SURVIVAL OF A HOMOLOGOUS PARATHYROID IMPLANT IN AN IMMUNOSUPPRESSED PATIENT

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Summary   A patient who had undergone subtotal parathyroidectomy while on chronic hæmodialysis became severely hypocalcæmic after receiving a well-functioning cadaveric renal graft. After a homologous parathyroid implant, there was a biochemical improvement in the patient, and at biopsy 6 months later the parathyroid graft was histologically normal. 21 months after the implant, serum calcium and phosphorus remain normal without calcium supplementation.

Introduction

ABOUT a hundred attempts at homologous parathyroid transplantation in man have been reported,[1-3] but with three possible exceptions there has been no histological proof of graft survival. Two of the three reports were published 50 years ago, and inconclusively described " remnants of three small glands which, although degenerated, had the histologic appearance of parathyroid tissues "[4] and " a nodule containing an array of aligned cells rather unusual in appearance, with an architecture revealing epithelial cell-like structures resembling parathyroid ".[5] In the third instance, histologically intact homologous parathyroid tissue was found in a millipore chamber that had been implanted for 5 months, but the patient had demonstrated no biochemical or clinical improvement.[6]

We report the morphological survival and apparent functioning of a homologous parathyroid implant in a
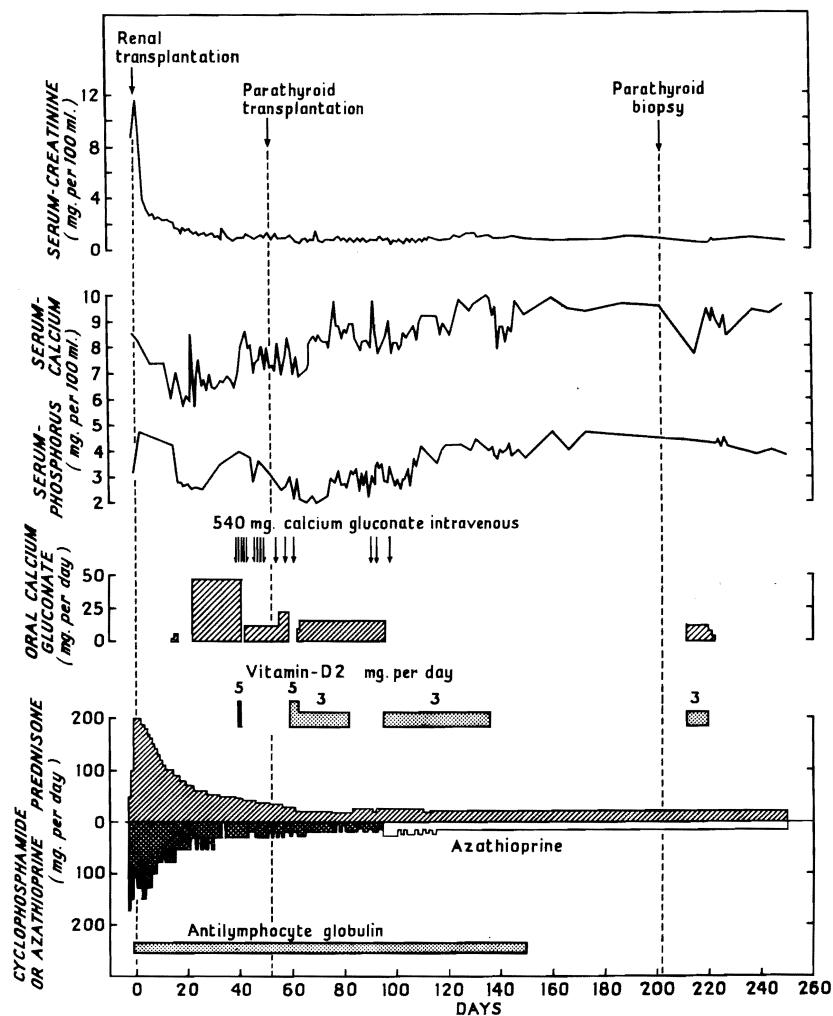
Fig. 1—Course and treatment after renal transplantation and subsequent parathyroid implantation.

Vertical arrows indicate intravenous infusion of 540 mg. calcium gluconate.

patient who, unlike the earlier parathyroid-transplant recipients, was immunosuppressed.

Case-report

A 46-year-old male with polycystic kidney disease had

been on chronic hæmodialysis since 1966. In 1969, skeletal pain, spontaneous rib fractures, and raised serum-calcium levels (11·5–12·2 mg. per 100 ml.) developed. Exploration of the neck in February, 1970, revealed parathyroid hyperplasia, and three and a half glands were removed. Postoperatively, serum-calcium was within normal limits and the bone disease improved.

After cadaveric renal transplantation at the Denver Veterans Administration Hospital on May 28, 1971, renal function became normal and rejection was never diagnosed (fig. 1). Postoperatively the patient was immunosuppressed with cyclophosphamide or azathioprine, prednisone, and antilymphocyte globulin (fig. 1). Other medications included reserpine, hydrallazine hydrochloride, and chlorothiazide. The first 2 postoperative months were complicated by recurrent convulsive seizures, dysphasia, and dyskinesia. Neurological examination only showed arteriosclerotic vessels by cerebral angiography. Subsequently, the patient's neurological condition improved slowly and at present only moderate dysphasia remains.

Immediately after the renal transplantation, serum-calcium dropped to subnormal levels (6–7·5 mg. per 100 ml.). Oral supplementation with calcium did not bring the serum levels to normal and calcium had to be administered intravenously (fig. 1). During this time, tubular reabsorption of phosphorus was 75 to 95%.

52 days after renal transplantation, four separate pieces of homologous hyperplastic parathyroid tissue (approximately 150 mg.) were implanted into the patient's pectoralis muscle. The grafts were obtained from another renal-transplant recipient undergoing subtotal parathyroidectomy. The donor was blood-group A, while the recipient was of blood-group O.

Initially, the recipient's serum-calcium remained below normal, necessitating further supplementation with calcium and vitamin D_2 (fig. 1). But 2 months after implantation, all supplementation could be stopped. In January, 1972, a biopsy specimen was taken from the site of the parathyroid grafting. This was followed by a transient drop in serum-calcium, and supplementary treatment was reinstituted for a few days (fig. 1). In the ensuing 12 months, serum calcium and phosphorus have been within normal limits.

Results

The parathyroid tissue used for implantation consisted microscopically of sheets of enlarged chief cells with occasional acini, characteristic of secondary hyperplasia. On biopsy 6 months after implantation, cords and clusters of chief cells were set in a fine, highly vascularised stroma characteristic of normal parathyroid tissue (fig. 2). Occasional interstitial collections of lymphocytes and plasma-cells suggested slight homograft rejection. Electron microscopy was
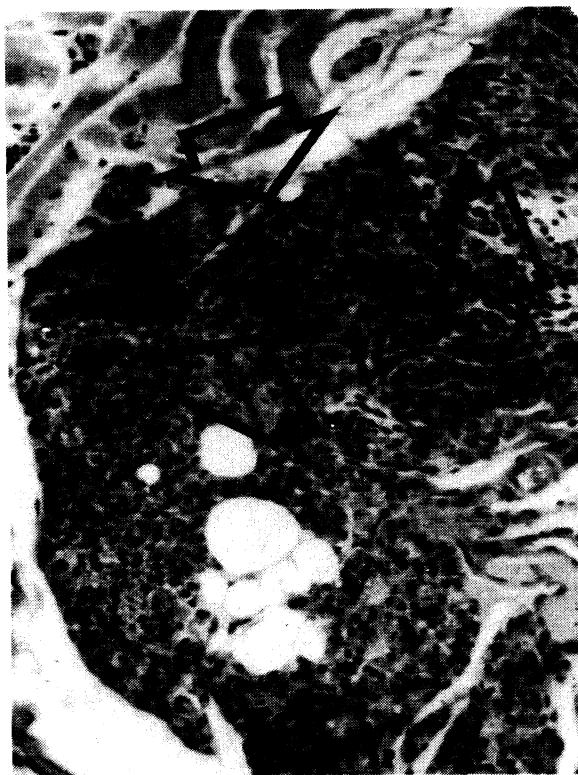
Fig. 2—Parathyroid tissue obtained at biopsy 6 months after homologous implantation.

The glandular tissue is surrounded by skeletal muscle. Area shown is focally infiltrated by lymphocytes and plasma-cells (arrows); most of graft was without such cells. (Hæmatoxylin and eosin. ×100.)

performed on tissue which had been embedded in a paraffin block and was thus poorly preserved ultra-structurally. However, large amounts of glycogen, occasional prominent arrays of rough endoplasmic reticulum, and secretion granules characteristic of functioning parathyroid cells [7] were apparent (fig. 3).

Discussion

The early assumption that homologous endocrine implants enjoy a major immunological privilege has never been substantiated. On the contrary, several experimental studies have shown that rejection of

thyroid-parathyroid grafts does occur.[8-10]

Parathyroid grafting during immunosuppression has not previously been attempted in man. Our patient was receiving immunosuppressive drugs after renal transplantation. Immunosuppression was highly effective, as judged by the uninterrupted and excellent functioning of the kidney graft thereafter. Consequently, it was not surprising that there was only slight evidence of rejection in the biopsy specimen of the parathyroid graft obtained after 6 months.
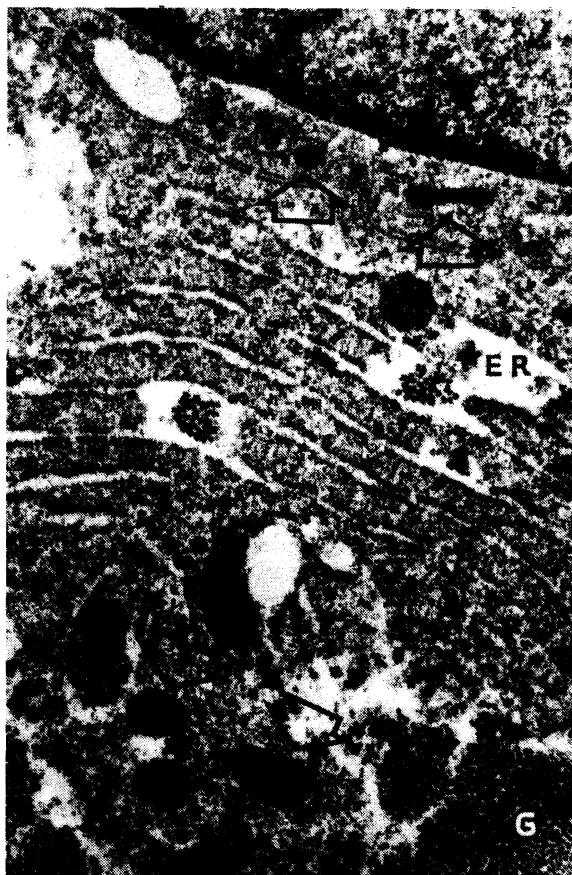
Fig. 3—Parathyroid tissue obtained at biopsy 6 months ^fter homologous implantation.

Granular endoplasmic reticulum (ER), glycogen (G), and secretory granules (arrows) are shown. (×21,000.)

There was strong biochemical evidence that hypoparathyroidism had developed after subtotal parathyroidectomy. When the artificial metabolic conditions of chronic hæmodialysis were followed by the normal renal function after transplantation, serum-calcium fell to extremely low levels. At the same time, the fractional tubular reabsorption of phosphorus far exceeded that usually recorded in patients with good graft function who are being treated with steroids and thiazides.[11]

Recovery from surgically caused hypoparathyroidism has been reported after temporary administration of vitamin D and may even occur " spontaneously ".[12] However, it seems more likely that in the present patient the restoration of normal calcium homœostasis was the consequence of hormone excretion from the graft. Indirect evidence for graft function was obtained from the electron-microscopic pictures of the biopsy specimen. The delay, in effect, could be attributed to the time required for revascularisation and healing of the free, grafted tissue. Efforts to measure parathormone levels in the stored sera from our patient gave results which were not reproducible and were consequently not as useful for following the postoperative course as were other serum levels which measured parathyroid function.

Better techniques for the measurement of parathormone will be invaluable for assessing parathyroid-homograft function. Parathyroid transplantation will probably be indicated in other recipients of renal homografts, since the removal of hyperplastic parathyroid glands to control bone disease is becoming more common. An accident to the residual glandular tissue could lead to the situation which developed in our recipient. Ironically, the best opportunities for obtaining a suitable homograft for such a patient will be provided by other members of the kidney-transplant population.

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