Clinical experience with intravenous immunoglobulin and tnf-a inhibitor therapies for recurrent pregnancy loss

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Editor,

We report on a 22 year-old non-smoking nulligravida who presented with her husband for in vitro fertilisation (IVF). She was in good general health and had five prior unsuccessful IVF treatments, all with implantation failure. While her TSH and T4 were normal, a strongly positive (1:25,600) thyroid peroxidase antibody (ATA) titre was noted. Their sixth IVF cycle included IVIG infusion x3 as had been used in the immediately preceding cycle. However, etanercept (Enbrel®; Immunex Corp., Thousand Oaks, California USA) was added for the first time as a series of 25mg subcutaneous injections commencing four weeks before ovulation induction and continued on four-day intervals thereafter. Eight etanercept injections were given until commencement of gonadotropins, and then discontinued. Two blastocysts were transferred fresh and two were frozen at day five. Following an unremarkable obstetrical course, the patient delivered male/male twins by Caesarean at 34½ weeks' gestation. While the strongly positive ATA titre finding in our patient was concerning, we admitted that the mechanism of how ATA impacts reproductive outcome is presently unknown. ATA have been documented more often in women with recurrent pregnancy failure than controls, and a prospective clinical trial of women with "immunologic abortion" evaluating multiple autoimmune variables found ATA to be the most frequently encountered immunopathology—present in 53% of patients[1].Our case, believed to be the first published report of its kind in Ireland, is parallel with those who have described a highly-circumscribed use of immunomodulators for refractory cases where an immune diathesis exists[2,3] and given only under closely monitored conditions. While immunomodulators are inappropriate in IVF for unselected populations and should not be regarded as first-line therapy, dampening of immune responses antagonistic to implantation and embryo development may be a derivative of IVIG + etanercept therapy. Should our patient decide to enlarge her family and return for transfer of cryopreserved embryos in future, the role of further immunomodulator treatment will require consideration.

Notes

The authors have no conflict of interest

References

1. Stricker RB, Steinleitner A, Bookoff CN, Weckstein LN, Winger EE. Successful treatment of immunologic abortion with low-dose intravenous immunoglobulin. Fertil Steril. 2000;73(3):536–40.[PubMed]

2. Sills ES, Perloe M, Tucker MJ, Kaplan CR, Palermo GD. Successful ovulation induction, conception, and normal delivery after chronic therapy with etanercept: a recombinant fusion anti-cytokine treatment for rheumatoid arthritis. Am J Reprod Immunol. 2001;46(5):366–8. [PubMed]

3. Clark DA, Coulam CB, Stricker RB. Is intravenous immunoglobulin (IVIG) efficacious in early pregnancy failure? A critical review and meta-analysis for patients who fail in vitro

fertilization and embryo transfer (IVF) J Assist Reprod Genet. 2006;23(1):1–13. [PMC free article] [PubMed]