First trimester concentrations of pregnancy associated plasma protein A and placent protein 14 in Down's syndrome

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Brambati et al reported that first trimester maternal serum concentrations of pregnancy associated plasma protein A (PAPP-A) were low in pregnancies associated with fetal aneuploidy. Of 13 pregnancies associated with Down's syndrome, seven were reported as having values less than or equal to the fifth centile. To examine the matter further and explore whether PAPP-A might be useful in screening for Down's syndrome in the first trimester we measured its concentration in sera previously used for measuring α fetoprotein, unconjugated oestriol, and human chorionic gonadotrophin concentrations in the first trimester. At the same time we investigated the endometrial protein known as placental protein 14 (PP14) as a possible additional first trimester serum marker.

Subjects, methods, and results

Serum samples were available from 19 of the 22 women with Down's syndrome pregnancies previously studied and 101 of the 108 original controls. The samples had been collected between 9 and 12 weeks' gestation and had been stored frozen in serum banks (United Kingdom, three cases; Israel, four cases; Germany, five cases; Italy, seven cases). Samples had been taken routinely from antenatal patients in the United Kingdom and immediately before chorionic villus sampling in the other countries. Cases and controls were similar with respect to gestational age and duration of storage of the serum sample and were balanced with respect to country of origin. Analysis of placentl protein 14 required a larger volume of serum, and sufficient material was available for only 11 cases of Down's syndrome and 64 controls. PAPP-A was measured by radioimmunoassay at the Royal London Hospital using a specific antibody (Dako, High Wycombe, United Kingdom) and purified PAPP-A prepared at the University of Odense, Denmark. Placental protein 14 was measured by radioimmunoassay with an antibody provided by Dr H Bohn.

We expressed results for PAPP-A in multiples of the control group median (MoM) using the overall median concentration for all the unaffected pregnancies without adjustment for gestation since there was no significant relation between concentration and gestational age. Concentration of PAPP-A was significantly lower in the women with Down's syndrome pregnancies than in the controls (p<0.001, Wilcoxon signed rank test) (figure). The median MoM was 0.23 (95% confidence interval 0.17 to 0.46) in the cases of Down's syndrome; 12 of the 19 women with affected pregnancies (63%) had values below the 10th centile value for the controls.

Placental protein 14 results were expressed in MoMs calculated from a weighted log-linear regression of the median concentration for each completed week of pregnancy on gestational age. The concentrations in women with affected pregnancies were similar to those in women with unaffected pregnancies (median value 0.93 MoM) with almost total overlap.

Comment

Our results show that PAPP-A is a useful first trimester serum marker for Down's syndrome. Measurement of serum PAPP-A concentration together with other markers and the use of maternal age may form the basis of effective first trimester screening for Down's syndrome.

Any physician should consider the possibility of ongoing domestic violence when confronted with a female patient lacking other obvious reasons for frequent hospital admissions.

References


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