

Infliximab Anaphylaxis in Siblings

To the Editor:

The need for antitumor necrosis factor alpha (TNF- α) therapies in siblings is a rare occurrence. Expanding indications, increasing incidences of authorized indications, and a rising awareness of anti-TNF- α strategies by physicians and patients has largely broadened the use of these drugs. Only two reports of well-tolerated infliximab infusions in both siblings have been published so far.^{1,2} It is conceivable that anti-TNF- α treatment of more than one family member will be more common in the future. We report the course and outcome of infliximab anaphylaxis following the sixth or seventh infusion in siblings with ulcerative colitis (UC) and Crohn's disease (CD), respectively.

The brother was born 1987 and CD of the colon with perirectal fistulae was diagnosed in 1996. Due to steroid-dependent disease, episodic infliximab therapy was started in October 2000 and he received six infusions until March 2002 with excellent clinical response. Shortly after the start of the seventh infusion he experienced nausea, emesis, generalized rash, and shortness of breath. This required urgent hospitalization, dimetindenmaleat, and high-dose prednisolone but resolved without sequelae. At that time, infliximab was discontinued. He later underwent repeat surgery for penetrating CD and has been in permanent remission since adalimumab was initiated in 2007.

The sister of this patient was born in 1985. At the age of 8 years left-sided UC was diagnosed. During the following years she experienced an uneventful course. With the exception

of one course of oral methyl prednisolone in 2006, she received only rectal mesalamine therapy or no therapy. In February 2010 she experienced a moderate flare with three or four voluminous bloody stools daily. Combined topical and oral mesalamine therapy did not induce remission. She lost six kg of weight and developed generalized arthralgia and pyoderma gangrenosum (PG) of the right lower leg. Therefore, she received 60 mg prednisolone (59 kg body weight), which induced clinical remission of the UC. However, the PG enlarged in diameter from 2 to 6 cm and got deeper. A short-term increase to 100 mg prednisolone q.d. for 1 week stopped further enlargement but did not induce healing. Moreover, the PG caused a slight but continuous bleeding, which frustrated our patient. Consequently, we infused the only authorized anti-TNF- α -antibody, infliximab (300 mg), on 18 March 2010 with close clinical and cardiopulmonary monitoring but without any adverse event.³ Fourteen days later only two PG lesions of 3 mm remained. We infused infliximab again, started 50 mg azathioprine t.i.d., and scheduled rapid prednisolone reduction. One month later complete clinical remission was achieved and a third uneventful infliximab infusion was applied. On 26 May 2010 prednisolone was stopped and she was treated with azathioprine and mesalamine only. Two month later a 3-mm recurrence of the PG was successfully treated with topical tacrolimus ointment (0.3 mg/1 mg). Another 2 months later, in September 2010, she experienced a rapid growth of the PG and two erythema nodosa on the other leg, but no UC flare. We therefore reintroduced infliximab with continuous cardiopulmonary monitoring after intravenous premedication with 4 mg dimetindenmaleat.

The infusion was uneventful and induced complete remission. We now scheduled regular infliximab infusions every 8 weeks. However, 20 minutes after the sixth infusion she experienced severe anaphylaxis with flush, tachypnea, abdominal cramps, generalized weakness, and ague. After administration of intravenous saline, dimetindenmaleat, and prednisolone she recovered completely within 1 hour and was treated with adalimumab off-label later on.

Our report illustrates that even in very different clinical courses infliximab anaphylaxis should be considered in patients with a family history of infliximab intolerance. One way to avoid familial anaphylaxis could be scheduled rather than episodic infliximab therapy, as many studies reported better efficacy, higher rates of mucosal healing, and fewer developed antibodies in patients with scheduled than those with episodic infusions.⁴

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