

Ventricular tachyarrhythmia after adalimumab therapy in a patient with Crohn's disease

P. Eder, L. Lykowska-Szuber, I. Krela-Kazmierczak, K. Stawczyk-Eder, K. Linke

Chair and Department of Gastroenterology, Human Nutrition and Internal Medicine, University of Medical Sciences in Poznan, Heliodor Swiecicki Clinical Hospital, Poznan, Poland.

To the Editor,

We report a case of a 19-year-old Caucasian male who was admitted to our Department in February 2010 because of the exacerbation of Crohn's Disease (CD) with a presence of an active perianal fistula. He was then qualified for the biological therapy. A routine electrocardiogram (ECG) performed at that time demonstrated a normal sinus rhythm – 75 beats/min. Subsequently, adalimumab was introduced in standard doses.

After two more weeks, the patient returned to our Department to receive the third dose of adalimumab. At the time of admission the patient was asymptomatic, he was in clinical remission. However, auscultation revealed an irregularity of the cardiac rhythm. A 12-lead ECG revealed numerous premature ventricular contractions (PVC's) such as bigeminy and occasionally trigeminy. The patient did not, however, complain of symptoms such as: chest palpitation, chest pains, dizziness, or fatigue; also, blood pressure was normal. We performed

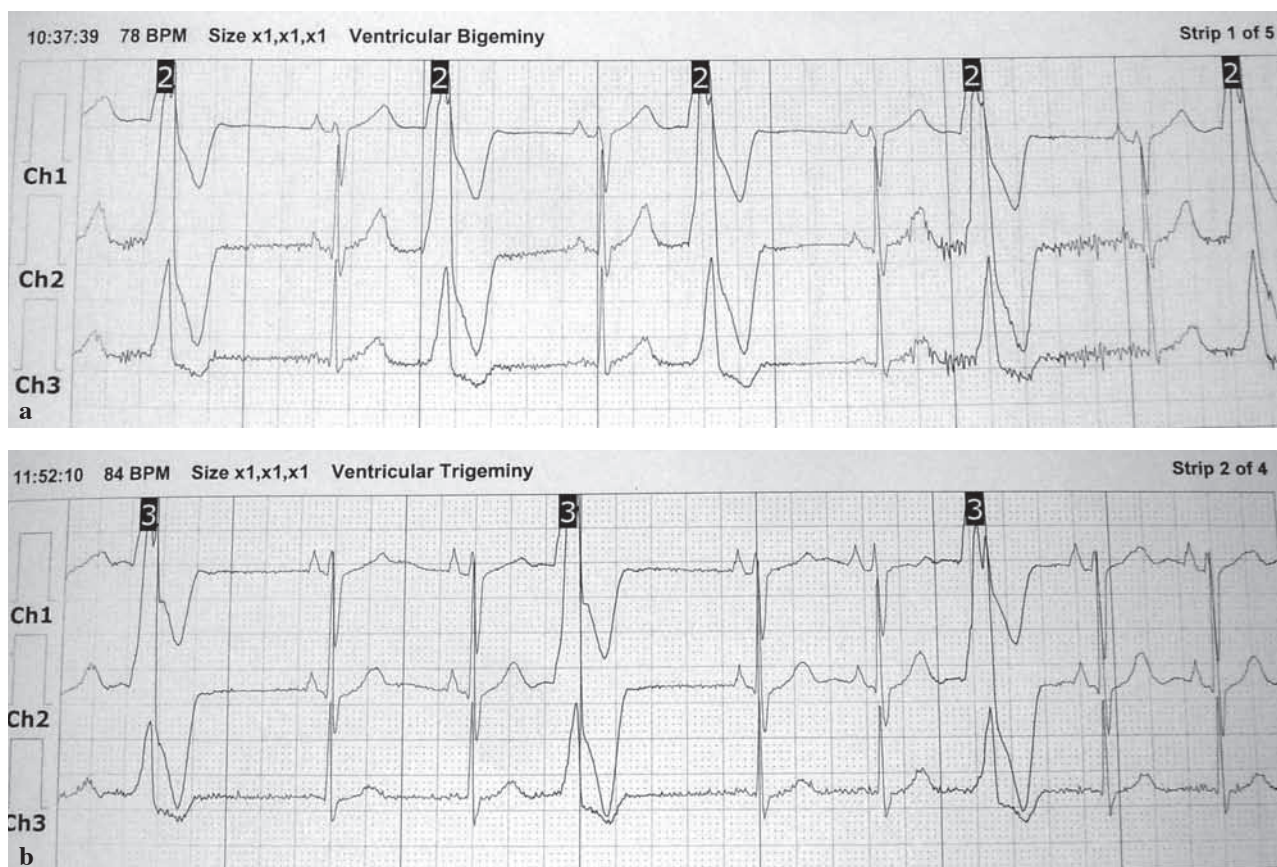


Fig. 1. — Holter ECG – ventricular tachyarrhythmia in a patient treated with adalimumab

- a) Ventricular bigeminy
- b) Ventricular trigeminy

Correspondence to : Piotr Eder, M.D., Chair and Department of Gastroenterology, Human Nutrition and Internal Medicine, University of Medical Sciences in Poznan, Heliodor Swiecicki Clinical Hospital, Przybyszewskiego Street 49, 60-355 Poznan, Poland. E-mail : piotr.eder@op.pl

Submission date : 31/05/2012

Acceptance date : 12/07/2012

a 24 h Holter ECG (Fig. 1) which revealed a sinus rhythm with numerous PVC's – 42509 ventricular ectopic beats/105779 total heart beats (40,2%). The echocardiography did not show any structural heart disease. Moreover, no abnormalities were revealed by laboratory tests – troponin T, creatine phosphokinase, CRP, ESR, serum electrolytes, thyroid hormones (fT3, fT4) and TSH were within normal ranges. The patient denied using any cardiotoxic drugs. Subsequently, the subject was examined by a cardiologist, who did not detect any organic heart pathology. Although there was a strong suspicion that it was adalimumab that caused cardiac arrhythmia, having consulted the cardiologists, we decided to continue the biological treatment. At the time, the patient was under strict control of gastroenterologists and cardiologists.

The patient was treated with adalimumab for 12 months. Two months later a follow up examination was performed. A 12-lead ECG demonstrated normal sinus rhythm - 70 beats/min, without any PVC's. A 24 h Holter ECG did not reveal any pathology as well ; PVC's were not registered (0% ventricular ectopic beats). These findings led us to the conclusion that adalimumab was the cause of numerous PVC's reported during the entire course of the treatment with that anti-TNF agent. Ileocolonoscopy and MR enterography revealed a sustained remission of CD.

At present, the patient is still in remission and is receiving azathioprine and mesalazine 2 g/daily. After another 4 months a 24 h Holter ECG was performed again, confirming the disappearance of PVC's registered during the adalimumab treatment.

There are only a few case reports of the influence of TNF- α inhibitors on cardiac rhythm. The vast majority of these concerns bradyarrhythmias caused by infliximab. For instance, Sote et al. reported a case of a 78-year-old woman with rheumatoid arthritis who developed complete heart block after her third dose of infliximab (1). To the best of our knowledge, there is only one case report of supraventricular tachycardia induced by infliximab, and just a few case reports of ventricular tachy-

arrhythmia resulting from treatment with anti-TNF agents (2).

Lazzerini *et al.* assessed the influence of infliximab on arrhythmias during infusion in patients with chronic arthritis. They estimated that the incidence of severe ventricular tachyarrhythmia was slightly higher, when compared to a group of subjects who had received placebo. In conclusion, they observed that patients with arrhythmias had a longer baseline-corrected QT interval and a more depressed heart rate variability. Although infliximab did not seem to influence the QT interval, it might produce a shift towards a relative vagal prevalence (3).

In contrast to infliximab, there are no case reports of any proarrhythmic influence of adalimumab, although "arrhythmia" is listed as a possible side effect in the drug prescribing information (4). In conclusion, to the best of our knowledge, our report is the first case report of cardiac arrhythmia transpiring after adalimumab injections, and one of few case reports of ventricular tachyarrhythmias after the administration of any anti-TNF agent at all.

To conclude, this report is important by calling the clinician's attention, that it is essential to look for various kinds of side effects of biological treatment in each individual subject. What we currently know about anti-TNF agents, nevertheless, continues to entail numerous questions and doubts, and we are still learning how to deal with these theoretically familiar drugs.

References

1. SOTE Y., GREEN S., MADDISON P. Complete heart block after infliximab therapy. *Rheumatology (Oxford)*, 2008, **47** : 227-228.
2. SINGH M., DIWAN M.M., PATEL K.C.R. A rare case of supraventricular tachycardia induced by infliximab : a case report. *Cases Journal*, 2009, **2** : 147.
3. LAZZERINI PE., ACAMPA M., HAMMOUD M., MAFFEI S., CAPECCHI P.L., SELVI E. *et al.* Arrhythmic risk during acute infusion of infliximab : a prospective, single-blind, placebo-controlled, crossover study in patients with chronic arthritis. *J. Rheumatol.*, 2008, **35** : 1958-1965.
4. Humira – drug prescribing information. <http://www.rxabbott.com/pdf/humira.pdf>. Revised March, 2011.