interval between vaccination and diagnosis, the absence of a measles exanthem, and the presence of giant cell hepatitis obscured the diagnosis. An underlying immunologic disorder should be considered before vaccination of children with growth retardation and frequent infections. Although the overall benefits of immunization outweigh the risks, this case and the current recommendations for pediatric immunization highlight the potential for complications in the severely immunocompromised child.[1]

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Free triiodothyronine toxicosis in two adolescents

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Two male adolescents had subtle symptoms and signs of thyrotoxicosis but normal levels of total and free thyroxine and total triiodothyronine. Serum concentrations of thyrotropin were undetectable in basal specimens and after administration of thyrotropin-releasing hormone; only free triiodothyronine values were elevated. An increase in serum levels of free triiodothyronine may be the earliest secretory abnormality of an overactive thyroid gland. (J PEDIATR 1994;124:276-8)

Most forms of thyrotoxicosis are associated with increased serum concentrations of total and free thyroxine and triiodothyronine. Less commonly, only the serum concentration of T_3 is elevated (T_3 toxicosis).[1] Bitton and Wexler[2] described three adult patients with hyperthyroidism and deficiency of thyroxine-binding globulin in whom free T_4 levels were normal but free T_3 concentrations were increased; they termed this entity *free triiodothyronine toxicosis*. Two male adolescents with a similar form of hyperthyroidism are now described.

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METHODS

Total and free concentrations of T_4 and T_3 were measured at Nichols Institute Diagnostics (San Juan Capistrano,

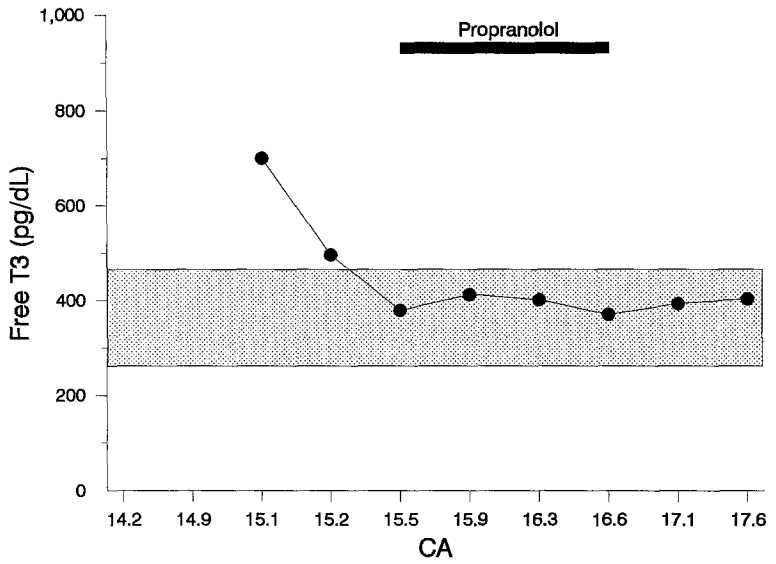

Figure. Serial concentrations of free T_3 concentrations in patient 1. (*Shaded area* represents normal range.)

Calif.) by radioimmunoassay and equilibrium dialysis.[3, 4] The interassay coefficients of variation of the assays for free T_4 and free T_3 are <12% and <15%, respectively. Control data are those of Nichols Institute Diagnostics and are specific for age and sex (T_4, 3.9 to 10.5 μg/dl; free T_4, 1.3 to 3.8 through 1990 and 0.6 to 2.0 ng/dl thereafter; T_3, 80 to 210 ng/dl; free T_3, 260 to 480 pg/dl). Serum concentrations of thyrotropin were measured before and after the administration of thyrotropin-releasing hormone by radioimmunoassay with reagents distributed by Hybritech (San Diego, Calif.) or by immunofluorometric assay with reagents from Abbott Laboratories (North Chicago, Ill.) (normal range, <5.0 μU/ml). The T_3 resin uptake was determined with reagents obtained from Abbott Laboratories (normal range, 25% to 35%). Antibodies to thyroglobulin and thyroid microsomal antigen were determined with kit reagents supplied by Burroughs Wellcome Co. (Research Triangle Park, N.C.).

CASE REPORTS

Patient 1. Hodgkin disease was diagnosed in a 6-year-old boy. The disease was managed by splenectomy and radiation therapy to the mediastinum and neck. At 12.6 years of age the patient was clinically well, the thyroid gland was of normal size, and thyroid function, including the thyrotropin secretory response to TRH (peak, 24.3 μU/ml) was normal (T_4, 6.6 μg/dl; T_3, 186 ng/dl; T_3 resin uptake 32%), but the titer of thyroid microsomal antibodies was increased (1:1600). When he was between 14 and 15 years of age, thyromegaly, fatigue, poor weight gain, and decreased school performance became evident. At 14.1 years of age the thyroid microsomal antibody titer was 1:25,600, and the thyrotropin secretory response to TRH was suppressed (peak, <0.2 μU/ml) despite normal serum levels of total T_4 (6.4 μg/dl) and T_3 resin uptake (28%). The thyrotropin secretory response to TRH remained suppressed at 14.9 years, but the thyroid microsomal antibody titer (1:102,000) increased. At 15.1 years the free T_3 concentration was first measured and was found to be elevated (700 pg/dl) (Figure); values for total T_4 and T_3 and free T_4 were in the normal range. Between the ages of 15.2 and 16.6 years of age, the patient received propranolol; free T_3 values returned to normal levels and clinical symptoms remitted. By 16.6 years the thyrotropin secretory response to TRH was normal (peak, 27.9 μU/ml), as were serum levels of total and free T_4 and T_3; the thyroid microsomal antibody titer was undetectable at this point. Adolescent sexual development began and progressed normally during this period, as did linear growth and weight gain. The patient remained free of symptoms, and with normal thyroid function (peak thyrotropin response to TRH, 14.1 μU/ml) for the ensuing year, although thyromegaly persisted and the thyroid microsomal antibody titer again increased (1:6400). Two years after cessation of propranolol therapy, the patient remained clinically euthyroid; results of basal thyroid function studies were normal (T_4, 7.8 μg/dl; free T_4, 1.5 ng/dl; T_3, 129 ng/dl; free T_3, 329 pg/dl, thyrotropin, 1.7 μU/ml), and the antithyroid peroxidase (microsomal antigen) titer was elevated (80.0 U/ml; normal, <1.0). The patient had graduated from secondary school with a B average.

T_4	Thyroxine
T_3	Triiodothyronine
TBG	Thyroxine-binding globulin
TRH	Thyrotropin-releasing hormone

Patient 2. A 16.4-year-old male adolescent was well until an asymptomatic right cervical mass was noted. Two months later physical examination disclosed a slim, apprehensive, sexually mature young man with blood pressure of 140/90 mm Hg, pulse 96 beats/min, and a 4.5 × 2.5 cm oval, freely movable mass to the right of the cervical midline. Serum values for T_4 (8.7 μg/dl), free T_4 (1.2 ng/dl), T_3 (202 ng/dl), and TBG (2.6 mg/dl) were normal, but the serum concentration of free T_3 was elevated (606 pg/dl). The basal thyrotropin concentration was <0.05 μU/ml and did not

increase after administration of TRH. Antibodies to thyroglobulin and to thyroid microsomal antigen were not detected. Technetium 99m was concentrated primarily within the intrathyroidal cervical mass. Seven days later, immediately before right hemithyroidectomy, the serum concentrations were as follows: T_4, 7.7 μg/dl; T_3, 282 ng/dl; and free T_3, 948 pg/dl. Pathologic examination of the lesion revealed a follicular adenoma with papillary epithelial configuration consistent with the hyperfunctional state. Fourteen months after operation, while the patient was receiving T_4, 0.1 mg daily, he was clinically euthyroid; serum thyroid hormone concentrations were as follows: T_4, 8.0 μg/dl; free T_4, 0.9 ng/dl; T_3, 129 ng/dl; free T_3, 195 pg/dl; thyrotropin, 0.7 μU/ml.

DISCUSSION

In patient 1, autoimmune thyroid disease occurred as a consequence of radiation therapy to the neck for treatment of Hodgkin disease.[5] Later, transient hyperthyroidism developed, manifested by subtle clinical symptoms, suppression of thyrotropin secretion, and an isolated increase in serum concentrations of free T_3. In patient 2, an autonomous hyperfunctioning follicular adenoma of the thyroid was manifested by radiographic findings, isolated increase in the free T_3 concentration, and suppressed thyrotropin secretion.

Bitton and Wexler[2] reported three women in the sixth decade of life who also had isolated increases in free T_3 levels. One woman had an untreated lymphoma. The other two patients had received radiation therapy to the neck; in one, external radiation had been administered 30 years earlier for unknown reasons, and the other had received iodine 131 for treatment of hyperthyroidism 1 year earlier. In all three patients the total T_4 and TBG values were decreased. The authors attributed the isolated increase in free T_3 levels to the low TBG values, but free T_4 concentrations were not elevated in these women. The TBG concentration was normal in our patient 2; it was not measured in patient 1, but there is no reason to believe that his TBG value was low, because total T_4 and T_3 resin uptake levels were normal.

The explanation for the isolated increase in free T_3 values in these patients is not clear. In patient 2 the increased free T_3 value may have represented an early biochemical abnormality of thyroid hyperfunction, because the total T_3 concentration was elevated within 7 days after its first measurement. However, in patient 1 this secretory aberration was more persistent; perhaps a subtle abnormality in the affinity of a serum T_3-binding protein for T_3 led to the isolated increase in free T_3 concentrations in this subject. Although three of five patients with "free T_3 toxicosis" had received cervical radiation, two had not. Therefore it is unlikely that radiation exposure per se was responsible for this biochemical finding.

The clinical findings (hyperactivity, wide pulse pressure, tachycardia, thyromegaly) and laboratory findings (elevated T_4 and T_3 concentrations with suppressed thyrotropin values) in the majority of children with hyperthyroidism are typical[6]; occasionally only total T_3 concentrations are increased. An isolated increase in free T_3 concentrations is unusual, and the free T_3 concentration should be determined only when the more common biochemical abnormalities are not present. However, there are patients and relatives of patients with autoimmune thyroid disease who are seemingly euthyroid and who have normal levels of T_4 and T_3 but suppressed secretion of thyrotropin. It may be of interest to determine free T_3 values in such patients.

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