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Transplantation and erectile dysfunction— is there a causative relationship?

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Using a comprehensive approach, 14 patients with renal transplants, two patients with combined renal and pancreas transplants and one patient each with a heart and single lung transplant were evaluated for erectile dysfunction. Erectile dysfunction was prevalent prior to transplantation in seven patients. Only one patient improved postoperatively. In 11 patients erectile dysfunction developed up to 10 years after transplantation, in seven there was a direct coincidence with the surgical procedure. Hormonal alterations were found in ten patients, arterial blood supply was compromised in four patients and five patients had abnormal venous drainage. Ten patients showed abnormal SPACE patterns, indicating autonomic dysfunction. All patients received a standard triple-regimen immunosuppression and six patients received antihypertensive medication. Erectile dysfunction in transplant patients is a problem of multifactorial origin, since pharmacologic, endocrine, neurogenic, vascular and psychogenic causes seem to play a significant role. A comprehensive work-up and a highly individualized therapy is necessary in this heterogenic group of patients.

Key words: impotence; transplantation; aetiology; diagnosis.

INTRODUCTION

Only few data are available about the prevalence of erectile dysfunction in the normal population¹. In patients with diabetes the prevalence of erectile dysfunction may be as high as 50%². Erectile dysfunction is also a relatively common finding in patients with chronic renal insufficiency and in dialysis patients³. Although there are only occasional reports in the literature, erectile dysfunction is also a common finding in transplant patients. The aetiology remains to be poorly understood, however, a multifactorial aetiology of vascular, metabolic, neurogenic, pharmacologic, endocrine and psychogenic aspects seems to be likely.

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This article reviews our experience with renal, heart, pancreas and lung transplant patients who underwent evaluation for erectile dysfunction.

PATIENTS AND METHODS

Fourteen renal, two combined renal/pancreas, one heart and one lung transplant patients were evaluated for erectile dysfunction. The mean age was 50.7 years (range 34–70). Two renal transplant patients had a second transplant 3 and 6 years after the first procedure. The mean time on dialysis (renal transplant patients) was 31.7 months (range 12–60 months). The mean time after surgery was 54.5 months (range 12–136 months). At the time of the study the transplants were functioning well in all patients. A comprehensive work-up consisted of a detailed history and physical examination, laboratory tests (CBC, electrolytes, BUN, creatinine, serum testosterone, estrogens, FSH, LH and prolactin), penile Doppler pharmaco-ultrasonography, intracavernosal pharmacotesting with vasoactive drugs, Rigi-Scan® real time monitoring under audiovisual sexual stimulation and single potential analysis of cavernous electrical activity (SPACE)⁴.

In one patient with primary erectile dysfunction and six patients with secondary erectile dysfunction impotence was present prior to transplantation. In 11 patients impotence developed after transplantation. All patients received a standard triple-regimen immunosuppression (cyclosporine, glucocorticoids, azathioprine). Anti-hypertensive medication was given in six patients (β -blocker in three patients, calcium channel blockers in three patients, angiotensin converting enzyme inhibitors in two patients, clonidine in one patient). Table 1 summarizes the predisposing factors for erectile dysfunction.

For intracavernosal pharmacotesting a mixture of papaverine and phentolamine (papaverine hydrochloride 15 mg/ml and phentolamine mesylate 0.5 mg/ml) was used in increasing doses up to a maximum of 2 ml. The responses were classified as follows: E0 no tumescence, E1 slight tumescence and no rigidity, E2 medium tumescence and no rigidity, E3 full tumescence and no rigidity, E4 full tumescence and medium rigidity, E5 full rigidity.

For SPACE evaluation a coaxial needle electrode (Dantec 9013 L) was inserted laterally into the cavernous body and advanced until the tip of the electrode was located centrally. The signals were processed by different electrophysiological units (WIEST SPACE; Dantec Neuromatic 2000), displayed continuously on a monitor

TABLE 1. Predisposing factors in 18 patients with renal, renal/pancreas, heart and lung transplants.

Renal failure	16	Hypertension	11
Diabetes mellitus	3	Peripheral vascular disease	2
Coronary artery disease	2	DVIU	2
Cardiomyopathy	1	TUR-P	1
Lumbar disc surgery	1	Peyronie's disease	1
Alcoholic abuse	1	Nicotine abuse	1
Depression	1	Peripheral neuropathy	1

DVIU—direct vision internal urethrotomy.

TUR-P—transurethral resection of the prostate.

screen (Dantec 2000, Tektronix) and simultaneously recorded (WIEST SPACE; Dantec 2000). The signals were analysed as described elsewhere⁴.

In six patients in whom a venous leak was suspected after completion of the noninvasive work-up, pharmacocavernosometry and -graphy was performed for evaluation of the venous occlusive system.

Rigi-Scan® monitoring and penile Doppler pharmaco-ultrasonography was performed as described elsewhere^{5,6}.

RESULTS

Physical examination of the genitalia was normal except in one patient with Peyronie's disease and one patient who developed an atrophic left testicle after transplantation of a renal transplant into the left iliac fossa. Oestrogen levels were slightly to moderately elevated in eight patients, testosterone levels were decreased in three patients and prolactin levels were slightly increased in three patients.

All patients showed abnormal results with Rigi-Scan® monitoring. Penile Doppler pharmaco-ultrasonography was normal in 14/18 patients, indicating intact arteriogenic blood supply. In the heart transplant patient both profunda arteries had decreased signal intensities with intact dorsal arteries. In three renal transplant patients the left profunda artery, right dorsal/right profunda artery and left profunda artery had decreased signal intensities, respectively.

Intracavernosal pharmacotesting with papaverine-phenolamine showed good functional results in 12 patients (nine patients E5, three patients E4). In four patients

TABLE 2. Response to pharmacotesting with papaverine/phenolamine and management in 18 transplant patients.

Patient (age)	Transplant	Pharmacotesting (ml p + p → response)	Management
64	renal	2→E3	Cavernosometry, -graphy
49	heart	0.5→E5	Autoinjection (0.5 ml)
51	renal	1→E5	Autoinjection (1 ml)
48	renal	1→E5	Autoinjection (1 ml)
45	renal/pancreas	1→E5	Autoinjection (0.5 ml)
70	renal	0.2→E5	Autoinjection (0.2 ml)
38	renal/pancreas	2→E2	Cavernosometry, -graphy
33	renal	2→E2	Cavernosometry, -graphy
58	lung	0.5→E5	Autoinjection (0.5)
59	renal	1→E4	Autoinjection (1 ml)
50	renal	1→E4	Autoinjection (1 ml)
51	renal	0.5→E5	Autoinjection (0.5 ml)
43	renal	1→E4	Autoinjection (1 ml)
47	renal	2→E2	Cavernosometry, -graphy
47	renal	1→E5	Autoinjection (SIN 1)
51	renal	2→E2	Cavernosometry, -graphy
36	renal	0.2→E5	Yohimbine, psychotherapy
44	renal	2→E3	Cavernosometry, -graphy

p + p — papaverine/phenolamine.

SIN 1 — Experimental nitric oxide donor.

TABLE 3. SPACE patterns, cavernosometric and -graphic results and management in six transplant patients with suspected venous leakage.

Patient (age)	SPACE	MF (ml)	Leakage	Ligation	Functional result after surgery	Management
64	Abnormal	30	Dorsal	+	No improvement	Autoinjection (CGRP→E4)
47	Abnormal	140	Dorsal, ectopic	+	No improvement	Prosthesis
51	Normal	65	Dorsal, ectopic	+	Full erection (E5)	Follow-up
33	Normal	80	Dorsal, ectopic	+	Improvement	Autoinjection (0.2 ml p+p→E5)
44	Abnormal	80	Dorsal, ectopic refused	—	—	Autoinjection (CGRP→E5)
38	Abnormal	10	—	—	—	Autoinjection (CGRP→E5)

MF—maintenance flow.

CGRP—calcitonin-gene related peptide.

p+p—papaverine/phentolamine.

with E2 and two patients with E3 responses a venous leak was suspected and pharmaco-cavernosometry and cavernosography was performed (Table 2).

Table 3 summarizes the cavernosometric and cavernosographic findings. Four of five patients, in whom a venous leak was diagnosed, underwent a venous ligation procedure. One patient had full erections after the procedure and one patient converted to a responder to autoinjection therapy with papaverine/phentolamine, another patient showed good results with calcitonin-gene related peptide (CGRP) injections. One patient failed pharmacotherapy and underwent implantation of a semirigid penile prosthesis. One patient who refused venous surgery, and another patient who did not show a venous leakage had full erections with CGRP.

Ten patients showed abnormal and eight patients showed normal SPACE patterns. Of the six patients in whom venous leakage was suspected after the standard work-up, two had normal SPACE patterns (Table 3); one of these two patients had a good postoperative result, the other patient converted to an autoinjection responder (to papaverine/phentolamine). Of four patients with abnormal SPACE patterns, two underwent a ligation procedure and failed (meanwhile one of whom received a penile prosthesis). Three patients were started on CGRP and showed a good response.

DISCUSSION

Erectile dysfunction in transplant patients seems to be caused by multiple aetiologies. Metabolic, endocrine, pharmacologic, vascular, neurogenic and psychogenic factors have been implicated^{7,8}. Metabolic factors do not seem to be most important, since preoperative erectile dysfunction in five renal transplant patients improved only in one patient. Interestingly, erectile dysfunction developed or worsened in three patients after TUR-P and direct-vision internal urethrotomy, indicating a significant impact of an additional surgical trauma on these 'borderline' patients.

In seven patients there was a coincidence between transplant surgery and the development of erectile dysfunction. In one of these patients unilateral testicular atrophy occurred; however, the hormone status was normal in this patient. The coincidence between transplant surgery and erectile dysfunction may be explained by pharmacological side-effects, since there is evidence that cyclosporine causes sympathetically-mediated elevations in arterial blood pressure⁹. An elevated sympathetic tone may influence the physiological response of the cavernous smooth muscle to sexual stimuli, causing a contraction of the cavernous smooth muscles. In addition, most patients receive β -blocker for treatment of hypertension, of which erectile dysfunction is a common side-effect¹⁰.

Abnormalities in the hormone status were detected frequently in our patient population. Hyperprolactanaemia, usually exceedingly rare in the normal population, was found in three patients. An elevation of total oestrogens, and a reduction of testosterone, was detected in eight and three patients, respectively. Oestrogen and testosterone abnormalities have been studied in uraemic patients and seem to be caused by an impairment of Leydig cell function^{11,12}. High prolactin levels also seem to be related to renal failure and haemodialysis¹³.

Five of six patients, in whom a venous leak was suspected after pharmacotesting, indeed showed malfunction of the veno-occlusive system in cavernosometry. Of four patients who underwent a venous ligation procedure two improved, both of whom had normal SPACE patterns. Both patients with abnormal SPACE patterns did not improve. These findings, yet in a very limited number, support the assumption that SPACE may prove to be a valuable diagnostic tool to differentiate 'true' venous leakage from cavernous myopathy, as suggested recently¹⁴.

Another important factor is the blood supply to the cavernous bodies. It has been reported that anastomoses to the hypogastric artery can cause erectile dysfunction due to a 'steal' phenomenon^{8,15}. Of four patients with diminished blood supply, as documented by Doppler pharmaco-ultrasonography, one patient was a heart transplant patient and three were renal transplant patients, of whom one patient had a second transplant with anastomosis to the hypogastric artery. Finally, the psychological impact of serious illnesses on erectile function cannot be overestimated.

Our results show erectile dysfunction after transplantation to be a problem of various aetiologies. Therefore, a comprehensive approach must be used in these patients, since a correlation to a direct aetiology could not be found. Further studies are needed to improve our understanding of the pathophysiology of erectile dysfunction in transplant patients.

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