THE VALUE OF RADIOIODINE (I^{131}) IN JUVENILE MYXOEDEMA DUE TO ECTOPIC THYROID TISSUE

BY

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(RECEIVED FOR PUBLICATION JUNE 24, 1954)

The value of radioactive iodine (I^{131}) in the investigation of disorders of the thyroid gland is now well recognized (Pochin, 1950; Myant, 1952; Wayne, 1954). While I^{131} has been used more frequently in adults than in children, its application to the study of abnormalities of thyroid function has added considerably to our understanding of the varied aetiology and pathogenesis of hypothyroidism in childhood (Hamilton, Soley, Reilly and Eichorn, 1943; Lerman, Jones and Calkins, 1946; Stanbury and Hedge, 1950; Stanbury, 1951; Hubble, 1953; McGirr and Hutchison, 1953; Silverman and Wilkins, 1953; Hutchison and McGirr, 1954).

We present here the results of I^{131} tests in two children which demonstrate the value of these tests in the diagnosis of ectopic thyroid tissue associated with juvenile myxoedema.

The techniques used in the I^{131} investigations have been described elsewhere (McGirr and Hutchison, 1953).

Case Records

Case 1. G.A., a girl, aged 13 years, was first seen by us on October 15, 1953. The second child of three, she was born spontaneously after a normal pregnancy. Her birth weight was 10 lb. She was breast fed and thrived. She sat up at the age of 6 months, walked at 1 year, and spoke single words at 1 year. Her early childhood was uneventful apart from measles, chicken-pox, and an operation for squint.

At the age of 11 years she developed tonsillitis and at that time a swelling was noticed under her chin in the mid-line. This was subsequently diagnosed as a thyroglossal cyst and removed in January, 1953. The specimen was reported histologically to be active thyroid tissue. The child's parents had noted that after the operation her speech had become thick and slow, that her hair had started to fall out, and she had become slower in her movements.

On examination the girl was found to be dwarfed (height 127 cm.) and underweight (weight 30.6 kg.). She was typically myxoedematous with coarse features, large tongue, supraclavicular pads, dry scanty hair, and coarse, cold skin. Mentally, however, she was of at least

average intelligence. There was a healed scar on the neck at the level of the hyoid bone. The thyroid gland was not palpable. The plasma cholesterol level was 593 mg. per 100 ml. The electrocardiograph showed low voltage with inverted T3. Radiographs of the bones showed no abnormality. The basal metabolic rate was -32%.

RADIOACTIVE IODINE TESTS. On October 26, 1953, she was given by mouth 72 μ c. of carrier-free I^{131} . The accumulation of I^{131} in the neck was negligible, amounting to only 7% of the dose at 24 hours, and 3% at 48 hours. Scanning of the neck by means of a Geiger-Müller counter (G.E.C. type G.M. 4) showed that such scanty thyroid tissue as was present was confined to the area of the operation scar (Fig. 1). The urine excretion values

FIG. 1.—G.A. Half-minute counts recorded with G.M. counter placed in contact with skin. Time after dose, 96 hours. Thigh count 10. Interrupted line indicates site of skin scar.

were 23.3% of the dose of I^{131} for the period zero to six hours; 12.2% for the period six to 24 hours; 20.8% for the period 24 to 48 hours. The total plasma radioactivity 48 hours after the dose of I^{131} was 0.89% of the dose per litre of plasma. The protein-bound fraction was 0.12% of the dose per litre; the butanol-extractable I^{131} was 0.10% of the dose per litre.

TREATMENT AND PROGRESS. On dry thyroid, gr. 1 daily, the girl has completely lost her myxoedematous features. Mentally and physically she is more active and in the first five months after starting treatment she has grown 5 cm. in height.

Case 2. S.M.J., a girl, aged 7½ years, was referred to us on November 30, 1953, because of failure to grow. An only child, she was born spontaneously after a normal pregnancy. Her birth weight was 7 lb. 14 oz. She was breast fed and thrived. She walked and spoke single words about the age of 15 months but did not cut her first tooth until the age of 16 months. She had always been constipated. Within a year of going to school at the age of 5 years she had measles, mumps and chicken-pox. She had done well at school and was in the normal class for her age.

Her parents had become increasingly concerned by

FIG. 2.—Photograph of S.M.J. illustrating dwarfism and somewhat infantile proportions in contrast with control of same age.

FIG. 3.—S.M.J. Half-minute counts recorded with G.M. counter placed in contact with skin. Time after dose, 24 hours. Thigh count 9.

her failure to grow since she was 3 years of age, and recently her class-mates had begun to tease her about her small stature.

On examination it was apparent that the child was dwarfed (height 104 cm.) and underweight (weight 17.68 kg.). Mentally she was above average intelligence. She had rather a dry, cold skin, a small umbilical hernia, showed a tendency to supraclavicular pad formation, but otherwise did not present the characteristic appearances of myxoedema (Fig. 2). The thyroid gland was not palpable in the normal position or elsewhere. The tongue looked normal even when examined with a laryngeal mirror. The blood cholesterol level was 183 mg. per 100 ml. The electrocardiograph showed low voltage in the three standard leads. Radiographs of the bones showed the ossification of a child at the age of 3 years.

RADIOACTIVE IODINE TESTS. On December 15, 1953, she was given by mouth 40 μ c. of carrier-free I^{131} . The accumulation of I^{131} in the neck was 30% of the dose at 24 hours. Scanning of the neck by means of a Geiger-Müller counter showed that there was no thyroid tissue in the normal site, and that the only thyroid tissue was in the region of the base of the tongue, just above the hyoid bone (Fig. 3). The urine excretion values were 20.0% of the dose of I^{131} for the period zero to six hours; 22.5% for the period six to 24 hours; 6.4% for the period 24 to 48 hours. The total plasma radioactivity 48 hours after the dose of I^{131} was 0.84% of the dose per litre of plasma. The protein-bound iodine fraction was 0.36% of the dose per litre, and the butanol-extractable I^{131} 0.28% of the dose per litre.

TREATMENT AND PROGRESS. There has been a striking improvement in the child's health, mental and physical, on dry thyroid gr. 2 daily. Her constipation has been completely corrected and in the first four months after starting treatment she has grown 5.2 cm. in height.

Discussion

Radioactive iodine has been used previously to confirm the diagnosis of ectopic thyroid tissue (Feitelberg, Kaunitz, Wasserman and Yohalem, 1948; Nachman, Crawford and Bigger, 1949; Crispell and Parson, 1950; Schilling, Karr and Hursh, 1950; Sicher, 1953). In all of the cases cited by these authors, however, the ectopic tissue, which was lingual, was producing local symptoms, such as swelling at the back of the tongue and difficulty in swallowing, and the diagnosis had already been made on clinical grounds alone. As far as we know our second case is the first patient in whom the diagnosis of ectopic thyroid has been determined by I^{131} tests alone and in the absence of local signs and symptoms.

Neither of these two children had thyroid tissue in the normal site. They were dependent for their thyroid hormone on the activity of the thyroid tissue at the base of the tongue. For a time both children had developed normally and it may be assumed that the thyroid hormone produced had been adequate for their needs. Ultimately, however, the body's demands outgrew the productive capacity of the available thyroid tissue, and signs of hypothyroidism appeared. The existence of a hypothyroid state in Case 1 even before operation is suggested by the degree of dwarfing found only nine months later. In this patient the ectopic thyroid tissue had visibly enlarged, and was removed under the erroneous belief that it was a thyroglossal cyst. It is probable that this visible enlargement had occurred because of excessive stimulation by thyrotrophin produced in response to a state of hypothyroidism. Nevertheless, the enlargement had failed to compensate for the fundamental lack of tissue and to supply enough thyroid hormone. Removal by operation of virtually all the thyroid tissue available to the patient had resulted in the development of the typical clinical features of myxoedema. In the absence of local symptoms the ectopic thyroid tissue might have been better left alone, and it should be possible in future to avoid such mistakes in diagnosis by the application of radioactive iodine tests to all mid-line swellings of the neck. In S.M.J., who was undoubtedly hypothyroid but without the gross features of myxoedema, the ectopic thyroid tissue had not become palpably enlarged by the time she was first seen.

In hypothyroidism protein-bound I^{131} in the plasma is usually negligible. It came, therefore, as a surprise to find that 48 hours after the ingestion of I^{131} by these patients there should be measurable amounts of protein-bound I^{131} in their plasma, namely, 0.12% and 0.36% of the dose per litre in G.A. and S.M.J. respectively. The finding that 0.10% and 0.28% of the dose per litre respectively were extractable by butyl alcohol, and not re-extractable by 5% Na_2CO_3 in 4N NaOH, suggests that the protein-bound I^{131} was mainly in the form of thyroxine or a thyroxine-like substance.

Blom and Terpstra (1953) have reported values for protein-bound I^{131} of 0.43% and 0.19% per litre at 48 hours in two patients who had become hypothyroid following subtotal thyroidectomy for thyrotoxicosis, and whose serum protein-bound I^{127} was low, namely, 1.3 $\mu\text{g. \%}$ in each patient. An attractive explanation of the appreciable amounts of protein-bound I^{131} found in such hypothyroid patients has been put forward by Riggs (1952), Blom and Terpstra (1953) and Wayne (1954) to the effect that scanty but very active residual foci of thyroid tissue, under intense stimulation with thyrotrophin, and with no storage capacity for organically bound iodine, are working to the maximum of a diminished capacity to meet the body's needs for thyroid hormone, and are turning over the iodine presented to them so rapidly that a relatively large proportion of the thyroid hormone molecules produced and released into the circulation contains radioactive atoms. Unfortunately, in our patients we were not able to estimate the levels of protein-bound I^{127} or to establish by chromatography that the thyroid hormone and not a premature thyroxine-like compound was being formed, and so we were unable to confirm the correctness of the hypothesis outlined above in relation to them, although obviously it would fit the facts of both cases.

Conclusions

Consideration of all the features of these two patients lends support to the opinion that some cases of childhood hypothyroidism may result from an insufficiency of thyroid hormone, which is relative and progressive rather than absolute (Hubble, 1953). Such a quantitative deficiency may arise, as in our patients who had no thyroid tissue in the normal site, from the ultimate failure of ectopic thyroid tissue to synthesize sufficient thyroid hormone for the body's needs.

Our experience in children suggests that the protein-bound I^{131} which may occur in hypothyroidism may arise in different ways. The

hypothesis discussed above, which envisages the rapid production of inadequate amounts of hormone with an unusually large number of its molecules labelled with I^{131} , affords a probable explanation of the appreciable amounts of I^{131} found in hypothyroid patients with scanty thyroid tissue. The high levels of protein-bound I^{131} , which we have previously reported in non-endemic goitrous cretins, appear to require a different explanation and to be due to an intrinsic defect in the synthesis of the thyroid hormone (Hutchison and McGirr, 1954).

Summary

The clinical features of hypothyroidism in two children, who were investigated with I^{131} , are presented.

The I^{131} studies indicated the absence of thyroid tissue in the normal site, and revealed that the only thyroid tissue was situated above the hyoid bone at the base of the tongue.

The value of scanning the neck for I^{131} accumulation in patients with mid-line neck swellings and in unexplained cases of juvenile myxoedema is discussed.

A probable explanation of the presence of appreciable amounts of protein-bound I^{131} in hypothyroid patients with scanty thyroid tissue is considered.

Thanks are due to the Board of Management, Glasgow Royal Infirmary, and the Rankin Fund, Glasgow University, for defraying the expenses of the radioiodine studies.

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