PRELIMINARY COMMUNICATIONS

Alpha-fetoprotein in Abortion

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Summary

The clinical value of maternal serum alpha-fetoprotein (AFP) as a guide to the outcome of threatened abortion was assessed. After the thirteenth week of gestation, abortion occurred more frequently (10/12) in women with abnormal serum AFP levels than in those (2/12) whose AFP concentrations were within the normal range. Low levels were present in women with blighted ovum and high concentrations were associated with intrauterine fetal death. In legal first and second trimester abortions, the circulating maternal AFP levels in postabortion samples were often higher than before abortion, irrespective of whether abortion was performed instrumentally or induced with prostaglandins. Maternal serum AFP levels provide a new means for prediction of the outcome of threatened abortion.

Introduction

Uterine bleeding is a common complication of early pregnancy. The biochemical assessment of viable pregnancies in women with threatened abortion includes the determination of urinary oestrogen and pregnanediol (Russell *et al.*, 1957; Brown *et al.*, 1970) and of circulating placental lactogen (Niven *et al.*, 1972). Human chorionic gonadotrophin levels in urine can be helpful in cases where trophoblastic tumours are suspected (Hamburger, 1944) and in doomed pregnancies, where the human chorionic gonadotrophin excretion drops below the positive pregnancy test level (Brown *et al.*, 1970). In contrast with biochemical methods, some investigators claim that vaginal cytology is a superior criterion in predicting the outcome of threatened abortion (Hughes *et al.*, 1964), although this has been disputed (Brown *et al.*, 1970).

The cumulative information of various criteria can serve as a more meaningful guide for clinical decisions concerning threatened abortions. It would be of great clinical value if the number of criteria for assessing fetal viability could be increased. We believe that determination of maternal serum alpha-fetoprotein (AFP) may have significance in this respect.

Alpha-fetoprotein is produced by the fetal liver and yolk sac (Gitlin and Boesman, 1967). During the embryonal period the highest serum AFP concentrations occur during weeks 12-14 of gestation, and the production of AFP begins to decrease around the 32nd week (Gitlin and Boesman, 1966). In the newborn serum AFP remains detectable for about five weeks postpartum (Seppälä *et al.*, 1967): until recently the occurrence

of AFP in maternal serum had been contested (Alpert and Zuckerman, 1970).

The application of a highly sensitive radioimmunoassay enabled quantitative measurement of AFP throughout pregnancy and even in normal human serum (Ruoslahti and Seppälä, 1971; 1972; Seppälä and Ruoslahti, 1972a; Purves and Geddes, 1972). During pregnancy the circulating maternal AFP levels increase during gestation, and the highest levels, about 500 ng/ml, occur during the mid-third trimester. The half-life of maternal serum AFP after delivery is about five days (Seppälä and Ruoslahti, 1972a).

We found recently that a noticeable increase in the maternal serum AFP concentration is often associated with fetal distress (Seppälä and Ruoslahti, 1972b) or intrauterine death (Seppälä and Ruoslahti, 1972c). The present study was undertaken to establish the maternal AFP levels during early pregnancy, and to evaluate the prognostic value of the AFP determination in patients with threatened abortion.

Patients and Methods

Sera from 82 pregnant women between seven and 24 weeks' gestation were studied for the normal range. Fifty-eight women with threatened abortion (vaginal bleeding, low abdominal pain) and 22 women admitted for legal abortion comprised the abortion material. The diagnosis of pregnancy was established in all cases by a positive pregnancy test for human chorionic gonadotrophin. Sera were collected on the day after admission from subjects with threatened abortion, and before treatment and the day after treatment from women undergoing legal abortion, which was carried out by suction curettage in 14 cases and induced with extra-amniotic prostaglandin $F_{2\alpha}$ in eight subjects. Sera were kept deep frozen until tested. No clinical decisions were based on the AFP determinations.

Alpha-fetoprotein was estimated by the radioimmunoassay technique (Ruoslahti and Seppälä, 1971) at serum dilutions of 1:10, 1:25, or higher.

Results

MATERNAL SERUM AFP CONCENTRATIONS IN NORMAL PREGNANCIES

At between seven and 12 weeks' gestation the AFP concentrations varied from 10 to 40 (median 16) ng/ml, at between 13 and 18 weeks from 18 to 150 (median 50) ng/ml, and at between 19 and 24 weeks from 26 to 360 (median 66) ng/ml (see Chart).

MATERNAL SERUM AFP CONCENTRATIONS IN THREATENED ABORTION

During the first trimester 22 of the 34 women with threatened abortion ended in spontaneous abortion, and pregnancies continued past 28 weeks' gestation in 12 subjects. No significant difference was found between the AFP concentrations in these groups (median values 11 and 16 ng/ml). Blighted ovum was diagnosed in two women whose AFP concentrations were about 10 ng/ml.

During the second trimester AFP levels in 12 of 24 women were within the normal pregnancy range (see Chart). Two of these (17%) aborted. Abnormal (either high or low) AFP levels were found in the other 12 women of whom 10 aborted (83%). The difference was statistically significant ($P < 0.01$). Maternal

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AFP concentration was 6,000 ng/ml in a case that was eventually diagnosed as missed abortion of 17-week-old twins. Intrauterine fetal death was also established in two cases where the maternal AFP levels were 2,700 and 415 ng/ml. A cervical cerclage was carried out in three women whose AFP concentrations were 300, 500, and 1,500 ng/ml at the time of operation. Macerated

Circulating AFP levels increased in five out of eight women whose midtrimester pregnancies were terminated using extra-amniotic prostaglandin $F_{2\alpha}$ (table II). No statistical difference was found between the group where abortion was carried out instrumentally and that induced with prostaglandin $F_{2\alpha}$.

TABLE II—Circulating Maternal Alpha-fetoprotein (AFP) Concentrations in Legal Midtrimester Abortions Induced with Prostaglandin $F_{2\alpha}$

Case No.	Pregnancy Week	AFP Concentration (ng/ml)	
		Before Induction	After Induction
1	14	25	220
2	15	50	60
3	15	50	405
4	16	75	55
5	16	90	140
6	16	100	90
7	19	60	40
8	24	55	105

Discussion

This is the first report describing the assessment of maternal AFP levels in early normal and pathological pregnancies. Of women with threatened abortion a significantly higher proportion (87%) of patients with abnormal AFP levels aborted spontaneously than subjects whose AFP levels were within the normal range (17%). We expect still higher predictive efficiency from maternal AFP levels if serial sampling is applied.

Highly increased AFP levels were associated with intrauterine fetal death. Tatarinov (1965), using immunodiffusion, reported a positive AFP reaction in maternal serum during abortion, but this finding could not be reproduced by others (Gitlin and Boesman, 1966). Our findings substantiate those of Tatarinov, since the concentration of 6,000 ng/ml was high enough to be detectable by immunodiffusion. It is likely that AFP levels giving a positive reaction in immunodiffusion indicate strongly that intrauterine fetal death has occurred, provided that malignant tumours are excluded. Presumably the high AFP level of 1,500 ng/ml was also associated with intrauterine fetal death in the case where cervical cerclage was performed. The present series indicates that maternal AFP levels might provide additional information in the monitoring of pregnancies where fetal and maternal defects must be distinguished.

The "background" level of AFP in non-pregnant Finnish adults is low, ranging from 2-16 ng/ml (Ruoslahti and Seppälä, 1971; 1972), but evidently higher concentrations are present in some African populations (Purves and Geddes, 1972; Elgort *et al.*, 1972). Before the thirteenth week the circulating maternal AFP levels increased above the non-pregnant level in about 50% of normal pregnancies and in 30% of threatened abortion. No information concerning the outcome of pregnancy was obtained from the maternal AFP levels during the first trimester. However, increased levels indicate that the fetus is or has recently been present, and this knowledge can be used to differentiate between choriocarcinoma or hydatidiform mole and normal pregnancy (Seppälä *et al.*, 1972). Absence of the fetus in blighted ovum might explain some of the low AFP levels of the present series.

Raised levels of the maternal serum AFP occurred in both spontaneous and legal abortions, where no fetal defects were expected. The increased AFP in maternal serum during abortion evidently originates from the fetal blood or amniotic fluid. Why these raised levels were infrequently present in spontaneous first trimester abortions may find an explanation from the interruption of fetal development before the ontogeny of the fetal liver has reached the stage where significant amounts of AFP are synthesized.

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Individual alpha-fetoprotein (AFP) concentrations in normal and pathological pregnancies. Broken line represents upper level in non-pregnant adults and hatched area is range of distributions during normal pregnancies. ● = One patient.

fetuses were aborted in these cases within 7-15 days. Fetal heart action was recorded in one patient whose AFP concentration was 1,070 ng/ml. The fetus died in utero 10 days later. Five women had abnormally low (non-pregnant) levels to AFP (see Chart). Two of these pregnancies continued past 28 weeks' gestation and three ended in abortion. Blighted ovum was diagnosed in one of these women.

MATERNAL SERUM AFP CONCENTRATIONS IN LEGAL ABORTIONS

In legal first trimester abortions the AFP concentrations in 13 out of 14 women increased (Table I). Exceptionally high AFP levels (550 and 950 ng/ml) occurred in one patient. Unfortunately, the case was regarded as clinically normal and the uterine contents were discarded after suction curettage.

TABLE I—Circulating Maternal Alpha-fetoprotein (AFP) Concentrations in Legal First Trimester Abortions (Suction Curettage)

Case No.	Pregnancy Week	AFP Concentration (ng/ml)	
		Before Abortion	After Abortion
1	8	12	85
2	9	14	27
3	9	15	25
4	9	34	275
5	9	38	30
6	10	10	30
7	10	13	25
8	10	15	120
9	10	15	170
10	10	20	60
11	11	10	26
12	11	15	30
13	11	25	45
14	12	550	950

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MEDICAL MEMORANDA

Fatal Paralytic Ileus due to Strongyloidiasis

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Strongyloidiasis is a chronic intestinal infection caused by the nematode *Strongyloides stercoralis*. It is widespread in tropical countries and is brought to temperate areas by immigrants. Infestation is usually asymptomatic but may produce rashes, abdominal pain, diarrhoea, anaemia, and malabsorption. A rare complication is paralytic ileus, which may present as a surgical emergency. Only one such case appears to have been reported from Britain; the diagnosis was not made during life. A further case is reported here, together with typical x-ray appearances of the upper small bowel.

Case Report

A 32-year-old Jamaican man was admitted to hospital with a two-week history of central abdominal pain, vomiting, and diarrhoea. He had anorexia and had recently lost weight. His motions had been unduly dark. Previously he had been well, had resided in England for 12 years, and had not returned home during that time.

On examination he was wasted and dehydrated. There was no abdominal tenderness or distension, and bowel sounds were present. The haemoglobin level fell shortly after admission from 11.0 to 8.6 g/100 ml. The W.B.C. was 14,500/mm³ (10% eosinophils). A barium-meal examination (see Figs. 1 and 2) showed dilatation, rigidity, and ulceration of the whole of the duodenum, with the

FIG. 1—Strongyloidiasis. Barium-meal study of duodenum.

FIG. 2—Barium-meal study of upper jejunum.

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