Successful challenge with the fully human EGFR antibody panitumumab following an infusion reaction with the chimeric EGFR antibody cetuximab

Infusion reactions are serious complications associated with modern antibody therapy. In order to reduce the incidence and severity of such reactions, the newer generations of monoclonal antibodies contain less or no mouse-specific protein sequences. We describe the clinical course of a patient who experienced an infusion reaction following the administration of the chimeric epidermal growth factor receptor (EGFR) antibody cetuximab and who was then successfully challenged with the fully human EGFR antibody panitumumab.

A 39-year-old white male with metastatic colon cancer was scheduled to receive cetuximab monotherapy as third-line treatment. Despite premedication with dexamethasone, clemastine and ranitidine the patient experienced an infusion reaction with massive urticaria mainly in the face and agitation 5 min after cetuximab was started. The infusion was then stopped and he recovered ~30 min later following another infusion with steroids and antihistamines. Ninety minutes later, the cetuximab infusion was restarted with reduced infusion rate but had to be stopped again 20 min later because of progressive urticaria and agitation. No subsequent cetuximab was given. Due to rapid tumor progression and lack of therapeutic alternatives, the patient was planned to receive panitumumab. For safety reasons, the patient was monitored on the intensive care unit during the first and second infusions with panitumumab. The patient was premedicated with cetrizine. No infusion reaction occurred and the patient

received in total six infusions of panitumumab 6 mg/kg i.v. >60 min every 2 weeks. Serum for antipanitumumab antibodies was collected before the first panitumumab infusion and at week 7; no antipanitumumab antibodies were detected.

To our knowledge, this is the first report of a patient with documented hypersensitivity to the chimeric EGFR antibody cetuximab who was then exposed to the fully human EGFR antibody panitumumab. The patient experienced no infusion reactions nor did the patient exhibit any symptoms indicative of a potential allergic response to panitumumab. Cetuximab has been associated with infusion reactions of any grade in ~19% of patients (severe infusion reactions in ~3% of patients) [1]. Severe events were characterized by rapid onset of airway obstruction, urticaria, hypotension and/or cardiac arrest [1]. The majority of infusion reactions (90%) occurred during the initial infusion despite antihistamine prophylaxis [1]. Infusion reactions to panitumumab are very rare. In the pivotal phase 3 trial of panitumumab plus best supportive care (BSC) versus BSC alone, no grade 3 or 4 infusion reactions occurred. One patient (<1%) had an infusion reaction (grade 2) to panitumumab and discontinued treatment (Peeters M, Van Cutsem E, Siena S et al., submitted for publication) [2]. These data and our case report indicate that there may be indeed differences in the hypersensitivity profile between anti-EGFR antibodies. Further studies of panitumumab focusing on infusion events in patients who are intolerant to cetuximab are warranted.

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