Neonatal Thrombocytopenia As Side Effect of Immunotherapy for Recurrent Spontaneous Abortion

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Case report

We report a case of a 38-year-old woman with recurrent spontaneous abortion who gave birth to a thrombocytopenic neonate after immunotherapy with husband’s leucocytes.

A 38-year-old healthy female consulted the Department of Immunology and Histocompatibility Center in Thessaloniki. Medical history taken from the woman revealed two abortions. She was pregnant in 1999 and aborted at approximately 12-weeks gestational age. The second pregnancy was spontaneously aborted at approximately 8-weeks gestational age. Personal and family history of the woman were free of autoimmune or other diseases.

Obstetrical investigation included hysterosalpingogram, laparoscopy, endometrial biopsy, cervical cultures, hormonal assignment and parental chromosomes. All examinations were normal. Immunological study in the patient included: antinuclear antibodies (ANA) panel (ANA titre, dsDNA, Sm, Rnp, Ro, La) negative, anti-cardiolipin: 4.0 U/mL, anti-β2glycoprotein IgA: 1.2 U/mL, IgG: 3.4 U/mL, IgM: 2.4 U/mL, anti-thyroid antibodies (antithyroglobulin: 50 U/mL, antithyroperoxidase: 40 U/mL, anti-phosphatidyl serine IgG: 5.1 U/mL, IgM: 6.7 U/mL), antigamma antibodies: 18 U/mL, complement (Sc5b-9 4.41 lg/mL, iC3b 3.1 lg/mL) immunoglobulins IgA: 320 mg/dL, IgM: 88 mg/dL, IgG: 800 mg/dL, immunophenotype, NK (CD16+CD56+): 10%, Cytotoxic (CD5+) B cells: 4%, cytokines IL-4: 4.5 pg/mL, IFN-γ: 1.0 pg/mL, TNF-α: 2.5 pg/mL, anti-paternal antibodies (Cross Match): negative. HLA typing (HLA-ABC, DRB1*, DQA1*, DQB1*) was performed in the couple and we confirmed sharing of HLA-DRB1, DQA1 and DQB1. Laboratory evaluation was negative for autoimmune diseases and thrombophilia. The patient was considered to suffer from recurrent spontaneous abortions (RSAs) of alloimmune aetiology.

Prior to pregnancy the woman received five paternal white cell immunizations (PLI), each PLI 4 weeks apart. Cross Match transformed to positive after the last dose of immunization. A girl baby of 36-weeks gestation was born by normal vaginal delivery. Clinical examination after birth was the following: weight 2920 g, length 35 cm, head circumference 35 cm and apgar score 1 min 8 s and 5 min 10 s. The neonate revealed generalized petechiae and purpura and was admitted in the Neonatal Unit of Hippokration Hospital of Thessaloniki Platelet count was 5000/mm.³ The diagnosis was neonatal thrombocytopenia. The treatment was immunoglobulin [intravenous immunoglobulin (IVIG)] 2 g/kg in bolus. The baby was
followed up for 1 year and thrombocytopenia did not relapse. The serological studies showed that maternal serum contain anti-HLA IgG against platelet antigens extracted from the father and the infant.

Discussion

Recurrent pregnancy loss is defined as two or more clinical losses before 20 weeks of gestation and occurs in 1% of couples desiring to have a child. All couples with history of unexplained pregnancy lose require accurate screening. In 50% of women who have RSA no anatomical anomalies or chromosomal disorders are recognized and not any infections etiology can be confirmed. Alloimmune recurrent abortions are treated by immunization of women with husbands’ lymphocytes or IgG IVIG. In our laboratory, we apply lymphocyte immunization in these cases with rate of success about 60%.

Paternal lymphocytes allogenic lymphocyte immunization is an effective treatment for unexplained RSAs. The beneficial effect of this procedure has been attributed to the induction of humoral factors and of immunoregulatory blocking factors, which may help to the implantation and fetal growth. The anti-paternal antibodies may play an important role and protect the foetus from rejection. The exact mechanism of immunotherapy is still not known, but it has been reported that lymphocyte immunization cause an increase in the progesterone induced blocking factor which may help to the implantation and fetal growth. The anti-paternal antibodies may play an important role and protect the foetus from rejection.

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References