Biochemical data in 63 transplanted patients. Values are means $\pm$ SE of mean

Concentrations	All patients (n = 63)	With avascular necrosis (n = 22)	Without avascular necrosis (n = 41)	Normal values
Serum calcium (mmol/l) ..	2.51 $\pm$ 0.01	2.48 $\pm$ 0.05	2.51 $\pm$ 0.02	2.25-2.62
Serum phosphate (mmol/l) ..	0.98 $\pm$ 0.04	1.01 $\pm$ 0.02	0.96 $\pm$ 0.04	0.80-1.40
Serum alkaline phosphatase (IU/l) ..	46.9 $\pm$ 2.4	50.3 $\pm$ 5.1	44.2 $\pm$ 2.5	20-90
Serum parathyroid hormone (μ g/l) ..	0.45 $\pm$ 0.04	0.48 $\pm$ 0.07	0.40 $\pm$ 0.04	<0.156-1.0
Serum 25-OHD (μ g/l) ..	25.4 $\pm$ 1.8	30.9 $\pm$ 3.6	22.4 $\pm$ 1.8*	3-40
Urinary calcium (mmol/24 h) ..	2.17 $\pm$ 0.19	2.11 $\pm$ 0.3	2.20 $\pm$ 0.25	
Urinary phosphate (mmol/24 h) ..	13.5 $\pm$ 0.9	12.9 $\pm$ 1.10	13.9 $\pm$ 1.30	
Creatinine clearance (ml/min) ..	79.4 $\pm$ 4.8	78.6 $\pm$ 7.9	80.5 $\pm$ 6.2	

*P < 0.05.

Conversion: SI to traditional units—Serum calcium: 1 mmol/l $\approx$ 4 mg/100 ml. Serum phosphate: 1 mmol/l $\approx$ 3.2 mg/100 ml. Urinary calcium: 1 mmol/24 h $\approx$ 40 mg/100 ml. Urinary phosphate: 1 mmol/24 h $\approx$ 0.031 g/24 h.

Hypercalcaemia was shown in a single sample from each patient and other factors which might have been responsible for it—for example, immobilization—were excluded. In the six hypercalcaemic patients, who had all received their grafts between three and eight years before this study, the serum parathyroid hormone concentration was within the normal range but perhaps not suppressed to the degree that might have been expected for the high concentrations of serum calcium. Circulating parathyroid hormone concentration was also normal in all but one of the remaining patients. No patient had a serum 25-OHD concentration below the normal range.

Comment

In this study the prevalence of radiological avascular necrosis of bone was as high as 35%. This is one of the highest reported but in most of our patients it would not have been recognised if radiological screening had not been done. Only four patients required hip replacement. Steroid treatment did not seem to have been responsible, as the incidence of graft rejection episodes was similar in patients with and without avascular necrosis and the maintenance steroid dosage was the same in both groups.

Hyperparathyroidism is a common complication of chronic renal failure and usually subsides after renal transplantation. In some successfully transplanted patients with normal renal function, however, parathyroid overactivity has been reported to persist for years^{1,2} and this has been implicated in the pathogenesis of avascular necrosis of bone.³

All but one of our patients had normal circulating parathyroid hormone concentrations. No difference in parathyroid activity could be shown between patients who had avascular necrosis and those who did not. Moreover, no differences in serum or urinary phosphate concentrations were found.

Measurements of serum 25-OHD concentrations can be used as an index of the vitamin D status in man. As we found, transplanted patients had normal 25-OHD concentrations and vitamin D cannot be implicated in the pathogenesis of avascular necrosis of bone. We therefore conclude that the avascular necrosis of bone in our transplanted patients was due neither to parathyroid overactivity nor to vitamin D deficiency and that other factors must be sought.

We thank the nurses and the secretary of the Fleming Ward of St Mary's Hospital for their help and co-operation. J L H O'Riordan is grateful to the National Kidney Research Fund for financial support.

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(Accepted 23 June 1978)

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Solitary diverticulum of transverse colon masquerading as polyp

Solitary diverticulum of the transverse colon is a rare developmental abnormality, which in the case we report gave rise to the appearances on barium enema investigation of a solitary polyp. This misleading radiological finding resulted in difficulty in locating the diverticulum, which was completely intramesenteric and therefore not visible except at colotomy. We present our experience as a caution to others.

Case report

A 52-year-old woman presented with a two-week history of passing bright red blood on defaecation. She had had no change in her bowel habit or loss of weight. Sigmoidoscopy showed no abnormality and proctoscopy only minor haemorrhoids. A barium enema showed a lobulated lesion in the region of the hepatic flexure (fig) judged to be a polyp. Laparotomy was performed but no polyp palpated at the appropriate site. Colotomy and thorough inspection of the colonic lumen also failed to show a polyp. It was concluded that faeces might have accounted for the "polyp" and the laparotomy ended. After convalescence another barium enema was performed and this showed the same abnormality to be present. Colonoscopy was

Solitary diverticulum of transverse colon, near hepatic flexure.

undertaken, but, mainly because of a long sigmoid colon, the hepatic flexure could not be visualised.

In view of the possibility of missed malignancy a second laparotomy was undertaken. Again no polyp was palpable and again a colotomy was performed. Thorough exploration showed the neck of a congenital diverticulum of 1-cm diameter in the region of the hepatic flexure. This was not visualised from the bowel exterior as it was completely intramesenteric, being three cm long. A localised resection of the hepatic flexure was performed and the patient made an uneventful recovery. Histological examination showed a simple diverticulum with no appreciable abnormality in sections of the mucosa. An adjacent lymph node was normal.

Comment

A review of British and American reports over the past ten years has shown none of a solitary diverticulum of the transverse colon presenting in this fashion. Solitary or congenital diverticula are rare developmental abnormalities found in the large bowel, and may be associated with vertebral defects.¹ They are found in the rectum and occasionally in the colon and commonly have a more or less complete covering of all bowel coats. The incidence of solitary diverticulum of the transverse colon is undetermined. Necropsy studies have put the incidence of solitary diverticulum of the caecum at between 2.5 and 5.0% of the general population.² These were all found to be thin-walled "false" diverticula. The same study found acquired diverticular disease in 43% of cadavers, but failed to find any case of congenital diverticulum in the 200 colons studied.

Chugntal and Ackerman described six patients with congenital solitary diverticula of the transverse colon all of which presented with

perforation.³ Perhaps, significantly (more so had the number of cases been greater), all six were women with an average age of 45. Our patient was also a woman, who was 52.

Our patient presented with rectal bleeding at defaecation. No such case has been reported. Possibly the bleeding may have been due to haemorrhoids, but against this no bleeding has occurred since resection of the diverticulum, despite her piles still being present and untreated. The barium enema findings strongly suggested the presence of a polyp and this led to erroneous diagnosis and difficulties at laparotomy. The confusion seems best explained by the partially barium-filled diverticulum overlying the barium-filled colon on the radiographs giving the appearance of "a lobulated lesion, probably a polyp." This phenomenon should be borne in mind by all those searching for elusive polyps.

We thank Mr R E C Collins for helpful discussion and advice and Miss Susan Stickells for typing the manuscript.

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(Accepted 21 June 1978)

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Thyrotoxic Graves's disease after primary hypothyroidism

We report a case of thyrotoxicosis following primary hypothyroidism in a 61-year-old man.

Case report

A retired local government officer presented in January 1976 with a six-month history of loss of energy and deepening voice. In 1957 he had had a total colectomy for ulcerative colitis. There was no family history of autoimmune disease. He was not taking any medication and weighed 78 kg. He looked hypothyroid and his thyroid gland was impalpable.

Investigations showed: protein-bound iodine (PBI) 180 nmol/l ($2.3 \mu\text{g}/100 \text{ ml}$) ($310-630 (3.9-8.0 \mu\text{g}/100 \text{ ml})$); Thyopac-3 121.5 (92-117); TSH 23.7 mU/l (<6); thyroid antibodies negative. Treatment with L-thyroxine was started in February 1976. By April he was clinically and biochemically euthyroid on $150 \mu\text{g}$, PBI 460 nmol/l ($5.8 \mu\text{g}/100 \text{ ml}$), and TSH 1.6 mU/l . He was discharged from the clinic, but one year later complained of weight loss and shakiness. He weighed 71 kg. His general practitioner reduced and eventually stopped the thyroxine in November 1977, when his weight was down to 67 kg. He was referred back to the clinic, where he was found to have lid retraction, tremor, and a small diffuse goitre. Thyroid function tests showed: serum thyroxine 149 nmol/l ($11.6 \mu\text{g}/100 \text{ ml}$), (60-140 nmol/l ($4.7-10.9 \mu\text{g}/100 \text{ ml}$)); serum tri-iodothyronine 4.6 nmol/l (3.0 ng/ml) ($1.2-3.0 \text{ nmol/l}$ ($0.78-1.9 \text{ ng/ml}$)); TSH values at 0 and 20 minutes after administration of $200 \mu\text{g}$ TRH were 1.5 and 1.3 mU/l , respectively. Thyroid stimulating immunoglobulin index 41 (normal >75),¹ but thyroid auto-antibodies remained negative. ¹³¹I uptake was 63% at six hours (thyrotoxicosis likely above 55%), with no suppression of uptake (74% at six hours) after administration of T3. A thyroid scan showed minimal general thyroid enlargement with uniform distribution of isotope.

He was started on treatment with carbimazole and, on a blocking dose with maintenance L-thyroxine, he is euthyroid and has gained weight to 73 kg.

Comment

In 1971 four cases were reported of thyrotoxicosis occurring during treatment of suspected primary hypothyroidism.^{2,3} In three cases the diagnosis of primary hypothyroidism was based on clinical findings and a raised serum cholesterol concentration. In the other case the diagnosis was made on the basis of a low PBI concentration only.

In our patient the diagnosis of primary hypothyroidism was clearly established by the low PBI, raised Thyopac-3, and raised TSH. The

cause was presumably atrophic thyroiditis, despite the absence of thyroid autoantibodies, and he was not taking any known goitrogen. The subsequent development of thyrotoxicosis is also well documented. Thyrotoxicosis medicamentosa is discounted by the raised 6-hour ¹³¹I uptake and failure of this to suppress with T3. The physical findings and the result of the thyroid scan exclude toxic adenoma and toxic multinodular goitre.

Together with the positive thyroid stimulating immunoglobulins these features are compatible with the diagnosis of thyrotoxic Graves's disease after primary hypothyroidism. Reported cases of this have been inadequately documented. The mechanisms by which this patient developed the above sequence of events is not clear. It was apparent that his thyroid was incapable initially of maintaining him euthyroid despite increased pituitary output of TSH, and yet two years later was responding excessively to the stimulus of thyroid stimulating immunoglobulins. Possibly his hypothyroidism was due to blocking of the TSH receptor by biologically inactive thyroid stimulating antibody, and that later this antibody became capable of stimulating the thyroid.

We acknowledge the contribution of Dr D Hurrell, the patient's general practitioner, and thank Dr B R Smith for carrying out the thyroid stimulating immunoglobulin assay.

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(Accepted 5 July 1978)

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Long-term tri- and tetra-cyclic antidepressants, myocardial contractility, and cardiac rhythm

Changes of the ECG revert to normal after prolonged administration of tri- and tetra-cyclic antidepressants (TCA),¹ but little is known about the long-term effect of TCA on myocardial contractility. Significant arrhythmias and sudden death have been reported particularly in patients taking toxic doses of TCA,² but only limited information is available on their effect in therapeutic doses.² We therefore investigated the influence of TCA on cardiac rhythm and myocardial contractility after prolonged administration.

Patients, methods, and results

Systolic time intervals (STI) and blood pressure were determined in five women aged 61 ± 13 years. The first tracing (A) was obtained three weeks after starting treatment and was repeated after 74.6 ± 1.8 months (B). The following antidepressants were used alone or in combination: maprotiline, amitriptyline, trimipramine, imipramine, desipramine, and clomipramine. In two patients STI were recorded one year after stopping treatment, which had lasted for 35.5 ± 4.9 months. STI were recorded as described by Weissler.³ In 18 patients 8 h-daytime-Holter monitoring was performed during treatment. The patients were divided into three groups. In group 1 the first Holter tracing was obtained before and the second during treatment, whereas in group 2 the second ECG was taken four weeks after stopping treatment. In group 3 only one Holter recording was obtained (during treatment).

STI—We found a significant further prolongation of pre-ejection period index (PEP_i) from $132.4 \pm 4.7 \text{ ms}$ (A) to $144.1 \pm 4.5 \text{ ms}$ (B). PEP/LVET (left ventricular ejection time) increased from 0.375 ± 0.032 (A) to 0.421 ± 0.030 (B) (fig). In two patients who had been taking TCA for 36 ± 4.9 months, PEP_i decreased from 135.2 ± 9.2 (C) to $125.3 \pm 6.5 \text{ ms}$ 11.5 months after treatment had been discontinued (D). The values for PEP/LVET were 0.412 ± 0.042 (C) and 0.356 ± 0.040 (D) respectively (figure). There were no significant changes of blood pressure between A and B and between C and D.

Holter monitoring—4/10 patients in groups 1 and 2 had no arrhythmias