Case reports

Raised alpha-fetoprotein levels in amniotic fluid and maternal serum associated with distension of the fetal bladder caused by absence of urethra

SUMMARY Raised alpha-fetoprotein concentrations were found at 29 and 30 weeks' gestation in the amniotic fluid and maternal serum of a woman who presented in her seventh pregnancy with apparent polyhydramnios. The fetus had multiple abnormalities including gross distension of the bladder resulting from absence of the urethra, intestinal atresia, and a congenital heart defect.

Several fetal abnormalities other than neural tube defects have now been reported where the amniotic fluid alpha-fetoprotein (AFP) was increased. These include congenital nephrosis (Kjessler et al., 1975; Thom et al., 1977), oesophageal atresia (Seppala et al., 1974), duodenal atresia (Weinberg et al., 1975), omphalocele (Nevin and Armstrong, 1975), and Meckel's syndrome (Chemke et al., 1977). In the present report raised amniotic fluid and maternal serum AFP levels were associated with multiple fetal abnormalities including gross distension of the bladder caused by absence of the urethra, intestinal atresia, transposition of the aorta, and an interventricular septal defect.

Fig. 1  Ultrasonogram at 30 weeks' gestation: transverse section 3 cm above umbilicus showing posterior placenta, right sided cystic area (amniotic fluid), and a larger cystic area (distended fetal bladder).

Two weeks later an ultrasonic scan showed the fetus to be pushed down into the pelvis by the excessive fluid, an appearance which was suggestive of a large loculated cystic mass. Further fluid was withdrawn; the AFP concentration was again 3.5 μg/ml. A week later, at 30 weeks' gestation, the ultrasonic scan clearly indicated a large cystic area occupying most of the uterine cavity separated by a septum from a smaller area of fluid in the right upper quadrant of the uterus with the fetal head compressed into the pelvis and the body in the right lower quadrant of the uterus (Fig. 1). Fluid was withdrawn from both areas; the AFP concentrations were 3.3 μg/ml and 72.0 μg/ml in the larger and smaller areas respectively (Table). The fluid from the smaller area was undoubtedly amniotic fluid having a total protein content of 10 g/l, albumin 6 g/l, and bilirubin 10 μmol/l, and also fetal cells. The fluid from the larger area contained no fetal cells and had a total protein content of 3 g/l, albumin 1 g/l, and no bilirubin. Thus this large cystic area was considered possibly to be an intrauterine cyst.

Case report

This 35-year-old patient's first four pregnancies each ended in a spontaneous abortion at 12 weeks' gestation, and her fifth, a female, had transposition of the great vessels with both atrial and septal defects. There was no family history of congenital heart abnormalities; a sister-in-law died with spina bifida. Her sixth pregnancy ended in a spontaneous abortion. Throughout her seventh pregnancy there was disparity between the period of amenorrhoea and the uterine size. At 23 weeks' amenorrhoea the uterine size corresponded to 30 weeks' gestation and within 4 weeks the uterine size was equivalent to 40 weeks' gestation. An ultrasonic scan excluded twins and showed excessive fluid, 30 ml of which was aspirated; the AFP concentration was 3.5 μg/ml.
The next day when the patient went into spontaneous labour, the uterus was observed contacting and the round ligaments were easily palpated during a contraction. Full dilatation was quickly reached.

Table *Alpha-fetoprotein in amniotic fluid, fetal urine and maternal serum*

<table>
<thead>
<tr>
<th>Gestation (w)</th>
<th>Fetal urine*</th>
<th>Amniotic fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>3·5</td>
<td>—</td>
</tr>
<tr>
<td>29</td>
<td>3·5</td>
<td>—</td>
</tr>
<tr>
<td>30</td>
<td>3·3</td>
<td>72·0 (1·4; 2·9)</td>
</tr>
</tbody>
</table>

Figures in parentheses show values of normal mean and 95th centile. *Normal fetal urine AFP range 0·1 to 3·4 µg/ml (Weiss et al., 1976).

During an attempted forcep delivery, the head separated from the trunk. It was apparent now that the appearance of polyhydramnios was the result of gross distension of the fetal abdomen. Decompression of the fetal abdomen was carried out with the removal of more than 2 litres of fluid. The trunk was delivered by internal version and breech extraction.

At necropsy, the abdominal distension which has persisted even after decompression resulted from an enormously enlarged bladder into which one (the left) dilated ureter entered (Fig. 2). The only kidney, which was hydronephrotic, lay slightly to the left of the midline in the upper abdomen. Behind the dilated bladder only one ovary and tube were present. There was no urethra and only a clitoris was identifiable. The small bowel which was of small calibre throughout measured 89·5 cm, with meconium only in the terminal portion. The large bowel which measured only 17 cm was also much contracted with a narrow lumen and ended in a blind mucus filled sac towards the apex of the bladder. There was no anal canal. The oesophagus, stomach, and pancreas were normal. The heart showed a patent foramen ovale, an aorta transposed arising entirely from the right ventricle, a hypoplastic pulmonary artery ending in a blind sac within the interventricular musculature, dividing into small right and left pulmonary arteries and joined to the aorta by a patent ductus. Pulmonary veins entered the left atrium. An interventricular septal defect (pars membranacea) was also present.

Discussion

In open fetal neural tube defects the origin of the increased amniotic fluid AFP is considered to be leakage of the protein from fetal serum and cerebrospinal fluid. This hypothesis is supported by the findings of high AFP levels in fetal serum and fetal cerebrospinal fluid between 15 and 20 weeks' gestation and also by normal amniotic AFP levels in fetal neural tube defects covered by a full thickness of skin (Brock, 1976). It has also been suggested that the raised amniotic fluid AFP may be the result of fetal serum transudation rather than a leakage into the amniotic fluid (Weiss et al., 1976).

In fetal abnormalities other than open neural tube defects, several different mechanisms have been postulated for the raised amniotic fluid AFP. In congenital nephrosis with a fetal proteinuria, raised amniotic fluid AFP has been observed (Kjessler et al., 1975; Thom et al., 1977). Recently, Chemke et al. (1977) have reported Meckel's syndrome without a neural tube defect in which the raised amniotic fluid AFP was attributed to polycystic kidneys. In gastrointestinal abnormalities, the raised amniotic fluid AFP is probably through disturbed or absent fetal swallowing (Weinberg et al., 1975). Intestinal atresia may disturb the normal passage of amniotic fluid through the fetal gut thus preventing normal absorption and/or degradation.

In our patient, the appearance of polyhydramnios was the result of distinct enlargement of the fetal abdomen caused by distension of the fetal bladder resulting from absence of the urethra. The fluid obtained transabdominally at 27, 29, and 30 weeks' gestation was fetal urine with AFP levels within previously reported normal ranges (Table). As fetal

![Fig. 2](http://jmg.bmj.com/) Necropsy appearance showing grossly distended bladder, and bowel ending blindly behind the bladder.
urine is a major source of amniotic fluid AFP, urethral obstruction alone would result in a low amniotic AFP level, as in disorders associated with renal dysgenesis. The raised amniotic fluid and maternal serum AFP is most probably caused by regurgitation of bile and gastric contents into the amniotic fluid due to intestinal atresia. Transudation of fetal serum as a result of the gross abdominal distension is unlikely. In omphaloceles with exposure of blood vessels, easy transudation of fetal serum will result in increased amniotic fluid AFP (Nevin and Armstrong, 1975; Weiss et al., 1976), but when the exomphalos is covered with skin amniotic fluid is normal.

Fortunately, in most instances where a high AFP level has been found in the absence of a neural tube defect, the fetal abnormalities have been so serious as not to compromise the validity of termination of the pregnancy because of the high AFP value.

N. C. NEVIN, A. RITCHIE, F. MCKEOWN, AND G. ROBERTS

Departments of Medical Genetics, of Midwifery and Gynaecology, and of Pathology, Institute of Clinical Science, The Queen’s University of Belfast, and the Department of Biochemistry, The Royal Victoria Hospital, Belfast, Northern Ireland

Primary hypogonadism in the Borjeson-Forssman-Lehmann syndrome

SUMMARY A 28-year-old man with mental retardation and multiple congenital malformations was found to have the classical features of Borjeson-Forssman-Lehmann syndrome. Endocrine evaluations showed primary hypogonadism as the underlying endocrine abnormality rather than hypopituitarism as suggested in earlier reports.

Borjeson et al. (1962, 1963) described 3 related males with an X-linked recessive syndrome characterised by profound mental retardation, microcephaly, peculiar fatty facies, and hypogonadism. Findings in an isolated case (Baar and Galindo, 1965) and in one of the original patients (Brun et al., 1973) suggested hypopituitarism as the basic endocrine abnormality.

We report here the clinical and endocrine findings in an individual with this syndrome.

Case report

The patient is a 28-year-old man who has resided in an institution for the retarded since age 11. Information on his past history is scanty as we have been unsuccessful in reaching any of his relatives. According to the records, there are no similar cases or mental retardation in the family. He was born with a weight of 2.6 kg to a 15-year-old primigravida. Bilateral inguinal herniorrhaphies were performed at age 3 months, but the operative reports are not available. He sat unsupported at 3 years of age, stood alone at 34 years, and walked at 4 years. By 4 years of age he was capable of some speech, but this has remained limited to the utterance of several phrases.

When admitted to the institution at age 11 years, his height was 127 cm (50th centile for 8 years) and his weight, 27.4 kg, was 5th centile for age. Major motor seizures occurred three times in the next seven years and at age 18, sodium pentobarbitone was prescribed intermittently because of increased frequency of seizures. Diphenylhydantoin, 32 mg orally, i.e., was started at age 20 and has been given regularly to this time. Seizures have been adequately controlled since age 23 when primidone, 100 mg, i.e., was added to this therapeutic regimen.

He has been admitted to hospital with cellulitis of the lower extremities on several occasions. Recurrent otitis media with bilateral tympanic membrane perforations necessitated a tympanoplasty at age 23. His
Raised alpha-fetoprotein levels in amniotic fluid and maternal serum associated with distension of the fetal bladder caused by absence of urethra.

N C Nevin, A Ritchie, F McKeown and G Roberts

doi: 10.1136/jmg.15.1.61

Updated information and services can be found at: [http://jmg.bmj.com/content/15/1/61](http://jmg.bmj.com/content/15/1/61)

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to: [http://group.bmj.com/group/rights-licensing/permissions](http://group.bmj.com/group/rights-licensing/permissions)

To order reprints go to: [http://journals.bmj.com/cgi/reprintform](http://journals.bmj.com/cgi/reprintform)

To subscribe to BMJ go to: [http://group.bmj.com/subscribe/](http://group.bmj.com/subscribe/)