

HYPERTHYROIDISM IN A PAIR OF IDENTICAL TWINS

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SYNOPSIS

Hyperthyroidism in identical twins is very uncommon. The first local pair of Chinese female twins with thyrotoxicosis are here reported. The literature, as regards its rarity, is briefly reviewed.

INTRODUCTION

Since Parry first described thyrotoxicosis in 1786, the precise aetiology of hyperthyroidism remains elusive. The role of heredity, however, is undoubted (Editorial, *BMJ*, 1973). Volpe *et al* (1972) in reviewing the pathogenesis of Graves' Disease noted that in dizygotic twins, the incidence of Graves' disease in both siblings is reported to be about 3 to 9%, while in monozygotic twins, the concordance rate was 30 to 60%. Case reports are here presented of the first local pair of Chinese twins who developed thyrotoxicosis, three years apart, while in their second decade of life.

CASE REPORTS

Case 1

(K.P.N.) The elder of a pair of identical twins presented in Jan. 1967 at age 14 years old with thyrotoxic symptoms and signs. The thyroid was diffusely enlarged with bruit. BMR was + 43%. The thyroid antibodies were positive (Table I). Patient responded satisfactorily to a course of Carbimazole (stopped in Nov. 1968) with weight gain (77 lb. to 97 lb.) and a BMR of—11%, only to relapse three months later. Because of the recrudescence of thyrotoxic features after an adequate trial of medical treatment, coupled with an enlarging goitre (gauged to be about four times normal size), surgery was advised and a subtotal thyroidectomy was performed in Nov. 1969. The histology was reported to show thyroid acini of varying sizes with scalloping of colloid; the picture was concluded to be consistent with treated thyrotoxicosis. Since the operation, patient continued to be well and when last seen in March 1975, was assessed to be euthyroid (confirmed with Free-thyroxine index).

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Case 2

(K.P.E.) The other twin presented at age 17 in May 1970 with palpitations, weight loss and excessive perspirations. The thyroid was diffusely enlarged (three times normal size) with bruit. There was also mild proptosis, lid retraction with lid lag. The Wayne's Diagnostic index was 42 (20 and over = toxic). PBI was 11.6 mcg. % with a BMR of +45%. Radioactive iodine uptake studies at 6 hr, 62.1%, and at 24 hr, 34.8%. Thyroid antibodies were also positive (Table I). Patient improved on Carbimazole, which was continued for 2 years, and when last seen in March 1975, remained clinically euthyroid (confirmed with Thyroid Function Tests).

Evidences for Monozygosity of twins

These include history of one placenta at birth, physical resemblance (Fig. 1), and determination of blood group antigens (Table II).

DISCUSSION

Hyperthyroidism in identical twins is extremely rare. Romberg was the first to record the familial occurrence of exophthalmic goitre when in 1851, he reported its presence in twin sisters, twenty years of age. Withusen, (1859), eight years later, was the first to suggest a hereditary factor in this disease, and in 1941, Bartels, in reviewing the World literature listed ten authenticated sets. Other subsequent reports include those of Carmena (1949), Cunningham and Kral (1959) and Lowenstein (1961). Jayson *et al* (1967) cited Harvard and Hauge's catamnestic investigations of Danish twins in which among forty one probands with thyrotoxicosis in monozygotic pairs, twelve of their co-twins were similarly affected, compared with fifty-nine thyrotoxic probands from dizygotic twins of like sex in which two co-twins had thyrotoxicosis.

The hereditary factor in Graves' Disease also appears to involve autoimmune aspects, as evidenced by the increased incidence in patients with Graves' Disease or in members of their families of other autoimmune disorders or manifestations, such as Hashimoto's disease or pernicious anaemia, and of autoantibodies against thyroid tissue components,

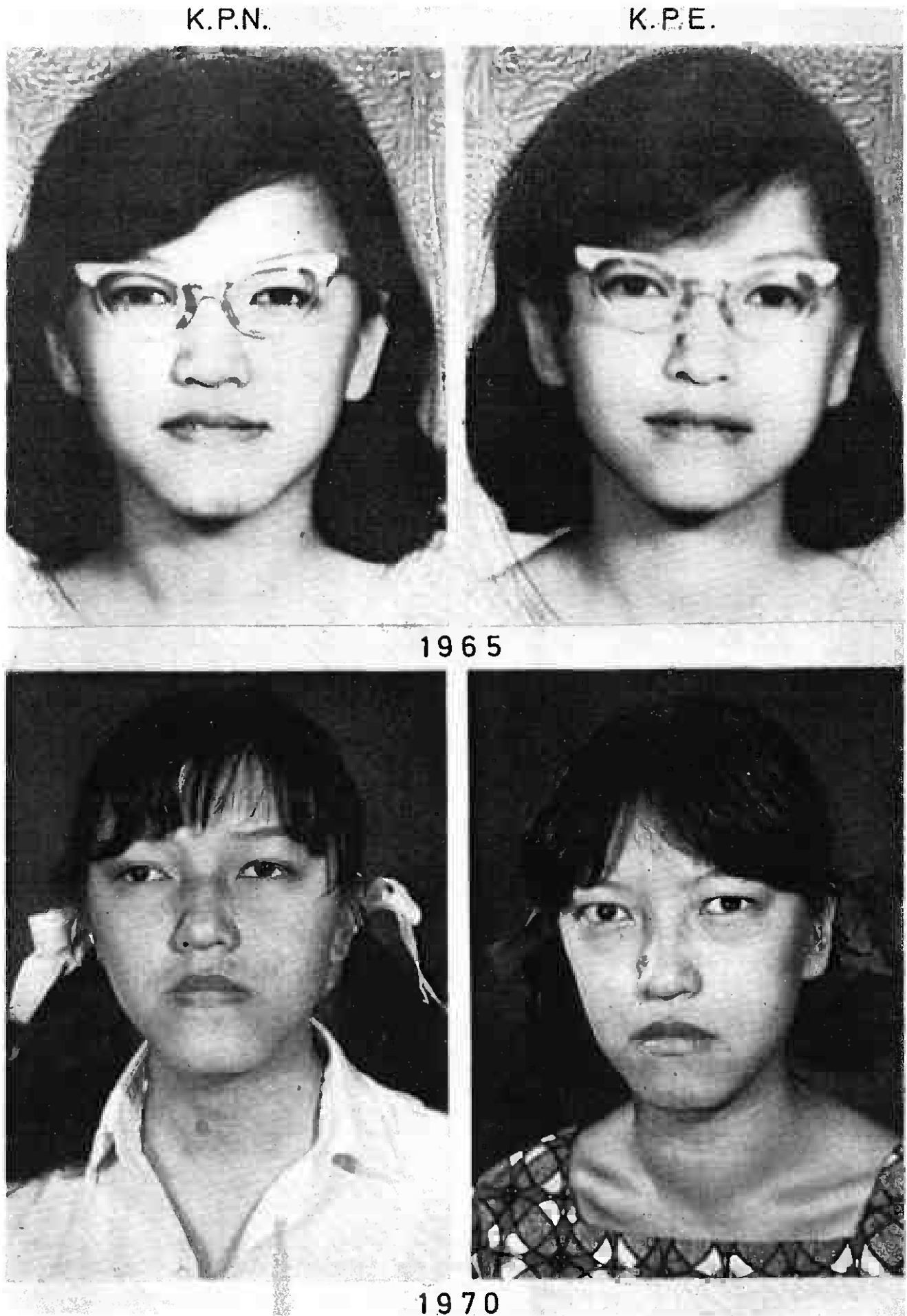


Fig. 1. Twins, KPN, KPE in 1965 and 1970. Note the thyroidectomy scar in KPN.

TABLE I
RESULTS OF TESTS FOR SERUM ANTIBODIES

Twin	Antibody to Thyroglobulin (tanned red-cell Haemagglutination Test)	Antibody to Thyroid Microsomal antigen (Immunofluorescent Test)	Antibody to Gastric Parietal cell antigen (Immunofluorescent Test)
K. P. N.	1 : 5	Positive	Negative
K. P. E.	1 : 25	Positive	Negative

TABLE II
EVIDENCE FROM BLOOD-GROUP ANTIGENS FOR MONOZYGOSITY OF THE TWINS

Twin	Blood Groups							
	ABO	Rh	Probable Genotype	MN	S	P ₁	k	Le ^a
K. P. N.	B	+	CCDee	MM	+	+	+	—
K. P. E.	B	+	CCDee	MM	+	+	+	—

gastric parietal cells, and intrinsic factor (Howel Evans *et al*, 1967). Hassan *et al* (1966) described four pairs of monozygotic twins with toxic diffuse goitre of which three pairs were concordant not only for significant titres of circulating complement-fixing antibody to thyroid microsomal antigen but also for that to gastric-parietal-cell antigen. These observations lend support to the concept that toxic diffuse goitre may evolve from an inherited defect of immunologic surveillance. The pair of twins described here had both antibodies to thyroglobulin and thyroid microsomal antigen but not to gastric-parietal-cell antigen. It is of interest that Jayson *et al* (1967) reported thyrotoxicosis and Hashimoto's goitre in a pair of monozygotic twins with serum long-acting thyroid stimulator (LATS). LATS has in fact been found in a significant proportion of euthyroid relatives of patients with Graves' disease (Wall *et al*, 1969).

The reason for the lack of concordance in 40-70% of identical twins as regards Graves' disease remains unclear. Volpe *et al* (1972) argued that environmental factors (including viral infections, trauma etc.) do not appear to be the additional elements necessary to induce the disease because, if these were important, it might be expected that both siblings should become hyperthyroid at the same time (particularly in the first two decades when environmental factors should be similar). Even in highly selective reports of studies in twins, the ages at onset of Graves' disease have varied greatly even as much as ten years in siblings under eighteen years of age. Our twins developed thyrotoxicosis three years apart while in their second decade of life. Because of the highly selective nature and limited numbers of the published case reports, it is not possible to apply sta-

tistical analysis to the differences between the ages at onset in monozygotic twins, although the limited data available suggest a random rate of appearance in a highly selective population. Hence, Volpe *et al* concluded that the age at which the disease commences in a monozygotic twin bears little relationship to the age at which the disease develops in the other twin.

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