Hypoglycaemia after initiation of treatment with etanercept in a patient with type 2 diabetes mellitus

E Bonilla, Y Y Lee, P E Phillips, A Perl

Ann Rheum Dis 2007;**66**:1688. doi: 10.1136/ard.2007.072256

Etanercept, a dimeric fusion protein consisting of the extracellular portion of the human p75 tumour necrosis factor α (TNFα) receptor and the Fc receptor of human immunoglobulin G subclass 1, has been used for the treatment of a variety of rheumatological conditions such as rheumatoid arthritis (RA), psoriatic arthritis, and ankylosing spondylitis.[1]

We report the case of a 54 year old white woman with a longstanding history of RA and type 2 diabetes mellitus who developed episodes of hypoglycaemia after initiation of etanercept treatment. The episodes occurred only on the day after she received her etanercept injection.

Before this, the patient had been on methotrexate and low dose prednisone for her RA. Her diabetes was well controlled with the use of a Humalog 75/25 insulin sliding scale before breakfast and before supper. She had always been compliant with the use of insulin and never had problems with hypoglycaemia. After initiation of treatment with etanercept at a dose of 25 mg subcutaneously twice weekly, self administered at night, the patient started to notice decreases in her glycaemia to the level of 40–50 mg/dl measured on her glucometer only on the morning after etanercept was injected. The situation was brought to the attention of her endocrinologist, who decided to decrease the dose of insulin by 10 units on the morning after her etanercept administration. In spite of this, her post-etanercept hypoglycaemia persisted and further reduction by 35 units in the dose of insulin has been required to avoid the problem. The hypoglycaemic episodes do not happen on the other weekdays and she never had this problem before the initiation of etanercept therapy. She has always been known to be compliant both with diet and insulin administration.

The metabolic effect of TNF blockade remains controversial.

There has been a previous report of marked hypoglycaemia in female mice two hours after the administration of TNFα.[2] The investigators suggested that the administration of TNFα produces the hypoglycaemia in order to serve increased lipogenesis in the liver and adipose tissue. On the other hand, Satomi *et al*[3] examined the association of hypoglycaemia and TNFα by presensitising the reticuloendothelial system with lipopolysaccharide in animals. Hypoglycaemia occurred only when TNFα production was induced after lipopolysaccharide administration but not when TNFα was given alone. More recently Gonzalez-Gay *et al*[4] found that a single infusion of the TNFα blocker infliximab improved insulin sensitivity and insulin resistance dramatically in non-diabetic RA patients. No significant changes in pre- and post-infliximab glycaemia were seen.

Our case shows that TNFα blockers may cause hypoglycaemia in humans, which has not previously been described. The exact mechanism by which this occurs remains obscure and should be the subject of further research.

Authors' affiliations
E Bonilla, Division of Rheumatology, Department of Medicine, State University of New York, New York, USA
Y Y Lee, Division of Endocrinology, Department of Medicine, State University of New York, USA
P E Phillips, Division of Rheumatology, Department of Medicine, State University of New York, New York, USA
A Perl, Division of Rheumatology, Department of Medicine, State University of New York, New York, USA

Correspondence to: Dr Eduardo Bonilla, Department of Medicine, State University of New York, College of Medicine, 750 East, Adams Street, Syracuse, New York 13210, USA; ebonill@twcny.rr.com

Accepted 3 June 2007

REFERENCES

1 **Spencer-Green G**. Etanercept: update on therapeutic use. *Ann Rheum Dis*, 2000;**59**(suppl I), i46–i49.
2 **Mahony SM**, Tisdale MJ. Metabolic effects of tumor necrosis factor alpha in NMRI mice. *Br J Cancer* 1990;**61**:514–19.
3 **Satomi N**, Sakurai A, Haranaka K. Relationship of hypoglycemia to tumor necrosis factor production and anitumor activity. *J Natl Cancer Inst* 1985;**74**:1255–60.
4 **Gonzalez-Gay MA**, DeMatias JM, Gonzalez-Juanatey C, Garcia-Porrua C, Sanchez-Andrade A, Marin J, *et al*. Anti-tumor necrosis factor alpha blockade improves insulin resistance in patients with rheumatoid arthritis. *Clin Exp Rheumatol* 2006;**24**:83–6.

CORRECTION

doi: 10.1136/ard.2006.063230.corr2

CA Stegeman is affiliated to the Department of Nephrology, Groningen University Medical Centre, University of Groningen, The Netherlands, not to the Department of Rheumatology and Clinical Immunology, as was previously stated in the journal.