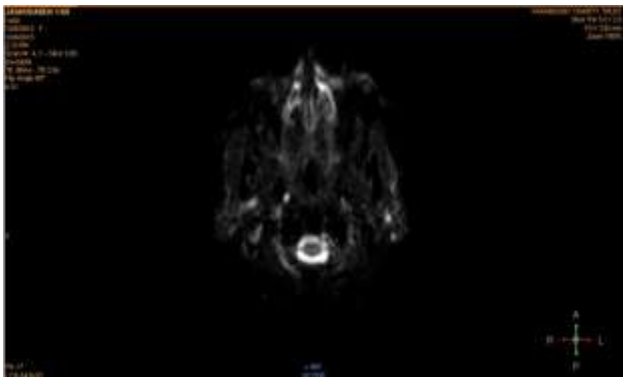

Figure 1: Abnormal hypointense areas in the bilateral parieto-occipital lobe on T1w section of MRI brain.

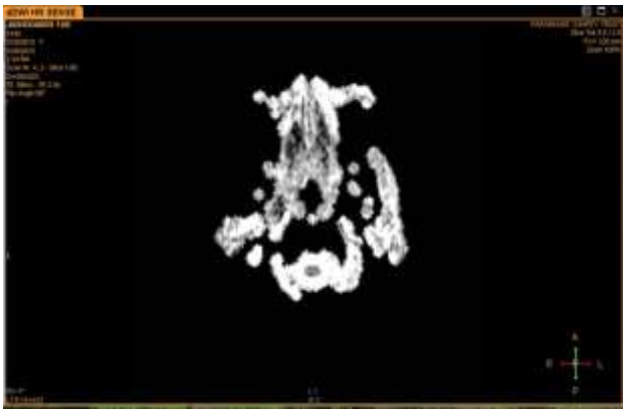

Figure 2: Abnormal hyperintense areas in the bilateral parieto-occipital lobe on T2w and FLAIR corpnal sequences.

After the ruling out all possible causes for this adverse reaction, gefitinib was suspected and its dose was reduced to 250 mg once a day from 09/10/2015. Patient was discharged after another 5 days, during which there wasn't any episode of convulsion. Also, she was advised for follow up every month and as and when needed.

DISCUSSION

There are many drugs associated with causing convulsions as side effect, e.g. anti-psychotics like clozapine, olanzapine, zotepine, CNS stimulants like cocaine, caffeine, theophylline, some anaesthetic agents etc. Many anti-epileptic drugs themselves can produce convulsions in toxic concentration. Sometimes these convulsions can be because of withdrawal of some drugs. Here, in our case an EGFR tyrosine kinase inhibitor, gefitinib is suspected for this episode of convulsion. Causality assessment was done for this reaction using WHO-UMC criteria and Naranjo scale and the reaction fell into "Possible" (not definite or probable) category in both.[4] This can be explained by the lack of previous data on this reaction and clinical and ethical considerations for dechallenge or rechallenge of the suspected drug. An open-label feasibility trial in 3 centres of Netherland, Spain and Belgium each by G. Giaccone et al evaluating safety and tolerability of gefitinib showed one case of grade 3 convulsion in one group of nine patients treated with gefitinib 250 mg/day and one case of grade 3 rash at 500 mg/day as dose limiting toxicity.[5]

CONCLUSION

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