ACUTE RENAL FAILURE, EOSINOPHILIA THROMBOCYTOPENIA AND EXPLIATIVE DERMATITIS ASSOCIATED WITH CAPTOPRIL THERAPY

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SYNOPSIS

A case of acute renal failure associated with captopril administration is reported. A man, age 62 with two-year history of mild renal impairment and hypertension was treated with captopril fro drug-resistant hypertension. The patient developed eosinophilia, thrombocytopenia, exfoliative dermatitis, and rapid deterioration of renal function after three weeks of captopril therapy. The renal biopsy was compatibie with acute tubular necrosis with pre-existing nephrosclerosis. The association of acute renal failure, eosinophila, thrombocytopenia, and exfoliative dermatitis constitutes an uncommon presentation of complications related to captopril therapy.

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INTRODUCTION

Captopril, and angiotensin I converting enzyme inhibitor, has been successfully used in the treatment of severe hypertension and congestive heart failure(1,2). However, as experience with this drug increases, a number of side-effects have been apparent: pruritis, skin rash, and less commonly, agranulocytosis, nephrotic syndrome and renal insufficiency(3,4). Acute renal insufficiency often occurs in patients with severe renal artery stenosis(5).

We report a patient with hypertensive nephrosclerosis who developed acute tubular necrosis after treatment with captopril. The association of acute renal failure, eosinophilia, thrombocytopenia, and exfoliative dermatitis constitutes an uncommon presentation of complications related to captopril treatment.

CASE REPORT

A 62 year old male with a two year history of hypertension and chronic renal failure was admitted to a community hospital with congestive heart failure. His hypertension and congestive heart failure were initially treated with furosemide (80 mg daily) and methyldopa (500 mg thrice daily). Administration of captopril (25 mg twice daily) was then begun because of uncontrolled hypertension and was increased to 50 and 75 mg thrice daily during the second and third weeks of catopril therapy. Methyldopa was ceased on the same day when catopril therapy was introduced, The complete blood picture prior to catopril therapy revealed: haemoglobin 11.1 gm%, normochromic and normocytic blood picture, leuccocyte count 7500/mm3, and platelet count 189,000/mm3. His serum creatinine and creatinine clearance were 189 umol/l and 39 ml/min respectively prior to captopril treatment. The renal function began to deteriorate after 20 days of catopril therapy and the serum creatinine rose to 505 umol/l at the beginning of third week of catopril treatment. There was no clinical event to suggest septicaemia, haemorrhage or hypotension leading to severe ischaemic insult to the kidneys during this period. The patient was then transferred to this hospital for further management.

On admission, he had a blood pressure of 120/80 mmHg, a regular pulse rate of 100 beats per minute, and a normal temperature of 36.7°C. No abdominal bruit was detected. Laboratory test revealed the following abnormal results: hemoglobin 8.8 gm%, leucocyte count 6800/mm³ with a total eosinophil count of 850, platelet count 75,000/mm³, blood urea nitrogen 32.5 mmol/l, serum mol/Kg. Urinalysis revealed a specific gravity of 1.010. trace protein, negative findings for glucose, five to eight white blood cells and 25 nonglomerular red blood cells per high power field, brownish granular casts and cellular debris and urine osmolatity 315 mosmol/Kg. Ultrasound of the kidnerys revealed normal sizes with no obstruction. A DTPA radionuclide renal scan showed suggestion of acute tubular necrosis with no evidence of unilateral arterial occlusive disease.

Four days after admission, he developed a diffuse, whole-body maculopapular rash. The rash progressed to extensive exfoliative dermatitis with involvement of the muco-cutaneous junctions including conjuctiva, oral cavity, urethra and anus. The captopril therapy was dis continued immediately. The exfoliative dermatitis improved slowly over the following two weeks with cessation of captopril therapy and corticosteriod therapy and the eosinophilia and thrombocytopenia improved simultaneously. The renal function continued to deteriorate despite the discontinuation of captopril dialysis because of

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uraemic symptoms. The patient died of bronchopneumonia ten days later.

A post-mortem renal biopsy revealed features of nephrosclerosis with tubular necrosis and mild interstitial fibrosis. Except for mild intimal thickening, the vessels were not remarkable. The immunofluorescent studies revealed no immunoglobulins nor complement depostion. The electron microscopy revealed wrinkling of glomerular basement membrane and loss of brush borders in the tubular cells. The overall interpretation was that the patient had acute tubular necrosis complicating nephrosclerosis. Significant renal artery stenosis was not found on post-mortem examination.

DISCUSSION

Captopril induced acute renal failure is uncommon. Apparently, this is more frequently ecountered in patients with severe renal arterial disease(5) and the renal failure is not uncommonly reversible(6).

The cause of captopril-induced acute renal failure remains controversial. An immunoallergic mechanism has been suggested by the frequent presence of fever and skin rash and in one patient patchy atrophy and inflammation were documented by renal biopsy(3). The other possible mechanism is hypotension-mediated acute tubular necrosis and this has been documented by renal biopsy in two patients(7,8). The renal biopsy of our patient revealed two pathologies, namely, nephrosclerosis and acute tubular necrosis. There was no evidence of allergic acute interstitial nephritis despite the clinical presentation of a drug reaction. Although severe hypotension and hypovolaemia did not occur in our patient, the combination of angiotensin I converting enzyme inhibitors and loop-diuretics may result in significant reduction of glomerular filtration in the hypoperfused kidneys hence resulting in acute tubular necrosis(8).

The occurrence of exfoliative dermatitis and acute renal failure complicating captopril therapy is extremely rare. Luderer and coworkers(9) reported a patient who developed haemolytic anaemia, diffuse maculo-papular rash, and acute renal failure with captopril therapy but renal biopsy was not performed. Steinman and Silva(7) described a patient with eosinophilia, acute tubular necrosis, and skin rash complicating captopril therapy. Lethal infected exfoliative dermatitis and irreversible renal failure has only been reported in one patient(4). The presentation of our patient with eosinophilia thrombocytopenia, exfoliative dermatitis and acute tubular necrosis has not previously been described with captopril therapy. The multi-system involvement would suggest that both immunoallergic and ischaemic mechanism operate in the complications related to captopril therapy.

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