Case Report

GRAVES' DISEASE IN A 5-YEAR-OLD CHILD

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Graves' disease in childhood and adolescence is still regarded as a rarity outside the USA, from where the only large series have originated.[1-3] To our knowledge, only neonatal Graves' disease, an equally rare but fundamentally different disorder, has been described in the South African literature.[4]

This fact, coupled with problems of therapy unique to this age-group, prompts reporting of a single case.

Case Report

Two weeks following tonsillectomy in May 1965, J.M., a 5-year-old White female, became increasingly irritable, fidgety and tremulous and began to sweat excessively. The right eye became prominent, the weight dropped, and the appetite was poor. Diarrhoea was not a feature. The mother noticed a period of rapid growth preceding the onset of these symptoms.

Examination revealed a tall child (height 45 inches), who was thin (weight 35 lb.), hyperactive and fidgety. A mild right-sided proptosis was noted, as was a tachycardia of 160 beats/min. and a diffuse, firm goitre (Fig. 1).

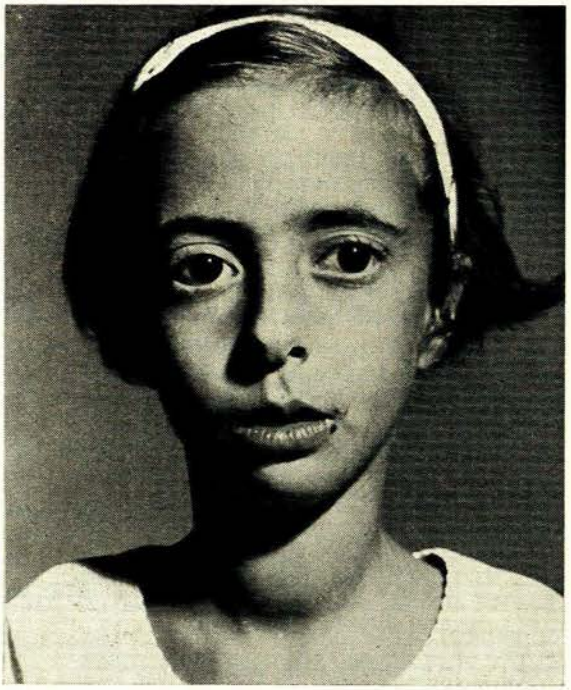

Fig. 1. Graves' disease in a 5-year-old child. Note the goitre and right proptosis.

Neck uptakes of tracer doses of ^{131}I were 94% and 94% at 6 and 24 hours respectively (upper limit of normal in our laboratories 40% and 50%). Red blood cell uptake of triiodothyronine (T3) was 46% (normal 13 - 19%) and serum protein-bound iodine (PBI) was 18·6 μg./100 ml. plasma (normal 4 - 9 μg.). Radiologic estimation of bone age was 7 years (Fig. 2).

Thus far she has been on methimazole therapy (20 mg./day) for 7 months and has improved progressively but very slowly. She has gained 9 lb. in weight, is less irritable and concentrates better at school. However, the pulse rate is still 110/min., the thyroid remains enlarged and a further 2¼ inches of linear growth has occurred. Exophthalmos, however, has regressed.

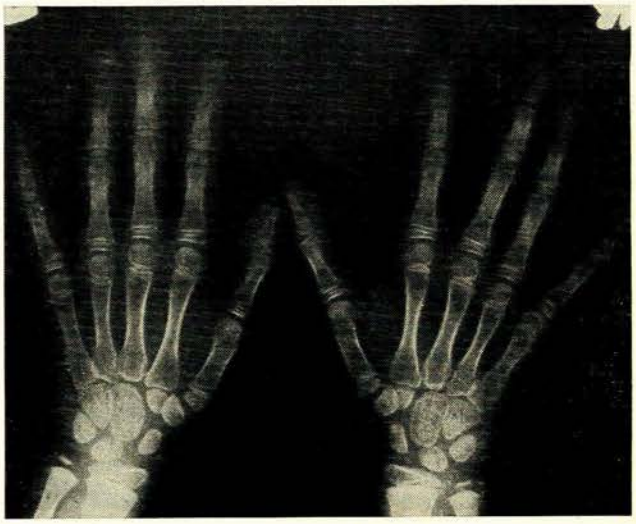

Fig. 2. Bone age estimated at 7 years (Pyle's Atlas) in a 5-year-old thyrotoxic subject.

DISCUSSION

Recent reviews[1,2] emphasize the clinical rarity of Graves' disease in childhood. Even rarer is its occurrence under the age of 5 years. Only 9 of 70 childhood cases reported by Saxena *et al.*[2] fell into this group.

The full-blown clinical picture resembles the adult disorder. However, early symptoms may be regarded as psychosomatic in origin, and the diagnosis is often missed until the disease is advanced. It is disturbing to note that the interval between the onset of symptoms and diagnosis exceeded one year in 10 of 33 cases recently reviewed.[5] A growth spurt is often associated with the disorder, and affected children are usually very tall with an advanced epiphyseal bone age. Occasionally they develop puberty precociously. Choreiform jerks are more common than the classical fine tremor. Diarrhoea is less manifest than in adulthood. Finally, psychic or other trauma appears to be a precipitating factor in a high percentage of cases.[2] The trauma of tonsillectomy might be incriminated in the case reviewed.

Fifty percent of children have family members suffering from thyroid disease,[2] raising the suspicion of genetic transmission of the tendency to develop the disorder. Ingbar *et al.*[6] found elevated ^{131}I uptakes in 22% of relatives, while Saxena[7] showed that of 11 thyrotoxic children with positive tanned red cell agglutination tests, 10 had a parent with a positive result. He suggested the possible importance of the genetic transmission of thyroglobulin antibodies in the pathogenesis of childhood thyrotoxicosis.

Regarding investigations, the PBI appears to be the most reliable, though the RBC uptake of T3 and neck uptake of ^{131}I are useful in following the progress of the disease. The long-acting thyroid stimulator (LATS) has been found in 3 of 17 cases,[2] an incidence distinctly lower than that found in adult Graves' disease where it approaches 60 - 75%.[8,9]

Neonatal thyrotoxicosis is a disorder with an entirely different pathogenesis. It is self-limiting and is caused by the placental transfer of LATS, a potent thyrotrophic substance, from an actively or recently thyrotoxic mother. Its course is limited by the temporary nature of circulating LATS in the newborn. As LATS activity diminishes spontaneously over 4 - 8 weeks, so does that of the thyrotoxicosis.

TREATMENT

In principle, thyrotoxicosis is treated along 3 main lines; antithyroid medication, partial thyroidectomy, or ^{131}I ablation.

In the adult, antithyroid medication is largely used to render the subject euthyroid before surgery. Because of the necessity for its prolonged use and a high relapse rate, it is rarely used as definitive treatment except in young females with very mild hyperthyroidism, in some pregnant thyrotoxics and in children; and even in the latter instance, its use is contentious. Some authorities regard this as the method of choice,[5] but it may have to be given for up to 4 years, and then only about 50% of patients will remit permanently.[2,3,10] The risk of the usual side-effects is ever present. It is however inexpensive and non-traumatic, an important consideration in childhood.

Partial thyroidectomy is the usual definitive treatment of adult Graves' disease under the age of 35 or 40 years. Its use is now standard and followed by a low rate of complication, though authorities are questioning the possible high incidence of subclinical hypoparathyroidism.[11] In childhood, results of surgery are much less uniform. Some report an 80% cure rate with negligible complications,[3] while others mention a 25% incidence of myxoedema.[10] Saxena *et al.*[2] find difficulty in achieving a compromise between a moderately extensive operation (leaving 4 - 5 G thyroid) with no complications but a high relapse rate on the one hand, and more extensive surgery (leaving 1 G thyroid) and 100% cure, but a high incidence of hypothyroidism and hypoparathyroidism, on the other.

^{131}I in ablative doses has found a permanent place in the treatment of thyrotoxic patients over the age of 35 - 40 years. However, the rising long-term incidence of myxoedema,[3,12] currently estimated at 30% 10 years after completion of therapy,[13] is causing some concern. In childhood there is much greater uncertainty regarding its use. Sheline *et al.*[14] feel nodule formation to be a side-effect, though others[15] are less certain of the correlation. A few cases of thyroid carcinoma[3] and leukaemia have been reported, but a statistical association is far from proven. No congenital anomalies in offspring of persons who have received ^{131}I therapeutically in childhood have been noted.[2] Though this is a simple, untraumatic and effective form of treatment, it is best avoided in childhood at present in view of the prevailing uncertainties mentioned above.

We favour medical treatment initially, and methimazole has been used in this case. This should be continued for 18 months. If relapse occurs on withdrawal of the drug, surgery should be considered.

SUMMARY

A case of Graves' disease in a 5-year-old child is reported. Diagnosis may present considerable initial difficulty, and a delay of up to a year from the onset of symptoms is not uncommon. Therapy is largely unsatisfactory compared to the adult disease—all forms have disadvantages. Long-term antithyroid drug treatment is favoured, followed by surgery if the disease relapses after withdrawal.

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