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SPECIAL ARTICLE

Vaccine model of antiphospholipid syndrome induced by tetanus vaccine

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Successful induction of antiphospholipid syndrome (APS) in two different non-autoimmune prone mouse strains, BALB/c and C57BL/6, was achieved by tetanus toxoid (TTd) hyperimmunization using different adjuvants (glycerol or aluminium hydroxide), and different adjuvant pretreatments (glycerol or Complete Freund's Adjuvant (CFA)). APS had different manifestations of reproductive pathology in BALB/c and C57BL/6 mice: fetal resorption (as a consequence of extreme T-cell activation obtained in the course of pretreatment), and lowering of fecundity (as a consequence of polyclonal B-cell stimulation), respectively. In BALB/c mice fetal resorption coincided with glycerol and CFA pretreatments, while in C57BL/6 mice lowering of fecundity was most obvious in CFA-pretreated mice immunized with TTd in aluminium hydroxide. Both molecular mimicry and polyclonal B-cell activation occur in APS induction, with molecular mimicry effects being dominant in BALB/c mice, and polyclonal cell activation being dominant in C57BL/6 mice. Confirmation of molecular mimicry effects, which in the condition of T-cell stimulation generated fetal resorptions in the BALB/c strain, was achieved by passive infusion of monoclonal antibody (MoAb) T-26 specific for TTd and anti-β_2-glycoprotein I obtained after TTd hyperimunization. High polyclonal B-cell activation in C57BL/6 mice prevented fetal resorption but induced fecundity lowering, as was the case in passive administration of MoAb T-26 in this mouse strain. Passive infusion of anti-idiotypic MoAb Y7 into C57BL/6 mice induced fetal resorptions and confirmed the above suggestion on the protective role of polyclonal B-cell stimulation in fetal resorptions. *Lupus* (2012) **21,** 195–202.

Key words: anticardiolipin antibodies; antiphospholipid syndrome; pregnancy

Introduction

Antiphospholipid syndrome (APS) is a systemic autoimmune disease that can have various clinical manifestations (thrombocytopenia, thrombosis, reproductive pathology). It is considered that this disease appears due to an increase in anti-phospholipid (aPL), anti-β_2-glycoprotein I (β_2GPI) antibodies (Abs) and/or β_2GPI-dependent aPL Abs. Manifestations of APS[1] in the mouse model include a decrease in fecundity and/or fertility. Various data that connect exposure to microbial antigens, either during infections[2–5] or vaccinations,[6–10] to autoantibody production have been published in recent years. Experimental evidence for infectious origins of APS came from mice, immunized with a panel of microbial preparations, which developed anti-β_2GPI Abs.[11] Pathogenic anti-β_2GPI Abs directed against the hexapeptide TLRVYK epitope are produced in mice upon immunization with common bacteria (*Haemophilus influenzae* or *Neisseria gonorrhoeae*), viruses, yeast and tetanus toxin.[12]

Our APS model differs from those previously described as it is generated through tetanus toxoid (TTd) hyperimmunization. Pathogenic anti-β_2GPI Abs in our model are thought not to be specific for the linear TLRVYK sequence present in TTd, but instead recognize TTd conformation, which is similar to that of β_2GPI. Anti-β_2GPI Abs per se are not necessarily pathological, but we were able to show their pathological effects on reproduction. The multifactorial aetiopathogenesis[13] of APS is

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