CASE NOTES

KERATOMALACIA ASSOCIATED WITH ADRENAL HYPOPLASIA IN A DEFECTIVE*

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XEROSIS epithelialis of the conjunctiva forms part of a general symptom resulting from malnutrition, usually a dietary deficiency in vitamin A and carotene which, in its fully-developed form, is characterized by:

- (1) Hypoplasia and metaplasia of the epithelium and mucus membranes, often accompanied by the invasion of the areas by micro-organisms and the production of local infective foci;
- (2) Degenerative changes in the medullated nerves in both the central and peripheral nervous systems.

So far as the eye is concerned, the clinical picture varies from a mild conjunctival epithelial xerosis, sometimes with hemeralopia, to an advanced state of keratomalacia and necrosis of the cornea, with its attendant tendency to hypopyon ulcers and panophthalmitis.

So far as the general condition is concerned, the clinical picture varies from one of very little disturbance to extreme debility, marasmus, and death from pneumonia.

While xerotic changes of this type have been observed from the earliest times, especially in time of war, when malnutrition, famine, fatigue, and debilitating diseases were rife, the first detailed clinical picture was given by Bitot (1863) of Bordeaux.

Since then, xerosis of the conjunctiva in its mildest form has been well recognized as occurring more particularly in children, especially boys, in association with night blindness. The condition is seen in the summer months, and the children need not be conspicuously ill-nourished. Improper diet after the cessation of breast-feeding is a common cause of its appearance, but the lesion also occurs in adults, although more rarely.

During the first years of life, children who are ill-nourished and marasmic and have typical intestinal disorders, may show a much more severe condition characterized by extreme xerosis of the conjunctiva and keratomalacia and necrosis of the cornea.

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After the 10th year of life these gross changes are much rarer, and are usually seen in adults suffering from severe debilitating diseases affecting especially the intestinal tract, such as acute and prolonged diarrhoea or dysentery (Duke-Elder, 1938).

It has also been suggested that there is a noticeable deficiency in serum proteins in this condition (Yap-Kie-Tiong, 1956).

Case Report

A male infant, born in England, the third child of Jamaican parents, was just under 1 year old when admitted to hospital on June 21, 1958.

Family History.—The father was aged 37 and the mother 31; both were apparently healthy. A brother 12 years old, living in Jamaica, a sister 2 years old, and an infant sister were all said to be quite healthy.

The mother had no illness during pregnancy, but had had a fall 2 days before the child's birth and "was in pain for some hours afterwards". The birth was said to have been normal, and the baby was born at full-term and showed no external abnormalities.

The midwife had guessed the infant's weight at 8½ to 9 lb.

There was, as far as was known, no history of mental illness or blindness on either side, and the baby had not been in contact with any infectious disease.

Medical History.—From birth, the child had been very difficult to feed and the mother had tried breast and bottle-feeding, the latter with a big-bored teat as well as the usual size, all with very little success.

On account of this difficulty and the infant's marked physical deterioration, he was twice admitted to the Paediatric Unit of the Royal Hospital, Wolverhampton. The first time was at 5 days old because he refused to feed. He weighed 7 lb. 5 oz. on admission, gained several ounces in hospital, and was discharged, only to be re-admitted 3 weeks later when his weight had dropped to 7 lb. 2 oz.

Examination.—When admitted at the age of one year he was a small, marasmic, microcephalic infant. Although he was nearly one year old he had the appearance of a neglected child of about 2 months old. His weight was 8 lb. and he was 22 inches in length.

The skin was dry and wrinkled, the head was covered with coarse black curly hair, and he was extremely emaciated. The terminal phalanx of the middle finger of the right hand was missing leaving an infected stump. (This, apparently, the baby had chewed off).

The central nervous system, heart, and lungs showed no abnormality.

The abdomen was lax and concave.

The mouth was clear, but the tongue was coated, and the child was edentulous.

He lay apathetically in his cot or in the nurse's arms and did not react to external stimuli of any sort.

He was admitted to hospital as a mental defective; the grade was not assessed as it was not known how much was, or might have been, due to the physical condition.

Treatment.—He was put on a diet of National Dried Milk, one scoop in 1 oz. water with sugar 3i hrly for 24 hrs.

This was increased to three scoops in 3 oz. water plus sugar 3i 2-hrly for 3 days.

On the 5th day he was given four scoops National Dried Milk in 4 oz. water plus sugar 3i 3-hrly for 24 hrs, and at the end of the first week he was receiving five scoops National Dried Milk in 6½ oz. water with sugar 3ii 3-hrly during the day, and 4-hrly at night. He was also having Penidural.

During the first week he was also put on cod-liver oil and rose-hip syrup.

On June 28, his weight was 8 lb. 9 oz. Bengers $\bar{3}i$ was added to all feeds, and Farex $\bar{3}i$ was added to the 10-a.m. feed.

During this time, he was still extremely difficult to feed, and took, at times, over an hour to complete one feed.

On July 2, his weight was 9 lb. 4 oz., and on July 3, the blood picture was estimated as follows:

Haemoglobin 75 per cent.; white blood cells 10,400 per cm.; polymorphs 41, leucocytes 55, monocytes 1, eosinophils 3, basophils 0.

The red blood cells showed slight hypochromia.

He was put on ferrous sulphate 1 gr. three times daily and ascorbic acid 50 mg. three times daily.

Progress.—On July 7, his weight was 9 lb. 14 oz. and he was taking (still very reluctantly) Farex $\bar{3}iii$ in half-milk mixture at 10 a.m. and 6 p.m., plus vegetable broth $\bar{3}iii$ and sieved prunes $\bar{3}iii$ with sterile water.

On this date, a slight stain of ? blood was noticed on his hands and face, but the source was not found until the following day when a tiny ulcer was apparent on the tip of the tongue.

As he was, or appeared to be, a placid child, the fact that he rarely cried was accepted as part of his make-up. The tear ducts appeared to be patent, but there were no tears.

On July 11 there was a loss of 4 oz. in weight and it was reported that he had been extremely difficult to feed as he blew out the food when it was placed in his mouth; he also had attacks of wind but he did not vomit and the stools were normal. On this date it was noticed that both eyes looked cloudy; he tried to put his fingers in his eyes and this had to be restrained by wrapping him in a shawl.

As the visiting consultant ophthalmologist Mr. H. Campbell Orr, was expected on July 13, the eyes were left until that date, but in the 2 days interval they showed very marked deterioration.

Ophthalmological Examination.—Keratomalacia was seen in both eyes with extensive ulceration of chronic type due to malnutrition.

Treatment.—Gutt. atropine 1 per cent. twice daily, Occ. Predsol. twice daily, and Ol. Morr. one drop each eye twice daily.

Progress.—After this the baby had one attack of vomiting, but his weight was satisfactory as he had gained 7 oz. between July 14 and 21, and then weighed 10 lb. 11 oz.

He still attempted to push his fingers into both eyes if at all possible, and it was noticed that this apparently caused no pain or discomfort.

On July 23, as the eye condition was obviously deteriorating even further, he was admitted to the Wolverhampton Eye Hospital, and remained there for 8 days. On July 31 he was transferred to the Paediatric Unit, Royal Hospital, Wolverhampton, and on August 1 came back to us. In this short period he had lost some of his hair and his weight had gone down to 10 lb. 4 oz.

The treatment ordered for the eyes was gutt. atropine 0.5 per cent. twice daily, gutt. ol. morrh. twice daily, and penicillin 15,000 units 3-hrly.

About this time he had isolated attacks of vomiting, and was still difficult to feed, but the stools were reported as normal, and he started to gain weight again.

Mr. H. Campbell Orr ordered occ. neomycin and gutt. ol. morrh. but the prognosis was considered to be quite hopeless.

On August 11, ulcers appeared at the corners of the mouth, but the weight had risen to 11 lb. 2 oz. On August 13 a loss of 4 oz. was noted, and he was put on Penidural again.

On August 13, the right central and left lateral incisors were apparent, he took his food

more satisfactorily for some days, and the mouth ulcers were clearing slowly. The lower central incisors were now about to break through.

An eye swab taken at this period showed "no growth", and a mouth swab showed "Scanty *Staph. saprophyticus* only". This organism was sensitive to penicillin, chloramphenicol, and novobiocin + + +, and to erythromycin and aureomycin - + +.

By August 25, his weight had gradually risen to 12 lb. 7 oz.; between that date and September 11, it varied, and he gained and lost from day to day, until on September 12 he weighed only 12 lb. 4 oz. There was little change in the eye condition and the corneae were glazed and apparently insensitive to touch. On September 12, a hypopyon ulcer appeared on the left cornea, and by the next morning the left cornea had perforated. He was again transferred to the Wolverhampton Eye Hospital, and the notes of admission state that the right cornea was likewise perforated and that there was excoriation of the corners of the mouth.

He was returned to this hospital on September 20, and the following treatment was ordered: gutt. atropine 1 per cent., occ. sulphacetamide 6 per cent., vitamin A and D 100,000 units daily intramuscularly, and oral penicillin $\frac{1}{2}$ teaspoon 6-hrly.

He now weighed 10 lb. 9 oz. and there were ulcers at both sides of the mouth.

Between September 20 and October 7, although the eye condition was hopeless, he took his diet more satisfactorily and his weight rose to 13 lb. 3 oz.

On October 9 a tiny swelling was noticed on the left temple; this was not investigated but looked and felt like a small cyst.

On October 12 he developed a "running" nose, which developed by the next morning into broncho-pneumonia in spite of initial treatment with Penidural and a mild expectorant mixture.

On October 14, he had what was described as a convulsion, and the temperature registered was 107°F. After this he had an attack of profuse sweating and the pulse was extremely rapid, but there was little change in the chest condition.

Early in the morning of October 15 his condition deteriorated rapidly, and he died within a short time.

Post-mortem Report (Dr. D. HEWSPEAR)

External Examination

Apparent age	Less than stated (15 months)
Height	27 inches
Rigor mortis	Moderate
Nourishment	Fair

A Negro child showing no obvious deformities, and no external evidence of injury or disease.

Internal Examination

Skull	Normal
Brain and meninges	Marked congestion of whole surface
Thoracic cavity	Air passages clear
	Pleura showed several petechiae
	Lungs showed terminal oedema
	Two small septic emboli noticed in lungs
	Pericarium contained excess fluid
	Myocardium showed several septic spots over surface, the contained blood was dark coloured
	No congenital abnormalities noted

Stomach and contents, peritoneum, intestine, and mesenteric glands	Normal
Liver	Moderate fatty degeneration
Pancreas	Normal
Spleen	Rather soft and of the septic type
Adrenals	Both very small, about half normal size. (The pituitary gland was smaller than normal)
Kidneys and ureters, bladder, urine, and generative organs	Normal
All other organs	Healthy

Cause of Death

- (1) Septicaemia (probably of the virus type).
- (2) Adrenal hypoplasia and mental deficiency.

Discussion

Cases of adrenal hypoplasia showing much in common with our infant and mainly of the male sex have been reported in the literature.

Provenzano (1950) reported a case of a male infant of 11 hours old and weighing 7lb. 1½ oz., who became listless with a weak cry and showed diminished response to stimuli. The sucking reflex was inadequate. There was marked loss of weight with dehydration. After treatment with adrenocortical hormones there was marked improvement. This patient died after the therapy had been withdrawn to establish the aetiological factor. There was definite pigmentation of the skin, and the *post-mortem* examination showed marked hypoplasia of the adrenal glands.

Sikl (1948) reported the case of a male infant who died at the age of 33 days. He was full-term and healthy but difficult as regards taking the breast. The skin showed discolouration at 3 weeks. Asthenia was not conspicuous. After rapid decline and death, a *post-mortem* examination showed very hypoplastic adrenals.

Geffert, Spencer, and Richmond (1950) reported the case of a male infant who died at the age of 20 months. He was admitted to hospital because of feeding problems, but after some months the case was diagnosed as one of adrenal insufficiency. At the age of 4 weeks he had "lost consciousness for 15 minutes". He was pale and undernourished but not acutely ill. He showed pigmentation at 8 weeks old. At the age of 13 weeks, after severe generalized convulsions, he was put on 5 cc. adrenalcortical extract (Eschaten P. D. and Co.) 3-hrly. He was also given daily doses of 5 mg. desoxycorticosterone acetate subcutaneously and 200 ml. normal saline orally. After some months the desoxycorticosterone was discontinued, and 6 months later he died. A *post-mortem* examination revealed small adrenal glands.

Mosier (1956) reported twin sibs; one child died when only 25 hours old and the *post-mortem* examination showed marked adrenal and pituitary hypoplasia.

Summary

A male Negro infant nearly 12 months old had a history of difficulty in feeding since birth because of an inadequate sucking reflex.

The development of keratomalacia was due to lack of essential vitamins particularly in the early months of life.

The rapid development of an acute chest infection after a simple catarrhal condition which showed no response to chemotherapy, led to death after convulsions and hyperpyrexia in 62 hours.

At a *post-mortem* examination the adrenal glands were found to be only half the normal size.

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