A SYNDROME OF MULTIPLE CONGENITAL MALFORMATIONS WITH ABSENT EXTERNAL GENITALIA, URETHRAL AND ANAL OPENINGS IN ONE OF TWINS

D. Sinniah
J. K. Manuel

SYNOPSIS

A syndrome of multiple congenital malformations with absence of the external genitalia, the fifth case to be recorded in the world literature is reported for the first time in one of diamniotic dichorionic twins and is associated with the longest survival yet recorded for this congenital abnormality. The various hypotheses on the pathogensis of this rare disorder are reviewed.

INTRODUCTION

Congenital absence of the external genitalia with absence of urethra, renal malformations, persistence of the primitive cloaca and imperforate anus have been described only on four occasions in the English literature including once in a sibling of a monoamniotic-monochorionic twin birth (Rukstinat and Hasterlik, 1939; Kirshbaum, 1950; Fitch and Artinian, 1973; Koffler et al., 1978). This first report in a diamniotic-dichorionic twin is associated with the longest survival yet recorded for this congenital abnormality. The various hypotheses on the pathogenesis of this rare disorder are reviewed.

CASE REPORT

The parents both Malays, aged 30 years old are unrelated. The father has twin brothers. The first pregnancy was normal and the male child is now aged two years. This is the second pregnancy and there was no history of toxaemia, hydramnios, or exposure to drugs, herbs or radiation. Pregnancy and delivery were uneventful at 36 weeks gestation in a private hospital. The first twin was a normal female, birth weight 2.67 kg. Apgar score was eight at one minute and 10 at five minutes, length 46 cm and head circumference 31 cm.

The second twin, the subject of this report, also had an uncomplicated delivery, birth weight 1.88 kg., length 34 cm and head circumference 31 cm. Apgar score at one and five minutes were eight and ten respectively. The placenta was dichorionic and diamniotic. The infant was transferred to the University Hospital, Kuala Lumpur, after birth.

On admission, the infant appeared active and not distressed. Abnormal physical findings were localised to the abdomen and perineum. The umblical cord contained two arteries and a vein and there was dribbling of urine through a persistent urachus. There was agenesis of the external genitalia and imperforate anus — the perineum was smooth except for a dimple at the centre of pubis.

**Departments of Paediatrics and Anatomy
University of Malaya,
Kuala Lumpur
Malaysia**

D. Sinniah, MA, MD, FRACP, FRCPI, DCH
Associate Professor of Paediatrics

J. K. Manuel B. Sc, MBBS
Associate Professor of Anatomy

Bilateral skin protrusions were noted in the region of the superficial inguinal ring (Fig. 1).

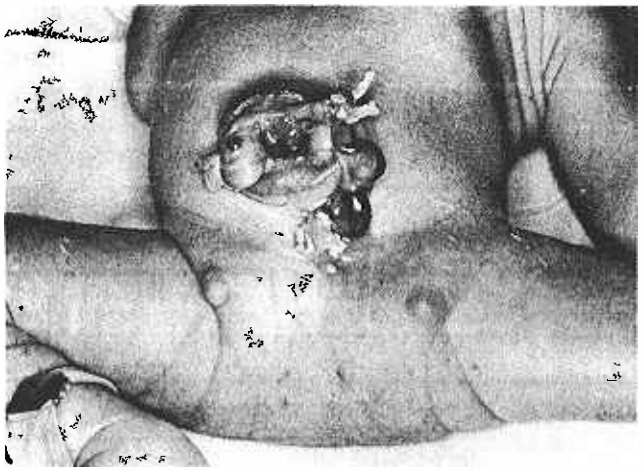

Fig. 1 Patient's abdomen and perineum showing deficiency in anterior abdominal wall, complete absence of external genitalia imperforate anus and skin protrusions at inguinal region.

Oral feeding was commenced after three days of intravenous fluids and defaecation was observed through a persistent vitello-intestional duct that lay in a malformation of the anterior abdominal wall around the umbilical region. Administration of larger feeds was followed within minutes by passage of unaltered milk and curds through the persistent vitello-intestinal duct (Fig. 2). There was no vomitting or abdominal distension.

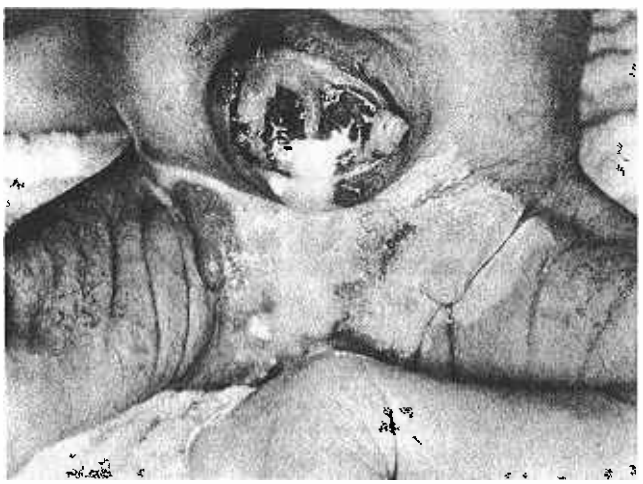

Fig. 2 Passage of unaltered milk and curds through persistent vitello-intestinal duct minutes after oral feeding.

Investigations revealed a haemoglobin of 8.8 gm/dl. Serum Na was 133 meq/1, K 6.0 meq/1, Cl 100 meq/1 and blood urea 24 mg/dl. X-rays showed no osseous abnormalities of the head, neck, thorax, upper and lower limbs but X-rays of the spine revealed sacral dysgenesis. Intravenous pyelogram disclosed excretion of contrast medium; the renal outlines were not clearly visualised but both pelvicalyceal systems, ureters and probably a cloaca appeared to be normal. Barium meal and follow-through revealed normal oesophagus, stomach and proximal small bowel which opened out at the umbilicus; no bowel was visualised distal to this area. Buccal smear revealed the presence of Barr bodies. Karyotype proved to be 46xx.

The infant remained well until the tenth day of life when she began to deteriorate. Blood urea and serum potassium increased to 156 mg/dl and 7.8 meq/1 respectively when she expired on the thirteenth day before sinogram studies were undertaken.

Surgery was not done as the defects were felt to be incompatible with prolonged survival and consent for autopsy was denied by the Muslim parents.

DISCUSSION

The primitive streak appears early in the third week of embryonic life, regresses caudally and disappears by the fourth week having given rise to the intra-embryonic mesoderm. Severe defects of the caudal axis are rare and usually occur sporadically giving rise to a wide range of abnormalities depending on the exact location of the lesion.

Potter's syndrome and the syndrome of caudal regression due to disturbances of structures derived from the caudal mesodermal axis of the embryo can extend to various cranio-caudal levels. A cranial insult would give rise to pulmonary disturbances while a more caudal insult gives rise to anal, genital and spinal disturbances and to sirenomelia (Kallen and Winberg, 1974).

The congenital abnormalities noted in this case resemble very closely the syndrome of caudal regression (Smith, 1976) without sirenomelia. The earlier four cases reported (Rukstinat and Hasterlik, 1939; Kirshbaum, 1950; Fitch and Artinian, 1973; Koffler et al., 1978) also did not posses sirenomelia. The gut distal to the vitello-intestinal duct in the index case was most probably atretic as no barium negotiated beyond this point and the presence of a cloaca rather than a urinary bladder could not be proved conclusively as permission for postmortem could not be obtained.

Various theories have been put forward for the stimultaneous occurrence of a number of malformations in an infant. In the case of a single umbilical artery, developmental anomalies may be due to disturbances of the blood supply to the caudal half of the body or to an interference in the growth of the umbilical mesoderm or to a disturbance in the hemodynamics of the embryo (Chaurasia, 1974). In this case however two imbilical arteries were present.

Teratogens have long been known to produce malformations but their exact mode of action in the embryo is still not known. The presence of various malformations in the same infant may be due to the presence of two or more teratogens, or the presence of one teratogen producing a malformation which results in a cascade of secondary anomalies or damage to various developmental processes at the same time. The occurrence of malformations in only one of twins however makes this unlikely.

An incoordination in growth rate, supply of 0_2 and programmed cell death during embryogenesis brought about by hypoxia due to a delay in the appearance of relevant small blood-vessels in an area is also thought to give rise to multiple malformations (Lloyd et al., 1977).

Of the five cases of congenital absence of genitalia recorded so far, two have occurred in twins. The aetiology

of early mesodermal death resulting in the defects described in this report remain speculative but is probably non-heriditary as one sibling of a monozygous twin was affected in the case reported by Koffler et al (1978). Congenital anomalies and abnormalities in placental circulation do occur more commonly in twins. The low hemoglobin level observed here suggests the likelihood of twin to twin transfusion via an abnormal placental circulation.

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