PENDRED'S SYNDROME IN SOUTH AFRICAN BANTU BROTHERS

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In 1896, Vaughan Pendred[1] reported the association of goitre and deaf-mutism in 2 female siblings of an Irish family. Brain[2] described 5 families with 12 cases of simple goitre associated with congenital deaf-mutism; he suggested a recessive mode of inheritance for this condition. It was not until 1958 that the metabolic defect in thyroxine synthesis was identified when Morgans and Trotter[3] found that, following the administration of a dose of ^{131}I, a proportion of the trapped ^{131}I was discharged from the thyroid gland by the subsequent administration of potassium perchlorate. This finding suggested a partial defect in the organic binding of iodine. Despite this enzyme defect, most of the patients are euthyroid. Fraser *et al.*[4] studied 18 families with 28 affected subjects and showed the deafness to be high-tone perceptive in type, the mode of inheritance simple recessive in nature and that ^{131}I in the thyroid was partly discharged by potassium perchlorate in all their cases. Recently Fraser[5] has presented a study of 207 families. He mentions that Pendred's syndrome has been reported among persons originating from the British Isles, Germany, Belgium, Holland, France, Italy, Greece, Sweden, Denmark, Poland, the Lebanon, the USA and Canada. Three Indian children described by Fraser represent the first report of this syndrome in non-White people.

We therefore thought it of interest to record the occurrence of Pendred's syndrome in 2 brothers, who are South African Bantu subjects.

CASE REPORTS

Case 1

T.M., a Bantu male aged 7 years, was admitted because of a swelling in the neck of a week's duration; he had been deaf and dumb since birth. His appetite was good and he had no pain or pressure symptoms that could be ascribed to the goitre. He did not come from an endemic goitre area.

Examination showed a well-nourished child with a large diffuse goitre, the right lobe being larger than the left. There was a systolic bruit over the gland. The heart rate was 80/min. and the blood pressure was 110/80 mm.Hg. There was no clinical evidence of hyper- or hypothyroidism. The height was 51 in. (129·5 cm.), which was at the 90th percentile, and the weight was 64 lb. (29 kg.), also at the 90th percentile.[6]

The following investigations were carried out: Mantoux test —negative; mumps complement-fixation test—negative on 2

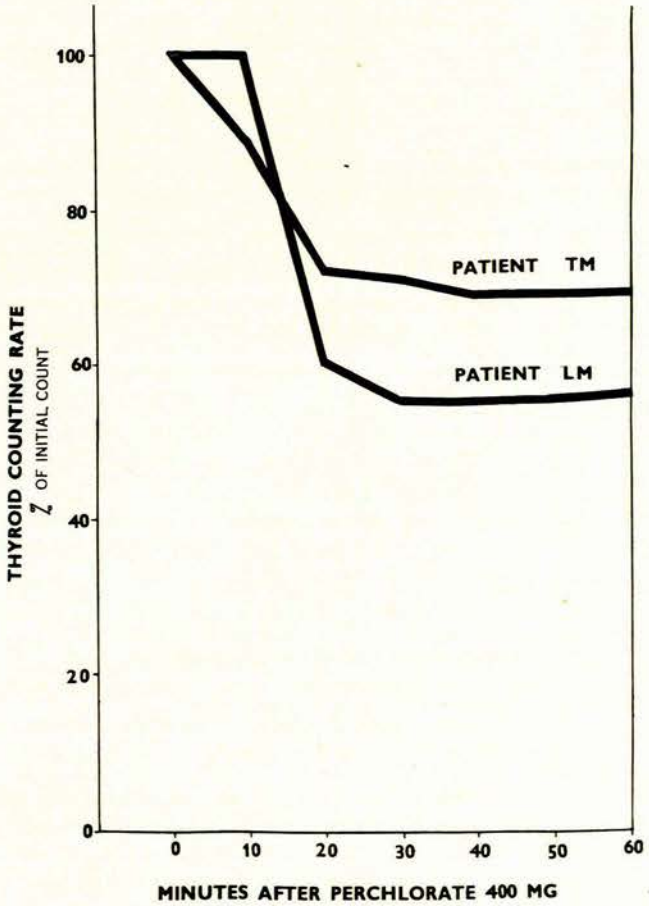

Fig. 1. Cases 1 and 2, potassium perchlorate discharge test after administration of ^{131}I.

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occasions; bone age—8 - 9 years as indicated by X-ray films of the wrist and elbows. Audiometry showed a bilateral high-tone deafness, slightly worse on the left side. The 4-hour ^{131}I-uptake was 50%. Thirty minutes after the administration of potassium perchlorate the count over the thyroid gland had fallen to 70% of the 4-hour level (Fig. 1). ^{131}I-labelled diiodotyrosine was administered intravenously, and chromatographic analysis of the urine subsequently collected showed that none of the diiodotyrosine was present in the urine, the radioactivity present being entirely in the form of inorganic iodine, thus indicating that there was no defect in de-iodination of iodotyrosines. The protein-bound iodine on admission was 3·8 μg.

TABLE I. PBI AND CHOLESTEROL LEVELS IN THE BLOOD OF CASE 1

Date	*4/10/1963*	*25/10/1963*	*12/12/1963*	*9/3/1964*
PBI μg./100 ml.	3·8	6·8	6·0	9·5
Cholesterol mg./100 ml.	190	190	185	190

which increased on ward diet, as shown in Table I. During this time, it was noted that the goitre had diminished in size, though it remained quite large. Measurement of the neck circumference ranged between 12 and and 12¼ in.

Treatment with l-thyroxine sodium was commenced at the beginning of January 1964, and the dose was increased to 0·1 mg. twice daily by March 1964. The goitre steadily decreased in size and a neck measurement in May 1965 was 10⅞ in.

Family history. The father was 73 years old and in good health. Two children were born of his first marriage, both males, now aged 25 and 21 years respectively; they are both normal. His second wife had 4 children: one male died at the age of 9 months, and a son aged 14 years is alive whose hearing is intact. Another son aged 11 years was attending a school for the deaf and dumb. The proband was the youngest member of the family. As a result of this history, arrangements were made to investigate the patient's deaf and dumb brother.

Case 2

L.M. was a Bantu male aged 11 years, weighing 76 lb. (34·5 kg.), and with a height of 56 in. (148 cm.), both measurements being at the 50th percentile. He was deaf and dumb and his nutritional status was satisfactory. The pulse rate was 72/min. and the blood pressure was 120/80 mm.Hg. There was a diffuse enlargement of the thyroid gland with the right lobe more prominent than the left. The over-all size of the goitre was less than that of his brother. There were no clinical signs of hyper- or hypothyroidism.

The following investigations were done: Mantoux test was negative; X-ray of the chest was within normal limits; the bone age was 10 - 12 years as indicated by X-ray films of the elbow. The haemoglobin was 13·7 G/100 ml. The leucocyte count was 6,000/cu.mm. and the platelets were normal. The serum proteins were 7·8 G/100 ml., of which 4·3 G was albumin. The protein-bound iodine was 6·3 μg./100 ml. and the blood cholesterol 190 mg./100 ml.

Audiometry demonstrated a bilateral perceptive high-tone deafness, the left ear being more severely affected than the right. The 24-hour ^{131}I-uptake was 34%. Subsequently the ^{131}I-uptake at 1 hr. was found to be 18% and 30 min. after the administration of potassium perchlorate the radioactivity over the thyroid had fallen to 55% of the 1-hr. value (Fig. 1). A scintigram showed diffuse uptake over the thyroid gland.

Treatment commenced with l-thyroxine sodium in a dose of 0·3 mg. daily. The neck circumference was 12¼ in. on admission and 12¼ in. 1 year after the commencement of therapy.

DISCUSSION

These 2 cases fulfil the criteria for the diagnosis of Pendred's syndrome, namely, the triad of goitre, high-tone perceptive deafness and a partial discharge of radio-iodine from the thyroid gland after the administration of potassium perchlorate. Both patients were euthyroid and this has been the case with the vast majority of reported cases. However, a few children have presented in early life as goitrous cretins.[5] More commonly, the goitre appears in middle childhood and even later in the case of males.

As a result of the partial block in thyroxine synthesis, it is thought that low blood levels of thyroxine stimulate the production of thyroid-stimulating hormone (TSH) by the anterior pituitary, thus inducing thyroid hyperplasia and the production of a goitre. This constant stimulation results in an extremely pleomorphic histological change in the thyroid gland, which has been interpreted by some authors as evidence of malignancy.[7] However, Fraser[5] is of the opinion that malignant change probably does not occur in these cases.

The use of thyroxine in treatment is aimed at suppression of the excessive TSH production in the hope of reducing the size of the goitre.[4] A striking response was obtained in the younger of our 2 patients, but not in his elder brother.

The recessive mode of inheritance of this condition is supported by the family history obtained. The first wife with 2 normal children was presumably not a carrier of the necessary gene defect, while the second wife and the father must be heterozygous carriers for 2 instances of Pendred's syndrome to have appeared among their 4 children.

Pendred's syndrome is not of infrequent occurrence in institutions for the deaf. Thould and Scowen[8] found an incidence of approximately 2% among children examined at 15 such schools. Fraser[5] found an incidence of 5·6% at normal and specialized schools for the deaf. This condition is, therefore, a numerically important cause of congenital deafness.

Deaf-mutism together with other forms of defective physical and mental development are known to occur with endemic goitre;[9] in these cases, however, there is an absence of thyroidal discharge after potassium perchlorate.[10] Pendred's syndrome has also been reported from an endemic goitre area in the Lebanon.[11]

SUMMARY

Two Bantu brothers with the classical features of Pendred's syndrome are reported from South Africa. These are thought to be the first such cases described from the African continent.

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