ANTENATAL DETECTION OF ANENCEPHALY BY AMNIOTIC FLUID AFP LEVELS

by

R. BAVEJA,* DG.O., M.S., Ph.D.

M. DAYAL,** D.G.O., M.S.

and

M. SINGH,*** M.D., D.C.P.

Introduction

Alpha-fetoprotein, a major plasma protein of early foetus, is synthesized by foetal liver (Gitlin and Boesman, 1967) and yolk sac (Gitlin, 1971). It represents a foetal element in amniotic fluid, maximum concentrations being found in 12 to 24 weeks of gestation. It is believed that even though the amniotic fluid is in intimate contact with the foetus, the protein turnover is comparatively slow. AFP reaches the amniotic fluid via the foetal urine and the levels follow closely the pattern of foetal serum levels.

Alpha-fetoprotein is becoming increasingly important in the antenatal detection of congenital defects. As the environmental component in the aetiology of neural tube defects remains unidentified, at present genetic counselling and early detection in utero with selective termination of an affected foetus are the only available methods for control of these malformations. A more widespread screening of pregnancy in women who have had atleast one previous infant with neural tube defect, is justified (Nevin *et al*, 1973).

The present study was undertaken with a view to detect neural tube defect in pregnancy.

Material and Method

Five antenatal cases suspected of congenital anomalies and 15 of normal pregnancy (26 to 42 weeks) were included in this study. A detailed history was taken with particular attention to diabetes, viral fever, drug intake, exposure to irradiation and previous history of congenital anomaly. Period of gestation was calculated from the date of last menstrual period. Clinical examination included fundal height, size of foetal head and amount of liquor.

Amniotic fluid was collected aseptically by transabdominal amniocentasis in all normal and 4 antenatal cases of hydramnios and with a syringe and needle from the bag of forewaters in early labour in 1. The samples collected were centrifuged at 1800 r.p.m. for 5 minutes. The supernatant fluid was stored in deep freeze until analysed.

Estimation of AFP was carried out by

*Professor and Head of the Department of Obstetrics and Gynaecology, M.L.N. Medical College, Allahabad.

**Pool Officer in Obstetrics and Gynaecology, M.L.N. Medical College, Allahabad.

***Lecturer in Pathology, M.L.N. Medical College, Allahabad.

radial immuno-diffusion by Behring werke's M-Partigen Alpha-Fetoprotein plates (Field *et al*, 1973) using standard serum of Behring werke's (22 mg/100 ml), for standardization of the test.

Observations

AFP levels were estimated in 5 suspected cases of anencephaly (Table 1) and 15 normal cases. The level of AFP varied from 3.2 to 5.5 mg/100 ml in normal pregnancy between 30-34 weeks of gestation (Fig. 1). The cases of anencephaly came to the antenatal clinic for the first time at 30 to 34 weeks because 4 had developed hydramnios and 1 had stopped feeling the foetal movements.

Two were primigravida and 3 multigravida. Previous siblings of the multigravidas were normal.

At 30 weeks amniocentasis was carried out in 2. AFP concentration was 29.6 mg/100 ml in one and 96.4 mg/100 ml in the other. Radiologically the diagnosis of anencephaly was confirmed. Both these patients refused admission for induction when told about the abnormality. They came back at 34 weeks with I.U.D. Labour was induced by oxytocin drip and both had stillborn anencephalic foetuses one of which was macerated.

Two cases presented with marked hydramnios and IUD at 31 weeks. AFP values were 25.2 mg/100 ml. and 36.3 mg/100 ml respectively. Labour was induced after radiological confirmation.

Fifth case came in labour at 34 weeks of gestation. She had marked hydramnios, dyspnoea and other pressure symptoms. Liquor was collected by a needle and syringe before A.R.M. The anencephalic foetus born was macerated. The AFP concentration estimated later on was found to be 17.5 mg/100 ml.

Discussion

The rise of AFP in anencephaly has been suggested to be due to enhanced leakage or transudation of foetal blood components in the exposed tissue of anencephalic skull into the amniotic fluid or via the cerebrospinal fluid, upto 36 weeks of pregnancy. Later on the amniotic fluid protein turnover increases through foetal swallowing and decreased leakage, which might be responsible for either normal or slight rise in AFP level in neural tube defects (Brock and Sutcliffe, 1972: Brock and Nelson, 1974). AFP values ranged between 17.5 mg to 96.4 mg/1000 ml. with a mean of 41 mg/100 ml at 30 to 34 weeks of gestation (Fig. 1). On comparing the data with normal which ranged between 3.2 mg to 5.5 mg/100 ml. for the same period of gestation, the AFP concentration was

TABLE I

AFP Concentration in Anencephaly

S. No.	Period of gestation (wks)	Level of AFP mg/100 ml.	Birth Weight (gms.)	Outcome of labour
1	30	29.6	1600	Male, S. B.
2	30	96.4	1200	Male, S. B., Macerated
3	31	25.2	900	Female, S. B.
4	31	36.3	1400	Male, S. B.
5	34	17.5	1500	Female, S. B.

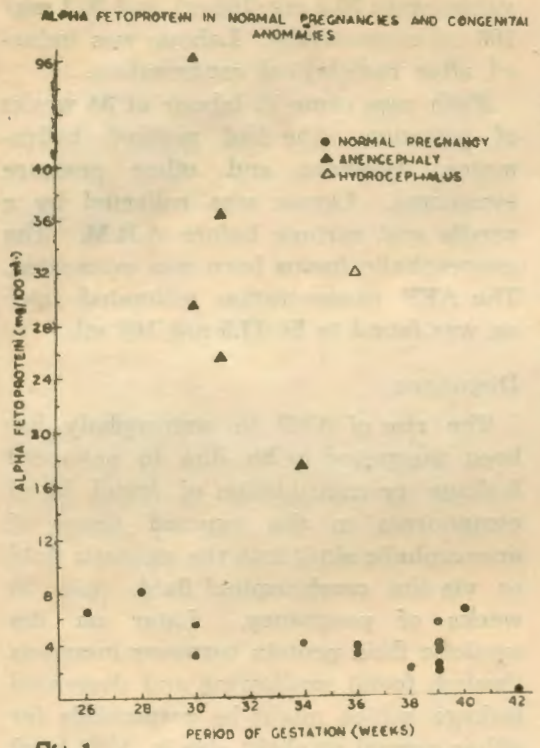

Fig. 1

Fig. 1

about nine times greater than the mean normal level (4.16 mg/100 ml.). Similar were the findings of Brock and Scrimgeour (1972), but at 18 weeks of gestation. Randle and Cumberbatch (1973) found significantly high AFP levels (29 times the normal range) between 26 to 38 weeks of anencephalic gestation.

Brock and Sutcliffe (1972) found raised AFP levels between 25 to 35 weeks of gestation. They suggested that for the diagnosis of anencephaly, amniotic fluid AFP should be measured before 36 weeks of pregnancy, Brock and Nelson (1974) reported similar observations before 36 weeks of pregnancy, after which AFP values were normal in all of their cases.

Field *et al* (1973) estimated AFP by similar method as in our series and reported high AFP value of 64.5 mg/100 ml. at 15th week of gestation in a case of anencephaly with mean normal level of 0.9 mg/100 ml. at 13-18 weeks. In the present series, the patients first came at 30 to 34 weeks of gestation and the highest level recorded was 96.4 mg/100 ml. at 30 weeks, the mean of normal cases at this period was 4.35 mg/100 ml.

High AFP levels were recorded in second trimester by various authors (Brock and Scrimgeour 1972; Allan *et al*, 1973; Randle and Cumberbatch 1973; Nevin *et al*, 1974; Lorber *et al*, 1973; Field *et al*, 1973; Milunsky and Charles, 1974; Laurence *et al*, 1975; Chandra, 1975) and they suggested that biochemical estimations of amniotic fluid AFP adds a new dimension to the early prenatal diagnosis of neural tube defects.

Vast literature has now accumulated on the significance of alpha-fetoprotein estimation. With literacy and awareness people are now gradually becoming conscious to come forward for antenatal supervision if there is a history of past mishaps. Majority still do not understand the significance and contribution of good ante-natal supervision.

Summary

Amniotic fluid Alpha-Fetoprotein levels have been measured in 5 cases of anencephaly by radial immunodiffusion method using Behring Werke's M-Partigen Alpha-fetoprotein plates and standard serum (22 mg/100 ml). Raised values of the range of 17.5 to 96.4 mg/100 ml. were obtained at 30-34 weeks of pregnancy when the patients presented first at the antenatal clinic. The mean AFP concentration was about 9 times higher than the mean normal level 4.16 mg/100 ml.

References

1. Allan, L. D., Ferguson-Smith, M. A., Donald, I., Sweet, E. M. and Gibson, A. A. M.: Lancet. **2**: 522, 1973.
2. Bergstrand, C. G. and Czar, B. (1956) Quoted by Lorrin Lau, H. and Linkins, S. E., Am. J. of Obstetrics and Gynaecology, **124**: 533, 1976.
3. Brock, D. J. H. and Sutcliffe, R. G.: Lancet. **2**: 197, 1972.
4. Brock, D. J. H. and Nelson, M. M.: J. Obstet. Gynec. Brit. C'welth. **81**: 177, 1974.
5. Brock, D. J. A. and Scrimgeour, J. B.: Lancet. **2**: 1252, 1972.
6. Chandra, R. K.: Indian Pediatrics. **12**: 545, 1975.
7. Field, B., Mitchell, G., Garrett, W. and Kerr, C. Lancet. **2**: 798, 1973.
8. Gitlin, D. and Boesman, M.: J. Clin, Invest. **46**: 1010, 1967.
9. Gitlin, D.: New Eng. Journal of Medicine. **285**: 1436, 1971.
10. Lorber, J., Stewart, C. R. and Ward, A. M.: Lancet. **1**: 1187, 1973.
11. Laurrence, K. M., Walker, S. M., Lloyd, M. and Griffiths, B. L.: Lancet. **2**: 81, 1975.
12. Milunsky, A. and Charles, D., Obstet. Gynec. **43**: 593, 1974.
13. Nevin, N. C., Nesbitt, S. and Thompson, W.: Lancet. **1**: 1383, 1973.
14. Nevin, N. C., Thompson, W. and Nesbitt, S.: Journal of Obstetrics and Gynaecology of the British Commonwealth. **81**: 757, 1974.
15. Randle, G. H. and Cumberbatch, K. N.: J. Obstet. Gynec. Brit. C'wealth. **80**: 1054, 1973.