



LETTER TO THE EDITOR

Transient menorrhagia without adalimumab discontinuation in a patient with Crohn's disease

Dear Sir,

Menstrual disorders are listed as possible rare side effects during infliximab or adalimumab administration but very few case reports regarding the management of such menstrual side effects exist.¹

A 32-year-old woman with ileal Crohn's disease was switched to adalimumab because of an allergic reaction during infliximab maintenance therapy. The patient was started on adalimumab but during the third dose of adalimumab induction scheme the patient developed severe menorrhagia lasting four days. In detail, the patient had to use approximately three times more pads daily as opposed to her previous 'normal' menstruation days. Menorrhagia resolved spontaneously in the fourth day and the patient was advised to continue adalimumab use and to use oral contraceptives in case of menorrhagia relapse. In next menstruations the patient had no recurrence of menorrhagia.

Inflammatory bowel disease, and more specially Crohn's disease have been related to menstrual abnormalities. These abnormalities are encountered either in the panel of disease extraintestinal manifestations or as the presenting or triggering factor of relapsing Crohn's disease.²

Abnormalities of endometrial blood vessels are among possible causes of anti-TNF α therapy related menorrhagia as many different factors affect endothelial cell growth, function and vessel remodeling in uterus, including TNF α . TNF α is a proinflammatory cytokine involved in a wide range of important physiologic processes. Increased production of proinflammatory mediators is considered central in the manifestation of events leading to irregular uterine bleeding or the polycystic ovary syndrome.³

Of note, adalimumab has been previously related to menstrual abnormalities but also to restoration of menstruation. Of interest, a woman who used adalimumab for psoriatic arthritis and experienced optimal response to adalimumab developed menorrhagia and severe menstrual pain.¹ By contrast, restoration of menstruation in premature ovarian failure after initiation of adalimumab has been also reported.⁴

Post-marketing data has noted that between 2003 and 2006 there were 1335 reports of side effects to adalimumab in 693 patients. Of these, five reports involved menstruation and uterine bleeding in patients using adalimumab, specif-

ically: two cases of dysmenorrhea, one case of menstruation irregularity, one case of menstruation with increased bleeding, and one case of menorrhagia.¹

Of note, the patient had no menorrhagia on infliximab. Post-marketing data related to infliximab described that between 1999 and 2006 there were 3914 noted reports of side effects in 1949 patients that included two cases of amenorrhea but no case of menstrual pain or increased menstrual bleeding. According to emerging data infliximab has been also related to menorrhagia but such an adverse reaction is extremely rare.⁵

The management of menorrhagia during anti-TNF α therapy is empirical. In one case, treatment with ethinyl estradiol and levonorgestrel together with adalimumab discontinuation were effective in abating symptoms.¹ According to our experience transient menorrhagia during adalimumab therapy may resolve spontaneously without discontinuation of therapy.

References

- Aslanidis S, Pyrpassopoulou A, Douma S, Poulakos P, Triantafyllou A. Restoration of menstruation in premature ovarian failure after initiation of adalimumab. *Scand J Rheumatol* 2008;**37**:488–90.
- Scheinfeld N. Menorrhagia and severe menstrual pain related to the use of adalimumab in a psoriatic. *J Dermatol Treat* 2008;**19**:188–9.
- Malik S, Day K, Perrault I, Charnock-Jones DS, Smith SK. Reduced levels of VEGF-A and MMP-2 and MMP-9 activity and increased TNF-alpha in menstrual endometrium and effluent in women with menorrhagia. *Hum Reprod* 2006;**21**:2158–66.
- Wakeman J. Exacerbation of Crohn's disease after insertion of a levonorgestrel intrauterine system: a case report. *J Fam Plann Reprod Health Care* 2003;**29**:154.
- Medical information Center of Centocor [data on file].

Konstantinos H. Katsanos

Vasileios E. Tsianos

Epameinondas V. Tsianos*

1st Department of Internal Medicine and Hepato-Gastroenterology Unit University, Hospital of Ioannina, Greece

*Corresponding author. Tel.: +30 26510 07501; fax: +30 26510 07016.

E-mail address: etsianos@uoi.gr (E.V. Tsianos).

15 February 2010