Pediatr Nephrol (1990) 4: 206

Pediatric Nephrology

Ask the expert*

Why is congenital nephrotic syndrome associated with a rise in the concentration of alpha-fetoprotein in the amniotic fluid?

Key words: Congenital nephrotic syndrome – Alpha-fetoprotein

In 1967 Seppälä et al. [1] observed increased alpha-fetoprotein (AFP) concentration in late pregnancy of a mother who then gave birth to a child with congenital nephrosis (CN). Several subsequent studies showed that amniotic fluid AFP was elevated in the second trimester of gestation associated with CN [2–6]. Furthermore, the AFP concentration was elevated in the maternal serum of these cases [6–8]. The latter observation led to a successful prenatal screening programme of CN in an area known to have a high incidence of the disease in Finland [9]. In contrast to these observations, a few published reports and several cases of unpublished clinical observations showed nephrotic syndrome in infants in whom the maternal serum and amniotic fluid AFP concentration had been within normal limits during pregnancy [10, 11]. This apparent controversy needs explanation.

AFP is a normal fetal protein which is synthesized in the fetal liver, yolk sac and gastrointestinal canal [12]. It is about the same size and with a similar electrophysiological charge to serum albumin. The fetal serum concentration reaches the peak around the 13th week of gestation and begins to decline 2 weeks later. The normal AFP concentration in the amniotic fluid parallels that of the fetal serum, but at a lower level. With all probability, the source of the normal amniotic fluid AFP is fetal urine [13]. Any pathological condition associated with diffusion or leakage of fetal proteins in the amniotic fluid is likely to increase the amount of AFP in the fluid. This was first shown in association with open neural tube defects [14] and later in a number of pathological conditions of the fetus [15].

Of all possible renal abnormalities fetal proteinuria is the almost exclusive cause of elevated AFP concentration in the amniotic fluid. Since AFP represents the fetal component of the amniotic fluid proteins, its amount shows the presence or absence of fetal proteinuria. The CN of so-called Finnish type (CNF) is the most common cause of fetal proteinuria. It appears that in this disease the protein-retaining barrier of the glomeruli is abnormal from the very beginning with ensuing proteinuria at the onset of fetal excretion of urine. Apart from CNF, increased amniotic fluid AFP has been described in a rare case of CN associated with defects of central nervous system differentiation [16].

The explanation for the cases of NS in infancy, but negative AFP values during pregnancy, is simple. The fetus did not have proteinuria at the time of the AFP determination. In these cases the renal lesion causing NS developed later in intrauterine life or after birth. Presently it appears that CNF is the only renal disorder associated invariably with increased amniotic AFP concentration, showing fetal proteinuria, in the second trimester of pregnancy. This feature may even be applied for differential diagnosis of the congenital and infantile nephrotic syndromes.

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References

1. Seppälä M, Tallberg T, Ehnholm C (1967) Studies of embryo-specific proteins. Physiological characteristics of embryo-specific alpha globulin. Ann Med Exp Fenn 45: 16–19
2. Kjessler B, Johansson SGO, Sherman MS, Gustavson K-H, Hultquist G (1975) Alpha-fetoprotein in antenatal diagnosis of congental nephrosis. Lancet I: 432–433
3. Seppälä M, Rapola J, Huttunen N-P, Aula P, Karjalainen O, Ruoslahti E (1976) Congenital syndrome. Prenatal diagnosis and genetic counselling by estimation of amniotic fluid and maternal serum alpha-fetoprotein. Lancet II: 123–125
4. Wiggelinkhuizen J, Nelson MM, Berger GMB, Kaschula ROC (1976) Alpha fetoprotein in the antenatal diagnosis of the congenital nephrotic syndrome. J Pediatr 89: 452–455
5. Milunsky A, Alpert E, Frigoletto FD, Driscoll SG, McCluskey RT, Colvin RB (1977) Prenatal diagnosis of the congenital nephrotic syndrome. Pediatrics 59: 770–773
6. Aula P, Rapola J, Karjalainen O, Lindgren J, Hartikainen AL, Seppälä M (1978) Prenatal diagnosis of congental nephrosis in 23 high risk families. Am J Dis Child 132: 984–987
7. Kjessler B, Johansson SGO, Lidbjörk G (1977) Alpha-fetoprotein (AFP) levels in maternal serum in relation to pregnancy outcome in 7,158 pregnant women prospectively investigated during their 14th–20th week past last menstrual period. Acta Obstet Gynecol Scand [Suppl] 69: 25–44
8. Thom H, Johnstone FD, Gibson JI, Scott GB, Noble DW (1977) Fetal proteinuria in diagnosis of congenital nephrosis detected by alpha-fetoprotein in maternal serum. Br Med J I: 16–18
9. Ryynänen M, Seppälä M, Kuusela J, Rapola J, Aula P, Seppä A, Jokela V, Castren O (1983) Antenatal screening for congenital nephrosis in Finland by maternal serum α-fetoprotein. Br J Obstet Gynecol 90: 437–442
10. Spriz RA, Soiffer SJ, Siegel NJ, Mahoney MJ (1978) False-negative AFP screen for congenital nephrosis Finnish type. Lancet II: 1251
11. Schneller M, Braga SE, Moser H, Zimmerman A, Oetliker O (1983) Congenital nephrotic syndrome: clinico-pathological heterogeneity and prenatal diagnosis. Clin Nephrol 19: 243–249
12. Gitlin D, Perricelli A, Gitlin GM (1972) Synthesis of α-fetoprotein by liver, yolk sac, and gastrointestinal tract of the human conceptus. Cancer Res 32: 979–982
13. Seppälä M, Ruoslahti E (1972) Alpha fetoprotein in amniotic fluid: an index of gestational age. Am J Obstet Gynecol 114: 595–598
14. Brock DJH, Sutcliffe RG (1972) Alpha-fetoprotein in the antenatal diagnosis of anencephaly and spina bifida. Lancet II: 197–199
15. Seppälä M (1978) Alpha-fetoprotein in the amniotic fluid in relation to neural tube defects and other congenital/genetic disorders of the fetus. In: Fairweather DVI, Eskes TKAB (eds) Amniotic fluid – research and clinical application, 2nd revised edn. Excerpta Medica, Amsterdam, pp 297–319
16. Palm L, Hägerstrand I, Kristoffersen U, Blennow G, Brun A, Jörgensen C (1986) Nephrosis and disturbances of neuronal migration in male siblings – a new hereditary disorder? Arch Dis Child 61: 545–548