OXALOSIS

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Oxalosis is a metabolic disturbance manifested by hyperoxaluria and leading to the deposition of calcium oxalate crystals in the parenchyma of the kidneys as well as in many other organs.

Until the end of 1957 only 22 cases of oxalosis had been reported: eight cases in adults and 14 in children. Le Poutre (1925) found calcium oxalate crystals in a renal biopsy taken from a child 4½ years old. Lass (1941) reported a similar finding in a man dying accidentally at the age of 25 years.

Davis, Klingberg and Stowell (1950) described the case of a 12-year-old boy who suffered from nephrolithiasis and died as a result of renal failure. Calcium oxalate crystals were found in the kidneys and in the bones. Chou and Donohue (1952) reported on a 7-year-old boy who suffered from nephrolithiasis and died of renal failure. Calcium oxalate crystals were found scattered throughout the bones, the heart, thymus, spleen and the pituitary gland. These authors were the first to consider the disease as an inborn error of the metabolism of the oxalates. Dunn (1955) termed the disease 'oxalosis', and because he found calcium oxalate crystals in the bone marrow advised diagnosis by sternal puncture. The relation of the disease to primary hyperoxaluria was demonstrated by Newns and Black (1953), by Aponte and Fetter (1954) and later by Archer, Dormer, Scowen and Watts (1957).

We present a case of oxalosis which slightly differs from the other cases reported because of extreme youth and the presence of calcium oxalate crystals in many different organs in addition to those already described.

Case History

A girl, 3 months old, was admitted to hospital because of convulsions lasting a few minutes, accompanied by vomiting. The parents and five other children were all in good health. The patient was born at home, the delivery being normal. Her weight at birth is not known. In addition to breast milk she was given buttermilk (Eledon) from birth. Her weight on admission was 2.9 kg., her temperature was 39° C., her general condition was poor and she was pale and dehydrated. At times she was very restless, and this phase was followed by general convulsions lasting a few minutes. Afterwards the child became apathetic.

Physical examination revealed nothing relevant. The cerebrospinal fluid, which was examined immediately after her admission, was normal in all respects. Haemoglobin was 8.1 g. %, erythrocytes 2,720,000, leucocytes 12,000. The urine contained albumin + + +, leucocytes were 20 per field, erythrocytes 3-7 and there were many calcium oxalate crystals; the pH was 5.8. Urine culture was sterile. Because of the small amount of urine excreted daily (about 20 ml.), the total excretion of calcium, phosphates and oxalates could not be determined.

The blood chemistry on admission showed: urea 178 mg. %, calcium 5.3 mg. per 100 ml. serum, phosphorus 13.4 mg. per 100 ml., alkaline phosphatase 19.4 BU. The CO₂ content was 20 vol. %.

The urea went up within seven days to 206 mg. % and rose to 275 mg. % before death.

The CO₂ content dropped to 14 vol. % after 12 days. Calcium was 3.7 mg. % after 12 days and 4.1 mg. % after 18 days, and phosphorus 14.0 mg. per 100 ml. serum. Potassium on the eighteenth day (one day before death) rose to 28.4 mg. per 100 ml. (7.3 mEq./l.). At the same time sodium values were 290 mg. % (126 mEq./l.) and chlorides 294 mg. % (83 mEq./l.). Total proteins on admission were 5.85 g. %, albumin 4.45 g. %, globulin 1.4 g. %. Electrophoresis of the proteins showed increase of α₂-globulin, and decrease of γ-globulin.

Radiographs of the bones were normal. Intravenous urography was not performed owing to the severely impaired renal function, but a plain radiograph of the abdomen did not show any pathological condition of the kidneys.

During her stay in the hospital the child vomited several times a day and later developed diarrhoea. A stool culture was negative. Treatment included infusions, sedatives and appropriate diet. Her condition deteriorated gradually and she died on the twenty-third day after admission.

Autopsy Findings. Macroscopically the kidneys were small, weighing 10 g. (normal 22 g.); the capsules, which stripped easily, revealed a smooth surface. On cross section the differentiation between cortex and medulla was obvious, the normal ratio being maintained. The pelves were of normal size, shiny and smooth. The ureters were normal and so was the renal pedicle. Three parathyroid glands were detected: two upper and one lower. They were dark brown in colour, the size of a pin head. None of the other organs showed pathological macroscopic findings.

Microscopically most of the tubules in the medulla

and the cortex of the kidneys were dilated and filled with bright yellowish polygonal crystals, arranged in a rosette formation (Fig. 1). The lining epithelium of the tubules

Microscopic examination of the parathyroid glands showed a uniform cellular structure, with no fat seen; many dilated vessels were apparent. The cells contained

FIG. 1.—Kidney. Crystals arranged in rosette formation in dilated renal tubules. H. and E. $\times 320$.

was flat, and, because of the pressure of the dilated full tubules on the unaffected ones, it was impossible to tell which part of the tubules was affected. The glomeruli were normal, free from crystals; so were the pelves and the ureters. The blood vessels of the kidneys were normal.

Crystals, similar to those found in the tubules, were detected in the myocardium, in the lungs, brain, thymus, thyroid, bone and cartilage. In the myocardium (Fig. 2) the crystals were seen in the muscle fibres, and in the lungs they were found in the septa between the alveoli. In the brain (Fig. 3) they were equally dispersed in the white and in the grey matter. Crystals were found also in the cerebellum. In the thyroid gland they were seen within the colloid only, and not in the interstitial tissue. They were also found in the bones and cartilages, especially concentrated at the osteochondral junction (Fig. 4).

FIG. 2.—Heart. Crystals in myocardium. H. and E. $\times 320$.

FIG. 3.—Brain. Crystals in white matter. H. and E. $\times 320$.

round nuclei, surrounded by clear protoplasm, presenting the typical appearance of water clear cells.

Sections of the kidneys were treated with various chemical agents in order to determine the solubility of the crystals. These were found to be soluble in concentrated hydrochloric and in sulphuric acids. In the latter, careful examination revealed needle shaped crystals presumably calcium sulphate crystals. Furthermore, the crystals were found to be insoluble in alcohol, ether, glacial acetic acid, lithium carbonate and ammonium hydroxide. With Von Kossa-reaction they stained black, but did not stain with the alizarin-red-S-stain.

Quantitative analysis for calcium in the kidney showed 188 mg. of calcium per 1 g. of net weight of renal tissue. With polarized light the crystals demonstrated birefringency. The Johnson incineration method gave a positive reaction.

FIG. 4.—Crystals in cartilage and bone. H. and E. $\times 320$.

Discussion

Discussing oxalate metabolism, Jeghers and Murphy (1945) stated that the source of the oxalates may be either exogenous (from food intake) or endogenous. Very little is known of the metabolism of oxalates from endogenous sources. The congenital defect which is supposed to exist in oxalosis is said to be unassociated with calcium metabolism, for it is not always calcium oxalate that is found, but other forms of oxalates. Origin from the Krebs citric acid cycle is not proven. Break-down of ascorbic acid has been suggested as a possible source. Recently Archer *et al.* (1957) emphasized the production of oxalic acid from glycine as a result of the failure to degrade this amino acid normally via glyoxalate to formate and carbon dioxide.

As our patient was fed on breast milk and butter-milk only, an exogenous source of the oxalate could thus be easily ruled out. It is, however, still to be decided whether the deposition of the oxalates is the result of insufficient kidney excretion or of excessive production of oxalates. Archer *et al.* (1957) in a series of examinations of oxalate excretion in the urine, conclude that it does not appear to result from a low renal oxalate threshold, but rather from metabolic over-production. Simkó (1957) suggested that oxalosis is initiated by a lesion of the distal portion of the renal tubuli. It is worth while to note that in our case a marked hypoplasia of the kidneys was found. However, it is impossible to decide in retrospect whether the hypoplasia was primary, causing failure of oxalate excretion, or secondary, caused by the large accumulation of oxalates leading to decreased activity of the kidneys.

We mention the severe metabolic disturbances of calcium, phosphorus and alkaline phosphatase, and the autopsy findings of marked hyperplasia of the parathyroid glands, which may be diagnosed as secondary hyperplasia of the parathyroids due to renal failure. In the case of Hollósi (1957) the clinical manifestations were osteoporosis, renal rickets and osteodystrophy, accompanied by parathyroid hyperplasia. The patients described so far have been between the ages of 4½ months (Carson,

1951) and 57 years (Zollinger and Rosenmund, 1952). In Carson's case the symptoms continued for 10 days and the child died of renal insufficiency. Calcium oxalate crystals were found in the kidneys only. Oxalate crystals in such large quantities and in so many organs as in our case were found only by Chou and Donohue (1952) in a child of 7, and by Hollósi (1957) in a 4½-year-old girl. The fact that the symptoms in our case became manifest as early as the third month led us to think that the metabolic disturbance might have already begun during intra-uterine life. Otherwise it is difficult to imagine such a massive and widespread deposition of crystals within three months of birth. We are also of the opinion that Dunn's (1955) recommendation of sternal puncture as an aid to diagnosis is appropriate. In our case, too, a large number of crystals were found in the sternum. Because several cases have been reported in one family, the urine of our patient's family was examined, but no oxalate crystals were found.

Summary

A case is described of a child, 3 months old, who died of renal failure. Autopsy showed calcium oxalate crystals in kidneys, heart, brain, thyroid, thymus, lungs, bones and cartilage. The accepted views on the aetiology and course of oxalosis are discussed.

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