SHORT REPORTS

Transient hypothyroidism after iodine-131 treatment for thyrotoxicosis

Many patients develop permanent hypothyroidism after being treated with iodine-131 (^{131}I) for thyrotoxicosis and require replacement therapy with thyroxine.¹ Transient hypothyroidism has been observed after subtotal thyroidectomy for thyrotoxicosis,² but whether this phenomenon exists after ^{131}I treatment is disputed.³ In 1977 we reported two cases of transient hypothyroidism after ^{131}I treatment,⁴ since when we have seen a further eight cases, which we report here.

Patients, methods, and results

The patients comprised seven women, median age 52 years (range 49-69), and three men aged 50, 59, and 67 years attending the thyroid clinic at this hospital. Thyrotoxicosis was confirmed biochemically and by an increased two-hour uptake of ^{131}I . None of the patients were receiving antithyroid drugs, and all had diffuse thyroid enlargement. Doses of ^{131}I ranged from 2.5 to 11.8 mCi (median 4 mCi). The diagnosis of transient hypothyroidism was based on a low serum thyroxine (T4) concentration. Serum T4, triiodothyronine (T3), and thyroid-stimulating hormone (TSH) concentrations were measured by radioimmunoassay. Normal ranges were: serum T4 60-140 nmol/l (4.7-10.9 $\mu\text{g}/100\text{ ml}$), serum T3 1.2-2.7 nmol/l (0.8-1.8 ng/ml), and serum TSH < 6 mU/l. Statistical analysis included Friedman's two-way analysis of variance test and Wilcoxon's matched pairs signed ranks test.

The figure shows the serum concentrations of T4, T3, and TSH measured immediately before ^{131}I treatment, when subnormal serum T4 concentrations were first found, and when serum T4 concentrations were first noted to be normal again. No patient became clinically hypothyroid when the serum T4 concentration was transiently low.

After treatment the median serum T4 concentration decreased from 211.5 nmol/l (16.4 $\mu\text{g}/100\text{ ml}$) (range 160-320 nmol/l; 12.4-24.9 $\mu\text{g}/100\text{ ml}$) to 38.5 nmol/l (3.0 $\mu\text{g}/100\text{ ml}$) (range 20-55 nmol/l; 1.6-4.2 $\mu\text{g}/100\text{ ml}$) and then increased to 92 nmol/l (7.1 $\mu\text{g}/100\text{ ml}$) (range 62-187 nmol/l; 4.8-14.5 $\mu\text{g}/100\text{ ml}$). Serum T3 concentrations fell from a median of 4.85 nmol/l

(3.2 ng/ml) (range 3.1-7.6 nmol/l; 2.0-4.9 ng/ml) to a median of 1.3 nmol/l (0.8 ng/ml) (range 1.0-1.9 nmol/l; 0.7-1.2 ng/ml) and recovered to a median of 1.95 nmol/l (1.3 ng/ml) (range 1.2-2.5 nmol/l; 0.8-1.6 ng/ml). The median serum TSH concentration rose to 21 mU/l (range < 2-50+) and then fell to 5.5 mU/l (range < 2-25). There was a significant difference ($P < 0.0005$) between each of the serum T4 and TSH concentrations obtained on the three occasions. Serum T3 concentration was estimated on the three occasions in only six patients, in all of whom there was a significant difference between each measurement ($P < 0.0002$). The low serum T4 concentrations were recorded from six to 24 weeks (median 12 weeks) after treatment, and the recovery concentrations from eight to 52 weeks (median 25 weeks).

The patients were followed up for seven months to four years (median 19 months), six for more than one year. Two of these six became clinically and biochemically hypothyroid after four years, requiring thyroxine treatment. Two had raised serum TSH but normal serum T3 and T4 concentrations and were clinically euthyroid, and two had normal serum TSH, T3, and T4 concentrations.

Comment

In seven of our patients low serum T4 concentrations were found within three months of ^{131}I treatment and had recovered by seven months. These changes were closely similar to those following subtotal thyroidectomy² and were probably due to the same mechanisms—that is, a fluctuating titre of thyroid-stimulating immunoglobulins and delayed recovery of suppressed pituitary thyrotrophs. None of our patients became clinically hypothyroid during the transient depression of thyroid hormones, which is consistent with the findings that biochemical hypothyroidism during carbimazole treatment can precede clinical hypothyroidism by many weeks.⁵ Thus not all patients developing biochemical hypothyroidism soon after ^{131}I treatment need to start lifelong thyroxine replacement therapy. Also, two of our patients now have mildly raised thyroid hormone concentrations, and thyroxine treatment in these patients may be harmful.

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¹ Toft, A D, *et al*, *Lancet*, 1975, **2**, 576.

² Toft, A D, *et al*, *Lancet*, 1976, **2**, 817.

³ Toft, A D, and Irvine, W J, *Lancet*, 1977, **2**, 1128.

⁴ Shalet, S M, MacFarlane, I A, and Beardwell, C G, *Lancet*, 1977, **2**, 1357.

⁵ Mortimer, C H, *et al*, *British Medical Journal*, 1977, **1**, 138.

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T4, T3, and TSH concentrations (with median) in 10 patients with transient hypothyroidism after ^{131}I treatment for thyrotoxicosis.

Conversion: SI to traditional units—T4: 1 nmol/l $\approx$ 7.7 ng/100 ml. T3: 1 nmol/l $\approx$ 0.65 ng/ml.

Is long-term immunosuppressive treatment necessary to maintain good kidney graft function?

In most centres immunosuppression is regarded as essential after kidney transplantation. Long-term non-specific immunosuppressive treatment, however, may result in diabetes, hypertension, obesity, tumours, etc owing to an inappropriate and generalised suppression of host immune responses.¹ During a study to evaluate the immunological states of patients with good renal function over three years after transplantation we found that one had stopped taking her immunosuppressive treatment. Her clinical and immunological state, however, was similar to that of the other patients. This suggested

Cellular immune variables in patient, other long-term (over three years) kidney transplant recipients, and controls

Lymphocytes in differential count											
White cell count ($\times 10^9/l$)	Total		Early E rosettes		E rosettes		Proportion bearing IgM		Proportion bearing IgG		
	No ($\times 10^9/l$)	%	No ($\times 10^9/l$)	%	No ($\times 10^9/l$)	%	No ($\times 10^9/l$)	%	No ($\times 10^9/l$)	%	
Patient											
36 months after transplantation	9.0	1.6	18.0	0.24	15.0	0.32	20.0	0.23	14.0	0.23	14.0
41 months after transplantation	7.5	0.9	12.0	0.22	23.0	0.49	54.0	0.09	10.0	—	—
47 months after transplantation	7.1	1.5	21.0	0.18	12.0	0.72	48.0	—	—	0.15	10.0
Other transplant recipients											
Mean $\pm$ SE	7.6 $\pm$ 0.60	1.6 $\pm$ 0.17	21.6 $\pm$ 2.0	0.58 $\pm$ 0.08	39.8 $\pm$ 3.4	0.88 $\pm$ 0.12	54.0 $\pm$ 3.3	0.10 $\pm$ 0.02	6.0 $\pm$ 1.1	0.11 $\pm$ 0.02	7.2 $\pm$ 1.2
Range	4.1–15.0 (n = 19)	0.6–3.5 (n = 19)	7.0–37.0 (n = 19)	0.2–1.3 (n = 17)	17.0–64.0 (n = 17)	0.25–2.2 (n = 19)	23–78 (n = 19)	0.02–0.25 (n = 13)	1.0–16.0 (n = 13)	0.01–0.24 (n = 12)	1.0–17.0 (n = 12)
Controls											
Mean	7.5 $\pm$ 0.42	2.4 $\pm$ 0.23	32.9 $\pm$ 2.3	1.03 $\pm$ 0.15	41.6 $\pm$ 3.2	1.46 $\pm$ 0.14	60.5 $\pm$ 1.4	0.23 $\pm$ 0.03	9.6 $\pm$ 0.6	0.22 $\pm$ 0.037	8.9 $\pm$ 1.1
Range	5.1–13.1 (n = 25)	1.4–3.5 (n = 25)	18.0–52.0 (n = 25)	0.3–1.8 (n = 22)	23.0–63.0 (n = 22)	0.78–2.6 (n = 25)	47.0–77.0 (n = 25)	0.08–0.31 (n = 21)	5.0–13.0 (n = 21)	0.06–0.49 (n = 13)	2.0–14.0 (n = 13)
Other recipient v controls*		P<0.01	P<0.001	P<0.025		P<0.005		P<0.01	P<0.01	P<0.02	

*Student's *t* test used for comparison.

that some patients might have their immunosuppressive treatment withdrawn without any untoward effects.

Patients, methods, and results

The patient, a 17-year-old girl, began haemodialysis in January 1974 and five months later received a cadaver kidney allograft. Matching for HLA histocompatibility was poor (donor: B+, HLA-A2, A10, B5, —; recipient: B+, HLA-A10, —, B8, —). Routine immunosuppressive treatment included corticosteroids, azathioprine, and antilymphocyte globulin. Peritoneal dialysis and haemodialysis were performed once. The postoperative period was uneventful. She had never had a rejection episode, and only three mild infections were recorded. In August 1975 she stopped her immunosuppressive treatment without informing the medical staff. When seen in 1977 she had good renal function, with serum creatinine concentration 72.5 μ mol/l (0.8 mg/100 ml); serum non-protein nitrogen concentration 42 mmol/l (59 mg/100 ml); no proteinuria; and a daily urine output of 1500 ml. The other patients in the series were taking azathioprine (1.5–3.0 mg/kg/day) and methylprednisolone (16 mg on alternate days).

Serum concentrations of IgG, IgM, and IgA (ICL Scientific) and C3, C4, and C3 proactivator (Behringwerke) were determined with commercial single radial diffusion plates. Whole serum haemolytic activity was measured. The ¹²⁵I-Clq-binding assay was used to detect circulating immune complexes in serum. Mononuclear cells were isolated from heparinised blood by Ficoll-Isopaque (MSL, Eurobio) density-gradient centrifugation. The E rosette test and early E rosette test were performed. Immunoglobulin-bearing lymphocytes were detected with fluorescein-labelled antisera (anti-IgM, anti-IgG; Cappel laboratories).

The table summarises the results in the patient, the other transplant recipients in the series, and a group of normal controls. No appreciable difference in any variable was observed between the patient and other transplant recipients except in the concentration of serum polyclonal IgMs, which was noticeably increased in the patient (10 g/l). Circulating immune complexes were detected in low concentration. There was a significant difference in most variables examined between the other transplant recipients and controls.

Comment

This patient stopped her immunosuppressive treatment because she was worried about its effect on her growth. (She and her mother admitted this spontaneously, so we have no reason to doubt it.) Nevertheless, she had good renal function. The lack of any clinical and immunological difference between the patient and kidney transplant recipients who were taking their immunosuppressive treatment suggests that the degree of immunosuppression was the same. This raises questions about the persistence of immunosuppression without immunosuppressive treatment, the possibility of graft acceptance without immunosuppressive treatment, and the relation between graft acceptance and immunosuppression. The persistent immunosuppression may have resulted from the massive immunosuppressive treatment given after transplantation. HLA histocompatibility matching was poor, so that spontaneous acceptance of the cadaver kidney allograft was unlikely.

Azathioprine is commonly discontinued to avoid bone marrow and liver toxicity,^{2,3} and some workers⁴ recommend stopping azathioprine two years after transplantation. Naik *et al*⁵ withdrew prednisone

after two years without untoward effects in renal transplant recipients given this treatment alone. Our findings confirm that this may be possible and suggest that some specific immunosuppression occurs in organ transplantation. Rejection may occur after stopping treatment,³ however, so that criteria must be sought to establish the real need for long-term immunosuppressive treatment after transplantation.

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¹ Thomas, F, *et al*, *Transplantation Proceedings*, 1978, **10**, 621.

² Bach, J F, *Transplantation Proceedings*, 1971, **3**, 27.

³ Dandavino, R, *et al*, *Transplantation Proceedings*, 1978, **10**, 655.

⁴ Sheriff, M H R, Yayha, T, and Lee, H A, *Lancet*, 1978, **1**, 118.

⁵ Naik, R B, *et al*, *Transplantation Proceedings*, 1979, **11**, 39.

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Polle syndrome: children of Munchausen

We report on a family in which the mother, who had the Munchausen syndrome, fabricated two different illnesses in her son and daughter in a highly systematic way. She was not suspected for six months, as her behaviour seemed normal.

Case reports

The daughter—This child was admitted in May 1976 aged 22 months with a five-day history of polydipsia, polyuria, and weight loss. Her urine contained 2% sugar. A glucose tolerance test was performed. The curve was an odd shape but definitely abnormal. She was diagnosed as having diabetes mellitus with a low renal threshold. She was stabilised on diet and Monotard insulin, and subsequent control was satisfactory.

The son—This 5-year-old boy was first seen in July 1976. Two months previously he had been accidentally knocked out. Soon afterwards he developed attacks of fever associated with headache, vomiting, abdominal pain, and diarrhoea. Later polyuria, polydipsia, and nocturia developed. His mother had seen blood and pus in his underpants and gravel in his urine. He