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A CASE OF CONGENITAL ADRENAL HYPOPLASIA AND REVIEW OF THE LITERATURE*

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Congenital adrenal hypoplasia is frequently observed in association with anomalies of the central nervous system. Adrenal hypoplasia which is seen without any malformation of the central nervous system is rather rare. It was first described by Sikl[1] in 1948. In 1959 Mitchell and Rhaney[2] reported the condition in two brothers and suggested that it could be familial. The case presented here is a male baby who was hospitalized with respiratory difficulties and cyanosis at birth. He died at the tenth hour of life. His adrenals were found to be a miniature adult type, and there were no anomalies of the central nervous system. This case emphasizes that congenital adrenal hypoplasia may also play a role in infant mortality.

Case Report

Ş.B., a male infant weighing 3000 gm, was delivered at term by cesarean section after an uneventful pregnancy. His Apgar score was 4 at one minute. The infant was born to a 25-year-old mother, gravida 4 para 0. He was brought to the Neonatology Unit of Hacettepe Children's Hospital because of respiratory difficulties and cyanosis. His blood sugar was 25 mg/dl when measured by "Dextrostix" (Ames). He was fed intravenously. The infant had a poor clinical course and died suddenly at the tenth hour of life. The parents were not related. Two sisters and a brother had also had cyanosis at birth and died within 24 hours after delivery.

Postmortem Findings

The infant had no external anomalies. Petechial hemorrhage was noted on the skin. The heart, great vessels and other thoracic organs were normal. No abnormalities

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were detected in the abdominal and pelvic organs, except that both adrenals were very small and showed an extremely thin cortical layer. Their combined weight was 150 mg (average normal weight is 6.5 gm for that age). Microscopic examination revealed that there was cortical differentiation between zona glomerulosa, zona fasciculata, and zona reticularis as can be seen in an adult (Figure 1). The medulla was normal. On microscopic examination of the lungs, amniotic fluid aspiration and pulmonary hemorrhage were found.

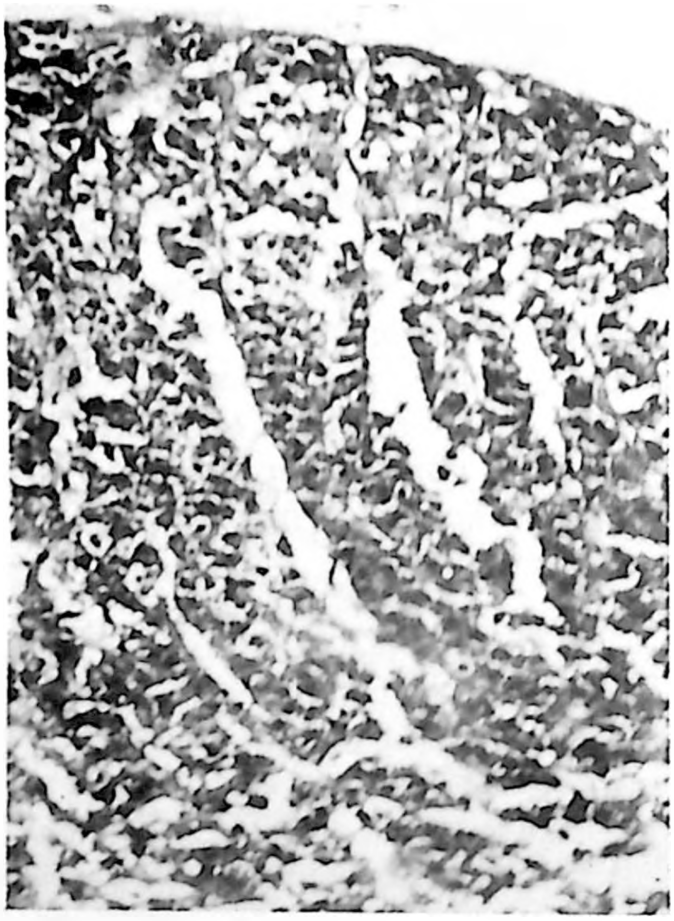

Figure 1.

Microscopic appearance of adrenal gland showing miniature adult pattern (H + E x 100).

Discussion

The causes of sudden death in infancy often remain unexplained despite extensive postmortem studies. Approximately 85% of infants who die suddenly and unexpectedly fall into the category of the sudden infant death syndrome, in which no specific pathological changes are found at postmortem examination. Less frequently, by careful examination at autopsy, a specific cause of death can be found.

The association between adrenal hypoplasia and anencephaly has been known since 1723 and several cases have been reported[3]. Although it is very rare without central nervous system malformations, it was first described by Sikl[1] in a 33-day-old infant. Subsequently, 3 cases were reported by Potter[4], and in 1965 Roselli and

Barbosa[5] reported 25 cases, including two of their own. To date individual or familial cases of congenital adrenal hypoplasia have been reported by various authors. These are summarized in Table I.

TABLE I

Cases of Congenital Hypoplasia of the Adrenal Glands Reported in the Medical Literature (1948 - 1977)

Reference	Sex	Age at onset	Age at death	Main clinical features
Sikl[1] (1948)	M	3 weeks	33 days	Diarrhea, melanoderma, sudden death
Roberts[6] (1949)	M	3 weeks	6 months	Vomiting, dehydration, electrolyte disturbances
Geppert et al[7] (1950)	M	Birth	20 months	Vomiting, electrolyte disturbances, melanoderma, convulsions, sudden death
Deamer and Silver[8] (1950)	M	Birth	10 months	Vomiting, electrolyte disturbances, melanoderma, convulsions, sudden death
Provenzano[9] (1950)	M	Birth	24 days	Shock, convulsions, sudden death
Welsh and Mehlin[10] (1954)	F	Birth	24 hours	Shock, melanoderma
Denys et al[11] (1955)	M	18 days	6 months	Vomiting, dehydration, electrolyte disturbances, shock
Weens and Golden[12] (1955)	F	Birth	22 days	Vomiting, dehydration, abdominal distension, two exploratory laparotomies
Williams and Robinson[13] (1956)	M	2 weeks	46 days	Vomiting, dehydration
	F	Birth	18 days	Vomiting, dehydration, prolonged jaundice
Mosier[14] (1956)	F	2 days	4 days	Vomiting, syncopal attacks, spasticity
	F Identical twins	6 hours	25 hours	Syncopal attacks, cyanosis
Blizzard and Alberts[15] (1956)	M	Birth	1 day	Cyanosis, apneic attacks, hypopituitarism and hypogonadism
Ehrlich[16] (1957)	M	2 days	15 months	Cyanosis, twitchings, convulsions, dehydration, coma
MacMahon et al[17] (1957)	M	15 days	3 months	Vomiting, diarrhea, electrolyte disturbances, gray skin, twitchings, shock (associated aorta coarction)
Brewer[18] (1957)	F	Birth	4.5 hours	Prematurity, cyanotic attacks
Gardner[19] (1957)	M	17 days	4 weeks	Vomiting, diarrhea, fever, electrolyte disturbances, respiratory difficulty, very low 17 ketosteroids, sudden death
Harlem and Myhre[20] (1957)	M	Birth	33 days	Vomiting, lethargy, melanoderma, convulsions, coma
Mitchell and Rhaney[2] (1959)	M	3 weeks	57 days	Vomiting, shock after laparotomy
Boyd and MacDonald[21] (1960)	M	4 days	4 weeks	Vomiting, dehydration, hypothermia, listlessness, marasmus, intestinal obstruction (volvulus), death on 8th postoperative day
	M Siblings	8 days	9 days	Vomiting, refusal to feed, dehydration, hypothermia, listlessness, gray color

TABLE I (continued)

Reference	Sex	Age at onset	Age at death	Main clinical features
Kerenyi[3] (1961)	F	5.45 hours	12 hours	Slight cyanosis, mottled skin, labored respiration, Cheyne-Stokes respiration, twitching of left side
Winquist[22] (1961)	F	25 hours	36 hours	Poor nursing, lethargy, respiratory distress, cyanosis, Cheyne-Stokes respiration, spasticity, convulsions
Roselli and Barbosa[5] (1965)	F	Birth	12 hours	Vomiting, cyanosis
	F	Birth	14 hours	Respiratory distress, cyanosis, convulsions
O'Donohoe and Holland[23] (1968)	F	Birth	16 months	Respiratory distress, vomiting, convulsions
	M	24 hours	28 hours	Cyanosis, gray skin
	M Siblings	Birth		Cyanosis, vomiting, dehydration
Uttley[24] (1968)	M	4 days	4 weeks	Refusal to feed, dehydration
Zondek and Zondek[25] (1968)	M	4 weeks	6 weeks	Diarrhea, dehydration
	M	Birth	27 days	Vomiting, refusal to feed
Favara et al[26] (1972)	F	1 year	22 months	Periodic vomiting
	M		4 months	Sudden death
	F		3.5 months	Sudden death
	M		2 months	Vomiting, dehydration
	M		2 years	Sudden death (during cleft palate operation)
	M		48 hours	Convulsions, apneic attacks
	M	Birth	17 hours	Respiratory distress
	M	1 hour	7.5 hours	Respiratory distress
	M	7 hours	9.5 hours	Cyanosis, hypotony, respiratory difficulty
	M	18 days	7 weeks	Diarrhea
Brook et al[27] (1973)	M	18 hours	–	–
Russel et al[28] (1977)	F	9 months	9 months	Sudden death

Analysis of the published cases discloses that cyanosis, respiratory and neurological signs, and syncopal attacks are the most frequent clinical features in the patients who die early (during the first 36 hours of life). Ten patients died during the first 36 hours of life. The patients who survive for a longer period more frequently have digestive disturbances such as vomiting and diarrhea, followed by severe dehydration, electrolyte disturbances and shock. The longest survival was 2 years in these series.

There are two types of congenital adrenal hypoplasias. The first, miniature adult adrenal type, is usually associated with anencephaly and/or pituitary abnormalities, consisting of either absence or hypoplasia of the gland itself, or decreased numbers of acidophils with an increased number of basophils. This type of adrenal hypoplasia has been found in both sexes and is thought to be an autosomal recessive condition[29].

According to Kerenyi[3], in the second type of congenital adrenal hypoplasia, the adrenal glands contain large irregular cells whose cytoplasm is eosinophilic and

finely granular. The layers of cortex cannot be identified. These changes, now called cytomegaly, are thought to represent remnants of the fetal cortex and may normally be present up to 18 months of age. In this type, the hypophysis is normal and patients survive for a longer time. This has been reported as an X-linked condition[29].

Kerenyi's classification[3] has been disputed by investigators reporting cases with miniature adult adrenal glands without cytomegaly and without pituitary or brain abnormalities[22,23,26]. Our case was miniature adult adrenal in type, and the hypophysis and brain were normal in appearance.

The adrenal hypoplasia cases present clinical findings such as listlessness, irritability, anorexia, vomiting, poor respiratory muscular action (dyspnea, cyanosis and pulmonary congestion); diminished Moro, grasping, and poor sucking reflexes; weight loss, dehydration; acidosis and convulsions. In these cases steroid therapy should be started without delay[9].

Adrenocortical hypoplasia and Addisonian crisis may be found as the cause of death in sudden infant deaths[28]. The case presented here also expired due to respiratory difficulties with cyanosis during the first day of life, and at the post-mortem examination his adrenals were found to be hypoplasic.

The familial incidence in this disorder has been reported by Uttley[24], O'Donohoe and Holland[23], Boyd and MacDonald[21], Zondek and Zondek[25], and Brook et al[27]. In the history of our case, mortality of brothers and sisters was noted. Since congenital adrenal hypoplasia may be inherited, it should be looked for in every case of sudden infant death so that appropriate genetic counseling can be given to prevent recurrence in the same family. When the diagnosis is made, all siblings should be examined to check for its presence in previously undiagnosed cases, since treatment will prevent death and is generally associated with a good prognosis.

Summary

A newborn male baby who died suddenly at the tenth hour of life is presented. His adrenals were found to be hypoplasic at the post-mortem examination, and he had no central nervous system malformation. Cases of adrenal hypoplasia which have been reported to date are also reviewed.

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