Raised concentrations of plasma atrial natriuretic peptides in cardiac transplant recipients

DONALD R J SINGER, MARTIN G BUCKLEY, GRAHAM A MACGREGOR,
ASGHAR KHAGHANI, NICHOLAS R BANNER, MAGDI H YACOB

Abstract

Plasma atrial natriuretic peptide concentrations were measured by radioimmunoassay six to 77 weeks after operation in eight cardiac transplant recipients with no appreciable evidence of cardiac failure or rejection and in eight control subjects matched for age, sex, race, and blood pressure. Plasma atrial natriuretic peptide concentrations were significantly higher in the cardiac transplant recipients (mean 19.4 (SE 3.9) ng/l) than in the controls (7.3 (1.2) ng/l $p < 0.01$). The mechanisms underlying these raised values were not clear.

These findings suggest that the transplanted atria may secrete atrial peptides and also that innervation is not obligatory for secretion of atrial natriuretic peptides to occur. Before this can be confirmed, however, it remains to be established what the relative contribution of donor and recipient atrial tissue is to the secretion of these peptides.

Introduction

There is increasing evidence that atrial natriuretic peptides are an important hormonal system for the regulation of sodium and water balance.¹ The mechanisms underlying release of atrial natriuretic peptides are not fully understood, however, and, in particular, what if any is the role of autonomic innervation to the atria. In view of the increased amount of atrial tissue present after cardiac transplanta-

tion, as well as the denervation of the donor heart,² we decided to study the plasma atrial natriuretic peptide concentrations of cardiac transplant recipients.

Patients, methods, and results

We studied eight cardiac transplant recipients (six men, two women; all white) with a mean age of 42 years and an average supine blood pressure of 135/90 (SE 4.2/2.5) mm Hg and eight control subjects matched for age, sex, race, and blood pressure (mean age 42 years, average supine blood pressure

Plasma atrial natriuretic peptide concentrations in eight controls and eight cardiac transplant recipients. Bars are means and SE ($p < 0.01$).

Blood Pressure Unit, Department of Medicine, Charing Cross and Westminster Medical School, London W6 8RF

DONALD R J SINGER, BMEDBIOL, MRCP, research fellow
MARTIN G BUCKLEY, BSc, biochemist
GRAHAM A MACGREGOR, MA, FRCP, senior lecturer

Cardiothoracic Unit, Harefield Hospital, Harefield, Middlesex

ASGHAR KHAGHANI, FRCS, senior transplant registrar
NICHOLAS R BANNER, MRCP, research registrar
MAGDI H YACOB, MD, FRCS, professor of cardiac surgery

Correspondence to: Dr Singer.

140/90 (5.1/2.7) mm Hg). All patients were well six to 77 weeks after transplantation, and none showed appreciable evidence of rejection in a cardiac biopsy specimen. One patient had a mild increase in venous pressure. In all patients the plasma creatinine concentration was less than 162 $\mu\text{mol/l}$ (1.8 mg/100 ml). Immunosuppression was with cyclosporin A and azathioprine. Five patients were receiving antiplatelet treatment with low dose aspirin and dipyridamole and two with aspirin alone. Six patients were also receiving vasodilator treatment with either nifedipine or hydralazine. All subjects were studied taking their normal diets. Blood was collected in the morning after 10 minutes' sitting and atrial natriuretic peptides measured by radioimmunoassay after extraction.³

Plasma atrial natriuretic peptide concentrations (figure) were significantly higher in the cardiac transplant recipients (mean 19.4 (SE 3.9) ng/l) than in the controls (7.3 (1.2) ng/l) ($p < 0.01$, unpaired *t* test and Wilcoxon rank sum test).

Discussion

The mechanisms underlying the raised plasma atrial natriuretic peptide concentrations in the cardiac transplant recipients are not clear. Recent studies have reported raised values in patients with congestive heart failure⁴ and high blood pressure.⁵ The single patient in our series with clinical features of cardiac failure, however, had one of the lowest atrial natriuretic peptide concentrations, and the patients and controls were well matched for blood pressure. In human cardiac transplantation the patient's own heart is removed (apart from the inflow tracts of the systemic and pulmonary veins) together with the posterior wall of the left atrium. The entire donor heart including the great vein inflow sites is transplanted, so that there is around a quarter more atrial tissue in the heart after transplantation is complete. This increased atrial tissue mass may have contributed to the raised plasma atrial natriuretic peptide concentrations in our patients. The transplanted

heart is denervated and remains so for many months after operation²; there is, however, residual innervation of the recipient heart.

From this study alone it is not clear to what extent denervation of the donor atrial tissue may have been responsible for the raised atrial natriuretic peptide concentrations. There was considerable variation among the patients in the concentration of plasma atrial natriuretic peptides, which was not related overtly to cardiac function, arterial pressure, plasma creatinine concentration, or type of drug treatment. These findings seem to suggest that the transplanted atria are secreting atrial peptides. In addition, these results appear to show that in man as well as in other species⁵ innervation is not obligatory for atrial natriuretic peptide secretion to occur. Nevertheless, this cannot be established from our study. To do so will require further studies to determine the relative contribution of donor and recipient atrial tissue to atrial natriuretic peptide secretion.

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Dialysis arthropathy: amyloid or iron?

N R B CARY, D SETHI, E A BROWN, C C ERHARDT, D F WOODROW, P E GOWER

Abstract

The clinical, biochemical, radiological, and pathological features in five cases of dialysis arthropathy were analysed. All patients were receiving long term haemodialysis and had had multiple blood transfusions. The arthropathy affected both large and small joints, was predominantly bilateral, and in all cases was associated with the carpal tunnel syndrome. In some instances joint pain was exacerbated during dialysis. In four cases the serum ferritin concentration was raised. Radiological examination showed a few juxta-articular cysts and erosions but most affected joints looked normal. All synovial tissue examined showed amyloid, which stained immunohistochemically for β_2 microglobulin. Large amounts of iron were present in synovial tissue from affected joints.

It is suggested that the deposits of iron, rather than amyloid, in synovial tissue may be the cause of the arthropathy. Iron may be derived locally as a result of haemarthrosis or it may be a manifestation of systemic iron overload.

Introduction

Dialysis arthropathy is a complication of long term haemodialysis.¹⁻³ It is predominantly bilateral, affecting both large and small joints, and is strongly associated with recurrent carpal tunnel syndrome. The cause is unknown but recent reports have emphasised the presence of amyloid in carpal tunnel tissue, bones, and synovium from affected joints.^{4,5} In the case of carpal tunnel tissue this amyloid has been characterised biochemically as β_2 microglobulin,⁶ probably derived from high circulating concentrations. The questions remain, however, whether the finding of amyloid in these joints is incidental and whether there is some other cause for the arthropathy.

Patients, methods, and results

We investigated five patients, who were representative of around 30 patients with dialysis arthropathy being studied. They underwent rheumatological assessment using a detailed form and were the first to have synovial tissue examined histologically. None had evidence of systemic amyloidosis.

Charing Cross and Westminster Medical School, London W6 8RF

N R B CARY, MA, MB, senior registrar, department of histopathology
D SETHI, MB, MRCP, research fellow, department of medicine
E A BROWN, DM, MRCP, senior registrar, department of medicine
C C ERHARDT, MD, MRCP, senior registrar, department of rheumatology
D F WOODROW, MB, PHD, senior lecturer, department of histopathology
P E GOWER, MD, FRCP, consultant physician, department of medicine

Correspondence to: Dr Cary.