The role of epidermal growth factor-like domain-related abnormalities, protein S Tokushima, and anti-protein S autoantibodies in pregnancy loss.

Abstract

BACKGROUND: Protein S (PS) deficiency and autoantibodies that bind to PS (anti-PS) have been described in patients with adverse pregnancy outcomes, including pregnancy loss. PS Tokushima is a congenital abnormality of the second epidermal growth factor (EGF)-like domain, and anti-PS has been reported to recognize EGF-like domains. OBJECTIVES: We evaluated the role of PS Tokushima and anti-PS in patients with pregnancy loss. METHODS: Patients with recurrent early pregnancy loss (n = 324; group A), those with one or more mid-to-late pregnancy loss (n = 196; group B), and infertile women having no pregnancy loss (n = 650; group C) were screened for PS type II deficiency and anti-PS. Patients who were diagnosed with PS type II deficiency underwent genetic analysis for the detection of PS Tokushima. RESULTS: The incidence of patients with PS Tokushima was 1.85 %, 5.10 %, and 1.23 % in groups A, B, and C, respectively. The incidence of patients with PS Tokushima was significantly higher in group B ($p = 0.0027$) than in group C. The incidence of patients with anti-PS was 20.1 %, 23.0 %, and 19.2 % in groups A, B, and C, respectively. The incidence of patients with anti-PS was significantly higher in groups A ($p = 0.0229$), B ($p = 0.0071$), and C ($p = 0.0288$) than in previously reported healthy nonpregnant women (7.1 %, 4/56). CONCLUSIONS: Our data suggest that PS Tokushima is associated with mid-to-late pregnancy loss, while anti-PS are associated with recurrent early pregnancy loss, mid-to-late pregnancy loss, and infertility.