

NIMOTUZUMAB-INDUCED HYPERTENSION: A MAIDEN CASE REPORT

BALAJI O, AMITA D, NAVIN PATIL*

Department of Pharmacology, Kasturba Medical College, Manipal, Karnataka, India. Email: navin903@gmail.com

Received: 30 December 2017, Revised and Accepted: 07 January 2017

ABSTRACT

Nimotuzumab is one among the latest humanized monoclonal antibody targeting against epidermal growth factor receptor (EGFR). It is approved for head and neck squamous cancer in India, Srilanka, Cuba and Argentina, for glioma in Cuba, Argentina and Ukraine and nasopharyngeal cancer in China. Hypertension is most common with bevacizumab and cetuximab, which are monoclonal antibodies against EGFR. Hence, we report here a case of nimotuzumab-induced hypertension in a 70-year-old man treated for vocal cord carcinoma.

Keywords: Nimotuzumab, Hypertension, Epidermal growth factor receptor, Adverse effects.

© 2017 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2017.v10i4.16868>

INTRODUCTION

Nimotuzumab is one among the latest humanized monoclonal antibody targeted against epidermal growth factor receptor (EGFR). It is approved for use in nasopharyngeal cancers, glioma, and squamous cell cancer of head and neck [1]. Common side effects associated with nimotuzumab include infusion reactions, skin rashes, and other dermatological adverse reactions, nausea, dizziness, vomiting [2]. Hence, we report here a case of nimotuzumab-induced hypertension in a 70-year-old man treated for vocal cord carcinoma.

CASE REPORT

Informed consent was obtained from the patient. 70-year-old male patient diagnosed of vocal cord carcinoma underwent surgery was started on nimotuzumab once weekly injection 200 mg IV infusion. Patient is not a smoker and nonalcoholic. His vitals were stable before the start of the treatment and other system examination were normal. Laboratory investigations were also normal with normal kidney function test. He was not a diabetic and his lipid profile was also normal. After patient received his first cycle of nimotuzumab infusion his vitals were stable and he was discharged home. During his next visit for second cycle chemotherapy, after nimotuzumab infusion of 200 mg, patient complained of dizziness and headache and his vitals were not normal. His heart rate was 110 beats per minute and blood pressure was 160/80 mmhg compared to 120/80 mmhg before and after start of first cycle chemotherapy (Table 1). He was treated with amlodipine 50 mg and was discharged home. Later nimotuzumab infusion was continued for four more cycles and blood pressure remained controlled with medications (Table 1). Causality, preventability, and severity assessment were done using Naranjo's scale, Thornton's scale, and Hartwig's scale, respectively.

DISCUSSION

Nimotuzumab is a Ig₁ type of humanized monoclonal antibody used against EGFR [1]. It acts as an antitumor agent by inhibiting angiogenesis, proliferation, and survival of cancer cells. It is approved for head and neck squamous cancer in India, Srilanka, Cuba and Argentina, for glioma in Cuba, Argentina and Ukraine and nasopharyngeal cancer in China. *In vitro* antiproliferative activity of nimotuzumab in squamous cell line culture also showed it inhibited vascular endothelial growth factor (VEGF) in dose-dependent manner. Randomized clinical trials have shown nausea, vomiting, dizziness, fluctuations in blood pressure, dermatological rashes, urticaria, infusion reactions, and pruritus are some of adverse reactions due to nimotuzumab [2].

Table 1: Blood pressure before and after treatment

Before start of chemotherapy	120/80 mm hg
After first cycle	120/80 mm hg
After second cycle	160/100 mm hg
After treatment with amlodipine along with chemotherapy	130/80 mm hg

Table 2: Adverse drug reaction assessment

Naranjo's scale Probable	Hartwig's scale Moderately severe	Thornton's scale Not preventable
-----------------------------	--------------------------------------	-------------------------------------

In our case, it was noted hypertension to be one of the side effects after infusion of 200 mg dose intravenously and presented at the end of second cycle. Mechanism that can be postulated as a reason for hypertension is mainly the VEGF inhibition by nimotuzumab and literature evidence says hypertension is observed in 80% of patients treated with anti-VEGF therapy and also cardiotoxicity is a noted side effect [3,4]. Hypertension is most common with bevacizumab and cetuximab, which are monoclonal antibodies against EGFR [5]. Other conditions causing hypertension was ruled out in our patient and causality assessment using Naranjo's scale [6] was done and a probable causal relationship was ascribed (Table 1). Adverse reaction was also found to be moderately severe and not preventable using Hartwig's scale [7], and Thornton's scale [8], respectively (Table 2).

CONCLUSION

Nimotuzumab, a very novel class of humanized monoclonal antibody against EGFR used in various cancers, has less side effects compared to other drugs in this class of antibodies but hypertension is a serious adverse effect as it can lead to life-threatening conditions. Hence, proper monitoring of vitals during and after infusion of nimotuzumab is required. Furthermore, large-scale prospective clinical studies can be done to find out the exact mechanism and incidence of hypertension associated with nimotuzumab treatment.

REFERENCES

- Chandel PA, Harikumar SL. Pharmaceutical monoclonal antibodies: Production, guidelines to cell engineering and applications. *Int J Pharm Pharm Sci* 2013;5(2):13-20.
- Ramakrishnan MS, Eswaraiah A, Crombet T, Piedra P, Saurez G, Iyer H, *et al.* Nimotuzumab, a promising therapeutic monoclonal for

- treatment of tumors of epithelial origin. In MAbs 2009;1:41-8.
3. Robinson ES, Khankin EV, Karumanchi SA, Humphreys BD. Hypertension induced by vascular endothelial growth factor signaling pathway inhibition: Mechanisms and potential use as a biomarker. *Semin Nephrol* 2010;30(6):591-601.
 4. Holla SN, Nayak V, Bairy KL, Tripathy A, Holla S. HER-2 gene, receptors and drug target: A systematic review. *Int J Pharm Pharm Sci* 2016;8(4):4-9.
 5. Fakhri M, Vincent M. Adverse events associated with anti-EGFR therapies for the treatment of metastatic colorectal cancer. *Curr Oncol* 2010;17 Suppl 1:S18-30.
 6. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981;30(2):239-45.
 7. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. *Am J Hosp Pharm* 1992;49(9):2229-32.
 8. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. *Hosp Pharm* 1992;27(6):538.