IDIOPATHIC RENAL ACIDOSIS IN TWINS

ALKALOSIS RESULTING FROM OVERDOSAGE OF A CITRATE MIXTURE

BY

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The literature and theories of the causation of idiopathic hyperchloraemic renal acidosis of infants have recently been reviewed by Latner and Burnard (1950). They describe the biochemical findings and give experimental evidence to show that the probable cause of the condition is faulty absorption of bicarbonate from the proximal tubules of the kidney. There is at present no evidence to show whether the disease is congenital or acquired but the former is more probable. The present description of the condition occurring in twins lends weight to this view.

Summary of Clinical, Biochemical and Necropsy Findings

The clinical features of the condition can be summarized as failure to gain weight, vomiting, constipation and hypotonia. In severe cases there is often a report that the child passes an abnormally large quantity of urine, and dehydration may be a prominent feature. The syndrome most commonly begins about the weaning period.

On laboratory investigation it is found that the urine is persistently alkaline (Payne, 1948) and often contains a few pus cells. In contrast to this, however, the child is in gross acidosis, the plasma bicarbonate being below 30 vol. CO_2% (13·5 mEq./litre) and the chloride raised. The blood urea level is often at the upper limits of normal.

At necropsy pathological findings are limited to the kidneys. These organs cut with a gritty sensation and radial calcification is seen in the medulla. On microscopy the calcification is found to be confined to the collecting tubules. It is best demonstrated by x-ray films of the kidneys taken after death. Theoretically it should also be visible in the x-ray films of the abdomen taken during life, and in gross cases this may be possible. Usually, however, the degree of calcification is not sufficient for it to be visualized, especially as the intestines are often full of gas.

Case Reports

The occurrence of the condition in twins is recorded below. They were studied at the Department of Child Health, Welsh National School of Medicine, Cardiff. This is believed to be the first time that the condition has been recorded in two members of one family. One of these twins died of a respiratory infection probably aided by too large a dosage of citrate mixture.

Case 1. Susan P., a twin, was delivered at full term (birth weight 5 lb.). She received cow's milk for the first six weeks, then the feed was changed to artificial dried milk. The child had received orange juice but no codliver oil.

There are five siblings, including a step-sister and the twin sister. None of the other children has had any illnesses in infancy or other relevant diseases, nor have any relatives had anything similar.

Apart from bronchitis at 3 weeks, progress was satisfactory until the age of about 6 months. The baby was first seen at the age of 8 months with a six weeks' history of 'taking feeds badly'. She would not suck from a bottle, but would take out of a cup. The milk was changed from National Dried Milk to cow's milk without any improvement. She was constipated and passed one or two hard motions a day. Urine was voided freely.

On examination the child was a small, pale infant, who appeared dehydrated and had obviously lost weight. On admission her weight was 15 lb. 5 oz. compared with her highest known weight of 18 lb. 6 oz. at the age of 6 months. The abdomen was scaphoid and the liver just palpable. The limbs were hypotonic. Nothing abnormal was detected in the chest or heart. A clinical diagnosis of idiopathic renal acidosis was made.

The following investigations were made before treatment was begun.

The urine was persistently alkaline (*p*H 7·5) and contained some pus cells. On one occasion a few colonies of *Staphylococcus aureus* were grown; two days later, however, another specimen was found to be sterile.

A blood count gave haemoglobin, 12·6 g. (85%); red blood corpuscles, 4·4 m. per ml.; white blood corpuscles, 22,800 per ml. (neutrophils, 65%, lymphocytes, 25%, monocytes, 10%). The blood urea level was 40 mg. per 100 ml.

A radiograph of the chest and abdomen revealed no significant abnormality. The Mantoux test (1:1,000) was negative.

The plasma bicarbonate level was 26 vol. CO_2%, and plasma chloride 750 mg. %.

The child had a temperature of 97° F. on admission, but on the next day it rose to 99° F., falling again to normal on the fourth day. Therapy with the sodium

citrate-citric acid mixture was begun on the evening of the sixth day and one dose of 60 ml. was given. The temperature by that time had risen to 102° F. Two further doses of 60 ml. each were given the next day and the temperature continued to rise to 104° F. and remained between 103° and 104° until the child died. On the seventh day after admission she developed convulsions, nystagmus and a right external rectus palsy. A catheter specimen of urine was normal. Further blood investigations showed a plasma bicarbonate level of 76 vol. CO_2 % and plasma chlorides level of 695 mg. %. Unfortunately this result was not known until the evening, by which time the third dose of citrate mixture had been given. The child's condition continued to deteriorate, convulsions being almost continuous despite 2 ml. of paraldehyde intramuscularly. On the eighth day blood investigations gave a plasma bicarbonate level of 81 vol. CO_2 % and a plasma chloride level of 759 mg. %.

The cerebrospinal fluid showed no abnormality.

The baby was given 5% glucose in water intravenously, intramuscular penicillin, 100,000 units three-hourly, and a total of 3 ml. of paraldehyde intramuscularly. Breathing became very distressed, and the trachea was sucked out under direct vision by Dr. J. Haley, a large quantity of mucopus being removed. Despite this, the child died in the early morning of the ninth day after admission.

NECROPSY. A necropsy was performed by Dr. D. B. Richards.

The right lung contained an area involving the posterior one-third of the upper and lower lobes which was of a uniform greyish-red. The left lung had a similar appearance. Microscopy of these areas revealed extensive bronchopneumonia.

Both kidneys were of normal size, and cut with a gritty sensation. The cortex was normal in appearance, but there were extensive foci of calcification outlining the periphery of the pyramids. On microscopy the calcification was seen to be confined to the collecting tubules.

Case 2. Christine P. was the twin of Susan P. (birth weight 5 lb. 8 oz.).

She was fed on National Dried Milk at first, later on cow's milk. Progress was satisfactory until the age of 7 months. The child then lost her appetite, started to vomit frequently, and became constipated. There was no history of passing abnormal quantities of urine.

On examination the child seemed rather small for her age (weight 16 lb. 8 oz.). There was no gross wasting or dehydration, but an extreme degree of hypotonia was apparent. Nothing abnormal was detected in the heart, lungs, abdomen, or central nervous system.

Before treatment the urine had a *p*H of 7·4. The plasma bicarbonate level was 29 vol. CO_2 % and the plasma chloride level 666 mg. %.

The child was started on 45 ml. per day of the citric acid-citrate mixture, and, after an initial loss, rapidly gained weight. Twenty days later the plasma bicarbonate was 43 vol. CO_2 %. Her general condition had improved and she had lost the hypotonia. Unfortunately she then developed a suppurative otitis media which proved somewhat resistant to treatment. She continued to gain weight well, however, and after a fortnight weighed 18 lb. 10 oz. The plasma bicarbonate level was then 36 vol. CO_2 % and serum chlorides 674 mg. %.

After discharge from hospital the child developed Sonne dysentery and lost weight again. Following this she gained weight well, but was found to be anaemic (haemoglobin 5 g. or 35%). The biochemistry gradually returned to normal, and apart from what appeared to be a febrile convulsion on one occasion she has remained well. She no longer requires the medicine, and appears to be a normal child both clinically and biochemically.

Discussion

It is very regrettable that when Susan P. died it was not appreciated that she was a twin. The other child at that time was apparently normal. It has, therefore, not been possible to prove that they were identical twins. The following factors are significant. They were always regarded as being identical and had to be dressed differently to distinguish them as babies. A photograph taken of the two children together reveals a striking similarity. When seen in hospital Susan had been ill for some weeks and Christine was still well so the resemblance was less obvious.

The causation of idiopathic renal acidosis has been very briefly referred to above. The fact that it can occur in twins indicates that it may be congenital in origin, but there is no evidence so far to suggest that it is a genetically determined condition.

A second point which emerges from consideration of these cases is the danger of overdosage with the citrate mixture; the following formula was used:

Citric acid . . . . 60 g.
Sodium citrate . . . . 100 g.
Water to 1,000 ml.

The initial dose should be about 45 ml. per day and may be increased as required.

The clinical and biochemical findings in Susan P. are very similar to those of a case recorded by Payne (1950). Both children had convulsions due to the profound alkalosis and both showed hyperelectrolytaemia, having a high blood chloride as well as the raised plasma bicarbonate.

Summary

Idiopathic renal acidosis in twins (probably identical) is described. One child developed hyperelectrolytaemia and bronchopneumonia following overdosage with the citrate mixture. The danger of this potent therapeutic weapon is stressed.

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