

Successful Administration of Panitumumab Alone After Severe Infusion Reaction to Cetuximab in a Patient with Metastatic Colorectal Cancer

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Abstract

The administration of monoclonal antibodies (MoAbs) can result in infusion reactions of various grades; severe reactions are seen in approximately 3% of patients after infusions of cetuximab (fatalities occur in approximately 0.1% of patients). We report a case of a patient who had a severe reaction to cetuximab (a murine MoAb) who then received panitumumab (a human MoAb) and tolerated it without any infusion reaction.

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Introduction

Patients with metastatic colorectal cancer in the United States currently have 2 monoclonal antibody (MoAb) treatment options that inhibit tumor cell growth by binding to the epidermal growth factor receptor: cetuximab and panitumumab. Cetuximab is a chimeric MoAb consisting of approximately 30% murine protein and is associated with severe infusion reactions in 3% of patients, with a fatal outcome in < 1 of 1000 patients (approximately 0.1%).¹ Panitumumab is a fully human MoAb associated with severe infusion reactions in approximately 1% of patients; none have been reported with fatal outcome.² Infusion reactions of any National Cancer Institute Common Terminology Criteria for Adverse Events grade were reported in 15% and 4% of patients receiving cetuximab or panitumumab, respectively.^{1,2} Herein, we report the results from a patient at our clinic who developed a severe infusion reaction to cetuximab but was later administered panitumumab without incident.

Case Report

A 55-year-old white man received cetuximab alone for recurrent stage IV rectal carcinoma with metastases to the

liver, bone, and regional lymph nodes. The patient was previously treated with adjuvant 5-fluorouracil (5-FU), FOLFOX (5-FU/leucovorin/oxaliplatin), and bevacizumab as first-line therapy and with FOLFIRI (5-FU/leucovorin/irinotecan) as second-line therapy. He received limited previous radiation therapy. Concurrent medications included tamsulosin, sulfamethoxazole, trimethoprim, hydrocodone (as needed), oxycodone HCl, and metaxalone. The patient was premedicated with 50 mg of oral diphenhydramine before his first dose of cetuximab. Five to 8 minutes after beginning the cetuximab infusion at a dose of 400 mg/m², the patient developed seizure-like activity, became unresponsive and diaphoretic, and experienced a severe drop in blood pressure, with a systolic reading of 73 mm Hg and no measurable diastolic pressure. His pulse increased to 148 beats per minute. The cetuximab infusion was stopped, and methylprednisolone sodium succinate, cimetidine, and epinephrine were administered. After calling 911, the patient was transported to the hospital, and his condition stabilized in the emergency room. He was admitted and observed overnight.

Five weeks after this severe infusion reaction to cetuximab, the patient was administered panitumumab 6 mg/kg on an every-2-week schedule. Concurrent with each 1-hour panitumumab infusion, the patient received hydrocortisone and lorazepam. No infusion reaction was observed. The patient developed a grade 1/2 rash, a characteristic toxicity of epidermal growth factor receptor inhibitors that appears to be a pharmacodynamic marker of on-target activity associ-

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ated with clinical benefit.³ This patient successfully received 13 panitumumab infusions over 26 weeks without any infusion reactions. The patient showed an improvement in disease-related symptoms, reported alleviation of pain and improvement in energy levels, and had a positive attitude about continuing panitumumab therapy because he felt better and tolerated the treatment well. Carcinoembryonic antigen levels decreased, and computed tomography (CT) scans indicated that this patient had a partial response (PR) to panitumumab. In addition, positron emission tomography was performed and supported the findings from the CT scan. After the PR to panitumumab was determined, therapy was withheld for 4 weeks to allow the rash to subside. Dosing was resumed, and to date, this patient has received a total of 16 panitumumab infusions without an infusion reaction.

Discussion

The severe infusion reaction this patient experienced with cetuximab is consistent with reactions observed in clinical studies, where approximately 90% of severe cetuximab infusion reactions are associated with the first infusion and are characterized by rapid onset of airway obstruction, urticaria, hypotension,

and/or cardiac arrest.¹ The incidence of severe reactions vary by region, as published by O'Neil and colleagues.⁴ They report that grade 3/4 hypersensitivity reactions have been observed in $\leq 22\%$ of patients in selected sites in North Carolina and Tennessee. Furthermore, this case report adds to the previously reported literature,⁵ which indicates that a patient unable to receive cetuximab because of a severe infusion reaction can clinically benefit from panitumumab administration, and more data should be collected to confirm these findings.

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