COMMENTS AND RESPONSES

Etanercept Treatment in Children With New-Onset Type 1 Diabetes: Pilot Randomized, Placebo-Controlled, Double-Blind Study

Response to Mastrandrea et al.

I read with great interest the article by Mastrandea et al. (1) discussing the potential of etanercept in pediatric patients with newly diagnosed type 1 diabetes. The authors performed a pilot randomized, placebo-controlled, double-blind study with etanercept and found lower A1C and increased endogeneous insulin production, suggesting preservation of β-cell function. These observations are promising and certainly merit further investigation, but I feel some points of balance would be usefully discussed. I concur that treatment with etanercept, a tumor necrosis factor-α (TNF-α) antagonist, may well be a very good candidate to modulate the progression of type 1 diabetes, simply because TNF-α plays an important role in the inactivation and destruction of β-cells. However, patients included in this particular study were all GAD-65 and/or islet cell antibody positive, and therefore specific autoimmune destruction of the insulin-producing β-cells is the most likely cause for the onset and progression of diabetes here. In this respect, I would like to speculate that a decline in GAD-65 and/or islet cell antibodies is responsible, at least partly, for the beneficial effect of etanercept, as titers of GAD-65 and/or islet cell antibodies are negatively associated with β-cell function (2). Consistent with this hypothesis, evidence from the field of rheumatology revealed that TNF-α blockade therapy significantly reduces titers of rheumatoid factor and/or anticitrullinated protein antibodies, and a decline in these antibodies correlates with clinical response (3,4). The possibility of a decline in GAD-65 and/or islet cell antibodies being responsible for the beneficial effects of etanercept is also noteworthy because other anti-inflammatory drugs with less severe drug advents, like methotrexate, may also be capable of lowering GAD-65 antibodies (5). In fact, in two rheumatoid arthritis patients with concomitant diabetes, we observed a significant decline in GAD-65 titers after receiving methotrexate treatment. Such observations of course need further study, but the point is that interpretation of TNF-α antagonists improving β-cell function through lowering levels of TNF-α may be too simplistic.

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