Before having received any insulin, the serum insulin level was abnormally low in relation to the blood glucose level (Table). At the time of diagnosis some degree of insensitivity to insulin was suggested since injection of 2 units crystalline insulin intravenously (1.0 unit/kg) caused a less than 50% decrease in blood sugar concentration after 30 minutes. The necessity for insulin treatment for only 21 days, and the improvement of the glucose tolerance test with time, could be interpreted as a maturation of insulin production by the β -cells.

Our patient appeared to have a transient inadequate secretion of insulin, and in addition perhaps some degree of insulin insensitivity.

Summary

A dysmature infant at the age of 3 weeks had a transient nonketotic hyperosmolar hyperglycaemia with glycosuria, hypermethioninaemia with homocystinuria, hyperlipidaemia, and relative hypoinsulinaemia. Methionine metabolism became normal after 5 days of insulin treatment.

At 9 months of age he responded normally to an oral glucose load.

A transient, inadequate secretion of insulin is suggested as causing the metabolic defects in the infant.

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Congenital Absence of Pituitary Gland and Adrenal Hypoplasia

Congenital absence of the pituitary gland and hypoplasia of the adrenal glands in an infant without anencephaly is rare, and we have been able to find reports of only 3 such cases (Blizzard and Alberts, 1956; Brewer, 1957; Reid, 1960). 3 further cases with similar, but not identical, congenital abnormalities of both the pituitary and adrenal glands have been described (Mosier, 1956; Dunn, 1966). Details of these 6 cases together with the case described in this paper are summarized in the Table. 2 of these 6 infants were boys, and the one described by Blizzard and Alberts (1956) had an extremely small penis.

In this paper we describe a further example of this syndrome in a boy who also had a very small penis. This finding may prove to be a useful external marker of a lethal congenital abnormality.

Case Report

This boy was born by normal vertex delivery at 41 weeks' gestation to a healthy 17-year-old primigravida, and weighed 3.22 kg. The mother had taken iron and folic acid during pregnancy.

Although the baby breathed spontaneously 30 seconds after birth, he remained cyanosed. He had no detectable abnormalities in his heart or lungs, and a chest x-ray was normal. He was noted to have a very small penis, but the testes were palpable in the inguinal canals. He was nursed in 30% oxygen and became pink but was unable to suck and was fed through a nasogastric tube. On the 5th day of life he had a number of generalized convulsions and became apnoeic. Investigations at this time gave the following results: blood sugar 30 mg/100 ml, serum calcium 7.8 mg/100 ml, blood urea 128 mg/100 ml, serum sodium 155 mEq/l., potassium 6.1 mEq/l., and bicarbonate 27 mEq/l., arterial pH 7.33, P_{CO_2} 38 mmHg. There were no cells in the CSF which was sterile on culture, and blood culture was also sterile. He was treated with intravenous dextrose and intermittent positive pressure ventilation, but died a few hours later.

The main findings at necropsy were bilateral bronchopneumonia, absence of the pituitary gland, and hypoplasia of the adrenal glands. Sections of the pituitary fossa revealed cartilage only, but unfortunately no attempt was made to exclude an ectopic pituitary in the track of Rathke's pouch. The adrenals measured $1.5 \times 0.6 \times 0.2$ cm and weighed less than 1 g each (normal 4 g). The kidneys were of normal size, and the relative sizes of the adrenals and kidneys were like those seen in the adult or anencephalic fetus. Histological examination of the adrenals showed absence of the fetal cortex, but the definitive adult cortex was twice as wide as normal in the newborn and in places was wider and had an irregular nodular appearance. The

TABLE

Necropsy Findings in 7 Cases with Congenital Abnormalities of Both Pituitary and Adrenal Glands

Author	Sex	Pituitary	Adrenals*	Testes	Penis	Ovaries	Thyroid
Blizzard and Alberts (1956)	M	Absent	Hypoplastic	Hypoplastic	Small	—	Hypoplastic
Brewer (1957)	F	Absent	Hypoplastic	—	—	Hypoplastic	Hypoplastic
Reid (1960)	M	Absent	Hypoplastic	Hypoplastic	Normal	—	Hypoplastic
Present case	M	Absent	Hypoplastic	Normal	Small	—	Normal
Dunn (1966)	F	Absent	Absent	—	—	Not recorded	—
Mosier (1956)	F } Twins	Hypoplastic	Hypoplastic	—	—	Normal	Hypoplastic
	F }	Not recorded	Hypoplastic	—	—	Not recorded	Not recorded

*All adrenals found to be devoid of fetal cortex.

medulla was also more abundant and better developed than is usual in the newborn. The thyroid was normal macroscopically and microscopically. The testes lay in the inguinal canals and were of normal size. Their histological appearance was probably within normal limits, though there was a moderate amount of loose connective tissue between the tubules. Interstitial cells were present, but not abundant.

Comment

The cause of this rare syndrome is unknown. The pituitary gland probably develops normally at first and subsequently atrophies, for the pituitary gland is required for early masculinization of the external genitalia, at least in experimental animals (Jost, 1953). The small size of the penis may reflect inadequate pituitary activity later in fetal life.

Normal development of the male genitalia in fetal life also depends on adequate adrenal and testicular function. Inadequate adrenal function, which occurs in the variety of congenital adrenal hyperplasia due to 3- β -ol-dehydrogenase deficiency, causes hypospadias and incomplete fusion of the labioscrotal folds (Hamilton and Brush, 1964). Inadequate testicular function leads to the development of the internal and external genitalia along female lines, regardless of chromosomal sex (Jost, 1953).

It is interesting that, despite the small size of the adrenal glands in our subject, adrenal activity in fetal life was sufficient to promote development of the external genitalia, and, after birth, to prevent hypoglycaemia and hyponatraemia from occurring.

Adrenal hypoplasia is presumably due to lack of adrenocorticotrophic hormone, for it is always found in association with pituitary hypoplasia in anencephaly (Potter, 1961). The thyroid gland may also be hypoplastic (Table) due to lack of thyroid stimulating hormone.

Summary

A male infant with a very small penis, who died

at 48 hours of age, is described. At necropsy no pituitary gland was found, and the adrenal glands were hypoplastic. The finding of a very small penis may prove to be an external marker of a lethal congenital abnormality.

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**Failure to Detect the Carrier
in Congenital Nephrogenic
Diabetes Insipidus**

Congenital nephrogenic diabetes insipidus is known to give rise to stunting of growth and possible mental retardation. Prolonged polyuria may result in urinary tract dilatation and hydrone-