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Częściowy powrót funkcji nerek u pacjentów leczonych przewlekłą dializoterapią

Streszczenie

Wstęp. Całkowity lub częściowy powrót funkcji nerek (RFR) u pacjentów leczonych hemodializami (HD) lub dializą otrzewnową (PD) obserwuje się stosunkowo rzadko. RFR zależy w dużym stopniu od pierwotnej choroby, prowadzącej do wystąpienia schyłkowej niewydolności nerek (ESRD); najczęściej są to: układowe zapalenia naczyń, choroby immunologiczne przebiegające z zajęciem nerek, pierwotne nadciśnienie złośliwe.

Cel. Celem pracy był opis przypadków 3 chorych z niewydolnością nerek wymagającą leczenia nerkozastępczego (RRT), u których po zastosowanym leczeniu immunosupresyjnym, obserwowano znaczną poprawę funkcji nerek i przerwano leczenie dializoterapią.

Materiał i metody. Obserwacje przeprowadzono u trojga pacjentów ze schyłkową niewydolnością nerek. Przyczyną schyłkowej niewydolności nerek w dwóch przypadkach było zaostrzenie układowego zapalenia naczyń z obecnością przeciwciał p-ANCA lub c-ANCA, w trzecim przypadku, zaostrzenie tocznia trzewnego (SLE) przebiegające z zajęciem nerek. U wszystkich pacjentów równocześnie z dializoterapią stosowano leczenie immunosupresyjne, a u dwóch chorych wykonywano także zabiegi plazmaferezy.

Wyniki. w następstwie zastosowanego leczenia u wszystkich chorych uzyskaliśmy znaczącą poprawę funkcji nerek, umożliwiającą odstąpienie od leczenia nerkozastępczego (RRT): w dwóch przypadkach przejściowego zaniechania dializoterapii otrzewnowej, w jednym przypadku stałego zaprzestania leczenia powtarzalnymi hemodializami.

Wnioski. Jednoczasowe stosowanie obok przewlekłej dializoterapii intensywnego leczenia immunosupresyjnego u chorych cierpiących na aktywne układowe zapalenia naczyń lub toczeń trzewny może skutkować poprawą funkcji nerek i możliwością zaprzestania dializoterapii. w naszej obserwacji powrót funkcji nerek stwierdzono częściej u chorych dializowanych otrzewnowo niż hemodializowanych.

Słowa kluczowe: powrót funkcji nerek, dializoterapia, zapalenie naczyń, toczeń trzewny, nadciśnienie złośliwe.

Partial recovery of renal function in patients treated by chronic dialysis

Abstract

Introduction. Renal function recovery (RFR), either complete or partial, in hemodialyzed (HD) or peritoneal dialyzed (PD) patients, is observed rather rarely. To a large extent it depends on primary disease leading to end-stage renal disease (ESRD), such as vasculitis, immunological disease associated with renal involvement, and primary malignant hypertension.

Aim. The aim of our study was presentation of three patients with end-stage renal disease (ESRD), needing renal replacement therapy (RRT). After immunosuppressive treatment performed in all patients, recovery of renal function was observed. The RRT was stopped in all patients.

Material and methods. The study was performed in three patients with end-stage renal disease. In two of three described cases the cause of ESRD was p-ANCA or c-ANCA positive vasculitis. In the third one the cause of ESRD was systemic lupus erythematosus (SLE) with renal involvement. In all described cases immunosuppressive therapy was performed parallelly to dialysotherapy. In two patients plasmapheresis was carried out as well.

Results. As a result of applying immunosuppressive treatment, together with renal replacement therapy, we obtained in all patients significant improvement in renal function, enabling us to withdraw them from the renal replacement therapy (RRT): in two cases of the transitional omission of peritoneal dialysotherapy, in one case of permanent ceasing of the treatment with repeatable haemodialyses.

Conclusions. Simultaneous application of chronic dialysis and intensive immunosuppressive treatment in patients suffering from vasculitis or systemic lupus erythematosus may lead to renal function recovery and to possibility to stopping dialysotherapy. In our study we observed renal function recovery more often in PD than in HD patients.

Key words: renal function recovery, dialysis, vasculitis, systemic lupus erythematosus, malignant hypertension.

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INTRODUCTION

The review of the literature suggests that complete or partial renal function recovery (RFR) in patients treated with haemodialyses (HD), or with peritoneal dialysis (PD) is relatively rarely observed [1-3]. It concerns most often the patients with systemic inflammations of small vessels (p-ANCA, and c-ANCA) running with renal involvement of violent glomerular nephritis; with primary malignant hypertension; with immunological illnesses like systemic lupus erythomatosus (SLE); with double-sided necrosis of the cortex of kidneys; infarction of the kidney and interstitial nephritis [2,4-6]. Exceptionally, RFR has rarely been observed in patients dialysed due to polycystic kidneys disease (0.1%) or diabetic nephropathy (0.4%) [2]. We are describing 3 cases, in which after applying the immunosuppressive treatment, a significant improvement in the renal function was observed and the dialysotherapy treatment was discontinued. In two cases the onset of the systemic vasculitis was the cause of the end-stage renal disease development (c-ANCA and p-ANCA); in third - the result was the advancing lupus nephropathy. In the described cases simultaneously with dialysotherapy, an immunosuppressive treatment was applied, and in 2 patients also plasmapheresis was applied. The obtained remission in 1 of 3 patients still continues. In two remaining patients, because of considerable worsening of the renal function a renal replacement therapy was commenced again.

AIM

The purpose of our study was the description of cases of three patients with kidney failure in the course of the systemic vasculitis or visceral lupus, requiring the treatment with renal replacement therapy (RRT), in whom after the application of immunosuppressive treatment, a major improvement of renal function was observed and dialysoptherapy was discontinued.

MATERIAL AND METHODS

Case 1

A 27-year-old woman was admitted to hospital in London in September 2006, with the diagnosis of erythrocyturia was stated, as well as with twenty-four hour proteinuria of 5.6g, and the presence of antinuclear antibodies (ANA) in titre of 1:640 and of anty-dsDNA antibodies - 1:820. Articular pains, raised temperatures and hypertension were being monitored, and in USG scan the kidneys were of the correct size. On account of the escalating renal impairment in November 2006, a renal biopsy was performed. The picture of „proliferative crescentic GN with positive crioglobulines" was stated. Systemic lupus erythematosus was diagnosed (SLE). The treatment with plasmaphereses and intravenous Endoxan (cyclophosphamide) infusions was undertaken. The treatment was continued applying Metypred (methylprednisolone) orally. The twenty-four hour diuresis was c 1500 ml. In December 2006, the patient reported to Nephrology Department in Lublin with features of the escalating renal insufficiency: urea 24.2 mmol/l (N: 2.5-6.7 mmol/l), creatinine 358 mmol/l (N: 60-130 mmol/l), enumerated scope of the glomerular filtration rate (eGFR) according to the MDRD formula amounted to 13.4 ml/ min/ 1.73 m^2, with significant anaemia (Hgb 4.88 mmol/l, Hct 0.22) and with high values of the blood pressure. Also a lowered level of the C 3 fraction of complement was stated - 81.3 mg/dl (N: 93-188mg/dl) with the correct C 4 level. USG scan of kidneys revealed their correct size and the preserved corticospinal structure. Following the activity of disease, consecutive doses of Endoxan i.v. were administered to the patient. Erythropoietin was included too. The increase in the level of urea to 37.9 mmol/l and creatinine to 527 mmol/l with the eGFR decline to 8.6 ml/min/1.73 m^2 made the personnel decide about beginning of peritoneal dialysotherapy.

The earlier immunosuppressive treatment resulted in the fall in the level of antibodies of the ds-DNA to the value of 1:40. In performed immunologic examinations p-ANCA the presence of antibodies wasn't stated, nor of c-ANCA, anty-dsDNA, antinuclear antibodies (ANA) or of antiphospholipid antibodies. Endoxan treatment was continued to July 2007, applying monthly intravenous infusions. Then correct values of the C 3 fraction and C 4 of the complement were stated. Dying down of the immunological activity of disease accompanied an improvement in the renal function; a twenty-four hour diuresis was continued above 2000 ml. After 13 months from commencing the treatment of renal replacement therapy (RRT),with the level of creatinine of 132 mmol/l, and urea of 11.3 mmol/l (eGFR- 43.1 ml/min/1.73 m^2), a decision was made to cease the dialysotherapy. Advancement of disease came after 18 months of the clinical and immunologic remission, with considerable worsening of the renal function and the necessity of the patient's return to the peritoneal dialyses program.

Case 2

A 54-year-old woman was admitted to the Nephrology Department in March 2004. Previously, the patient had been hospitalized in the medical ward of the regional hospital due to the infection of the upper respiratory tract and articular pains. Then, the increased parameters of the renal function were stated: urea ranging from 6.5-14.8 mmol/l; creatinine 206-246 mmol/l, twenty-four hour diuresis of c 1800 ml. Proteinuria of the value of 0.78g/day was monitored, increase of blood pressure value to 170/100 mmHg and anaemia: Hgb 5.81 mmol/l, Hct 0.28 with the correct leucocytosis: 7.4 x 109/l. In the urinalysis, leucocytes and areas filled with leached erythrocytes were stated. The eGFR value accounted according to MDRD formula was 18.7 ml/ min/1.73 m^2. The culture of urine, ASO and the Waaler-Rose reaction were negative. USG scan of the abdominal cavity revealed kidneys of correct echostructure and erased corticospinal diversity. The patient with the suspicion of an acute renal failure in the course of acute glomerulonephritis was moved to the Nephrology Department. Gradual advancement of kidney failure was observed (creatinine 306 mmol/l, urea 14.4 mmol/l) with increased anaemia requiring transfusion of erythrocyte mass, persistence of elevated values of the blood pressure. In the sediment of urine: insignificant proteinuria, leucocyturia and erytrocuturia (fresh erythrocytes and leached ones) were observed. a further decline in

eGFR value was registered to the level 15.1 ml/min/1.73 m^2. After moving to our department, it was revealed that the patient since December 2003 had already suffered from raised temperature, decrease of the body weight, reduced appetite and articular pains. Quickly progressing decline of the diuresis, increase of urea to 24.5 mmol/l and of creatinine to 1229 mmol/l, and anaemia, forced us to commence dialysotherapy. The eGFR level was 4.1 ml/min/1.73 m^2 then. In the performed immunological examinations, positive values of p-ANCA antibodies and the presence of antibodies against the glomerular basement membrane (anty-GBM) in the titre of 1:160 were stated.

In view of the situation the patient underwent 3 plasmaphereses, as well as intravenous infusions of Endoxan and Solu-Medrol (methylprednisolone hemisuccinate) were given. The renal function didn't improve so the decision was made to commence for the treatment with peritoneal dialyses along with monthly Endoxan pulses and oral Encorton (prednisone) therapy.

A twenty-four hour diuresis of c 1700 ml and normalization of the blood pressure were obtained along with the gradual improvement in the renal function: concentration of creatinine and urea were 221 mmol/l and 10.7 mmol/l, respectively and eGFR was 21.9 ml/min/1.73 m^2. Since May 2005 to March 2007, because the acceptable parameters of renal function were kept, the patient wasn't dialysed. In March 2007, the creatinine level suddenly increased to 618.8 mmol/l; urea to 34.5 mmol/l; Hgb level decreased to 5 mmol/l and Hct – to 0.23. It was connected with a rise in blood pressure values to 160/100 mmHg. The 24-hour diuresis also decreased to 700-800 ml. The eGFR value was reduced to the level of 6.4 ml/min/1.73 m^2. Relapse of the renal function followed after the episode of an infection of the upper respiratory tract. In USG scan distinct reduction of the size of kidneys was stated. Peritoneal dialysis with the use of a cycler was started. Due to mycotic peritonitis in October 2009 the patient was transferred to the haemodialysis. The next episode of severity of the disease with the massive intra-alveolar bleeding was the cause of death of the patient in March 2010.

Case 3

A 32-year-old man was admitted to the Nephrology Department due to violent progression of chronic nephropathy in the course of the vasculitis with the presence of c-ANCA antibodies. On admission to our department, the patient reported myalgias, the progressing weakness and the increased perspiration. Physically high blood pressure, slight swelling of lower limbs, raised temperature, and small-blemished rash on the skin of the torso and lower limbs were stated. The 24-hour diuresis was c 2000 ml, eGFR 10.81 ml/min/1.73 m^2. We also observed anaemia (Hb 5.93 mmol/l), leucopenia (3.5x109/l), daily proteinuria of 1.36g and hyperpotasemia (6.6 mmol/l). In USG scan, kidneys were of normal size and presented hyperechogenic cortex. On account of the advanced kidney failure with accompanying hyperpotasemia, hemodialisotherapy was decided instantly. Systemic vasculitis with the c-ANCA presence of antibodies of titre 93.98 U/ml (met. ELISA) had been recognized in patient 10 months earlier in other medical condition. Then chronic nephropathy was stated (eGFR value was 43.6 ml/min/ 1.73 m^2, according to MDRD formula). The patient was treated with pulses of Solu-Medrol with the continuation of orally given Metypred. The treatment was suspended for unknown for us reasons.

In view of continuing features of the immunological disease activity with the c-ANCA presence of antibodies in the titre of 20.30U/ml, a decision about resuming the immunosuppressive treatment was undertaken. a pulsating treatment with Solu-Medrol with Endoxan and then oral continuation with Encorton was applied. After 3 weeks a distinct improvement in the general state and the renal function was obtained. The diuresis took out c 2500 ml/day, whilst eGFR indicated a value of 53 ml/min/1.73 m^2. The patient didn't require dialysotherapy any more; he was treated with Endoxan i.v. pulses and orally given Encorton.

Unfortunately after the 3rd Endoxan pulse an essential leucopenia developed which forced us to cease that. After 6 months, a relapse of the renal function (eGFR 13.7 ml/ min/ 1.73 m^2) with the fall in the diuresis below 1500 ml/day was observed. For the second time a treatment with haemodialyses was commenced. The return to the monthly pulsating treatment with steroids was performed, obtaining the next clinical remission: after 3 months the treatment with haemodialyses was ceased; the renal function was essentially improved – eGFR value increased to 50 ml/min/1.73 m^2, but the level of c-ANCA antibodies still remained high at the value of 16.1 U/ml. The remission in this patient is still lasting. The renal function is stable, with the eGFR equal 57 ml/ min/1.73 m2. The diuresis is about 2500 ml/day. The patient is being treated at present with the custom therapeutic method with the application of Cell-Cept (mofetil mycofenolate) in a dose of 2 x 1 g/day and doesn't need renal replacement therapy (RRT).

RESULTS

As it was presented above, in the process of long-term observation of three patients with kidney failure, requiring the treatment with renal replacement therapy (RRT), as a result of the applied immunosuppressive treatment, in all the patients we obtained significant improvement in the renal function, enabling us to withdraw from the renal replacement therapy: in two cases of the transitional omission of peritoneal dialysotherapy, in one case of permanent ceasing of the treatment with repeatable haemodialyses.

DISCUSSION

The authors who analysed a large number of patients treated with dialysotherapy, think that the renal function recovery (RFR) fluctuates in the ranges of 1%-2.8% [1-3,7] (Table 1) Lindblad and Nolph [2] analysing retrospectively 23771 CAPD treated patients in the United States observed RFR at 281 patients which accounts for 1.2%. Craven et al. obtained similar results [1] with a group of 24663 patients treated with the peritoneal dialysis in which RFR was observed in 253 individuals (1%). Cancarini et al. studies differ from the above results [8]. They demonstrated RFR in as many as 8% of the dialysed patients. Such a high score was a result of the lack of uniform criteria of RFR recognition. Authors

TABLE 1. Partial recovery of renal function in patients treated with peritoneal dialysis – literature review.

	Authors	Literature source	Number of patients treated with peritoneal dialysis	Partial renal function recovery
1	Cancarini GC et al.	Perit Dial Bull. 1986;6:77-9	75	(8%)
2	Rottembourg J. et al.	Perit Dial Int. 1989;9:63-6	300	(3.3%)
3	Michel C. et al.	Nephrol Dial Transplant. 1989;4:499-500	198	(4.5%)
4	Michel C. et al.	Nephrologie. 1989;10:suppl. 53-5	400	(3.9%)
5	Sekkarie MA et al.	Am J Kidney Dis. 1990;15:61-5	7860	(2.8%)
6	Lindblad AS, Nolph KD	Perit Dial Int. 1992;12:43-7	23771	(1.2%)
7	Goldstein et al.	Perit Dial Int. 2003;23:151-6	1200	(2.4%)
8	AM S. Craven et al.	Perit Dial Int. 2007;27:184-91	24663	(1%)

included in this group 2 patients with diagnosed acute glomerular nephritis, complicated by acute renal failure. RFR depends to a large extent on the primary illness leading to the end-stage renal disease. These are systemic vasculitis, running with immunological affecting of kidneys, primary malignant hypertension and other more rarely appearing problems. In two of our patients, kidney failure was a result of the vasculitis connected with the c-ANCA or p-ANCA antibodies presence.

As a result of the applied immunosuppressive treatment including plasmaphereses, a significant improvement in the renal function was obtained. The affected kidneys in the vasculitis with the ANCA antibodies presence were named "ANCA associated glomerulonephritis". At present a governing classification of inflammations was drawn up on the basis of International Consensus Conference held in 1994 in Chapel Hill. Four disease types were included to inflammations associated with the development of ANCA antibodies and affecting kidneys: Wegener's granulomatosis, microscopic polyangitis (MPA), Churg-Strauss syndrome (CCS) and pauci-immune crescentic necrotizing glomerulonephritis. Before implementing the immunosuppressive treatment, the patients usually died after a few months since establishing of the diagnosis [9]. Treatment of systemic inflammations is one of the most important challenges of contemporary medicine. The outlines of treatment have changed fundamentally over the last years. However, the standard therapy still depends on combining application of prednizolone and cyclophosphamide [10]. The cyclophosphamide is also an essential element of therapy associated with other immunosuppressive agents (azathioprine, tacrolimus, mofetil mycophenolate). In most difficult cases of vasculitis, affecting lungs and kidneys, immunosuppressive treatment is joined with the plasmapheresis [11-14]. Hauer et al. [10] demonstrated that the improvement in the renal function and the withdrawal from dialysotherapy appears mainly in patients, in whom in the biopsy of the kidney, active changes are stated. Active changes more often appear in patients with the presence of MPO-ANCA (p-ANCA) antibodies when compared with PR 3 - ANCA (c-ANCA).

Similar plans of treatment, as in systemic inflammation with the p-ANCA or c-ANCA presence are applied in lupus which affecs kidneys [15]. In our patient with diagnosed lupus nephropathy, after the Metypred treatment and consecutive therapy with Encorton and cyclophosphamide „pulses" connected with plasmaphereses, a clinical and immunologic remission was obtained. The dialysotherapy was stopped and the obtained remission continued for 18 months. After this period the relapse of the activity of disease caused the necessity to return the patient to peritoneal dialyses (PD). Many authors showed that RFR definitely more often appeared in PD-treated patients as compared with those treated with HD [1,7,8].

This peculiarly concerns the patients in whom malignant hypertension coexists with the increase in the rennin activity of plasma, concentration of the angiotensin II and aldosterone. During HD treatment, as a result of the fast dehydration and sodium loss, there comes to a further increase in the plasma rennin activity. In these cases a peritoneal dialysis should be a method of choice. In our study more often we also observed the improvement in the renal function in patients treated with the peritoneal dialysis.

CONCLUSIONS

The diagnosis of advanced kidney failure in the course of the active systemic vasculitis or systemic lupus erythematosus, points to continuing of the intensive immunosuppressive treatment at the same time commencing the treatment of renal replacement therapy (RRT). Such proceedings can bring a benefit in the form of the renal function improvement and possibility of the omission, although temporary, of the treatment with dialyses. On account of the probable improvement we propose to include such patients in the program of peritoneal dialyses.

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