

Long-time survival of a female with primary amyloidosis treated by peritoneal dialysis

Agnieszka M Grzebalska¹, Jarosław Sak^{1,2}, Andrzej Prystupa³, Andrzej Książek¹

¹ Department of Nephrology, Medical University of Lublin, Lublin, Poland

² Department of Ethics and Human Philosophy, Medical University of Lublin, Lublin, Poland

³ Department of Internal Medicine, Medical University of Lublin, Lublin, Poland

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Abstract

Introduction. Amyloidosis, both primary and secondary, is a systemic disease characterized by extracellular deposition of fibrillar protein in vital organs, leading to their injury and even insufficiency. It results in a poor diagnosis, especially for patients with primary amyloidosis. Kidney involvement is typical and usually manifests by proteinuria, mainly nephrotic range, leading to end-stage renal disease (ESRD). Patients with ESRD need renal replacement therapy (RRT). Some data claim that better results and longer patient survival are observed in peritoneal dialysed rather than in haemodialysed patients.

Case report. The case is described of 19-year-old Caucasian woman with primary amyloidosis. Inherited primary amyloidosis with abnormal apolipoprotein A-I was established. The patient was successfully treated with peritoneal dialysis for 87 months. After this period, she was transferred for haemodialysis. Such a long survival time on peritoneal dialysis (PD) in a patient with primary amyloidosis has not been found. It is believed that the lowering of immunoglobulin levels in blood and normalization of total protein in serum effectively removed, through dialysate, the pathological polyclonal proteins. This effect probably also sustained cardio-circulatory sufficiency of the patient and significantly prolonged her survival.

Conclusion. Peritoneal dialysis is an effective and recommended method of treatment in patients suffering from primary amyloidosis. Peritoneal dialysis should be the first choice therapy in ESRD patient; contrary to haemodialysis, peritoneal dialysis removes pathological proteins and allows the avoidance of intra-dialytic hypotension.

Key words

Amyloidosis, kidney failure, peritoneal dialysis, end-stage renal disease

INTRODUCTION

Amyloidosis is a systemic disease characterized by homogenous protein fibrils depositions present in many organs and leading to their injury. The prognosis is rather poor – the median survival is usually less than 18 months [1]. In both types of amyloidosis, primary and secondary, kidney involvement is typical and frequent [2, 3, 4]. It usually manifests by proteinuria, mainly of nephrotic range [2, 5]. The standard treatment of amyloidosis, e.g. using kolchicine, melphalan with prednisone or cyclophosphamide with prednisone, can extend the median survival of patients [1]. Nowadays, the most effective treatment is a high-dose of melphalan followed by autologous stem cell transplantation. Further renal transplant has even been postulated [4]. Amyloid deposition, prolonged proteinuria and performed treatment of amyloidosis can injure the kidney, and finally lead to end-stage renal disease (ESRD) [2, 4]. If ESRD occurs, patients can be treated with all standard types of renal replacement therapy (RRT): peritoneal dialysis (PD), haemodialysis (HD) or renal transplant. Some authors suggest that better patients' survival in PD than in HD [6]. In most available reports, amyloidosis patients on PD the survival rate was satisfactory but not impressive [2, 3, 7]. The case is presented of a woman with primary amyloidosis successfully treated with PD for more than seven years (87 months).

CASE REPORT

In May 1995, a 19-year-old Caucasian woman was hospitalized because of generalized oedema and proteinuria, nephrotic range (up to 10.0 g/day) (Tab. 1). Normal blood pressure was observed (120/70 mmHg), normal renal function (urea-24 mg%, creatinin 0,7 mg%), hipoproteinaemia (4,6g/L), albuminemia (30,6%) and hiper- γ -globulinemi (21,4%).

Immunoglobulins were moderate elevated: IgG-1500 mg/dl (n. 850–1350 mg/dl), IgA-460 mg/dl (n.160–330 mg/dl), IgM-500 mg/dl (n.95–165 mg/dl). Secondary reasons of nephrotic syndrome (chronic inflammatory process, neoplasms) were excluded, and renal biopsy performed, which failed. No biopsy of rectal or oral tunica mucosa was performed. The patient was given intravenously 3 pulses of methylprednisolone of 1g each, followed by prednisone (40 mg/day). A decrease in proteinuria was achieved. In May 1998, because of a sudden decrease in renal function (creatinin 1.7 mg%), another renal biopsy was performed and found typical features of amyloidosis: positive Congo red stain deposits of amyloid in glomerulus, blood vessels walls, interstitium and even in the basement membrane of tubules (Tab. 1). Inherited primary amyloidosis with abnormal apolipoprotein A-I was established. From then on, the patient was treated with 0.5 mg/day colchicines, administered orally. Pulses of cyclophosphamide 400 mg/month i.v. were given. Creatinin level established at 2.1–3.1 mg%, but nephritic range proteinuria was still (up to 7g/day). Low levels of total protein – 4.8 mg/dl and albumin 1.6 mg/dl were found, together with high levels of all types of immunoglobulin; IgG-2300 mg/dl was especially high (n. 850–1350 mg/dl).

Address for correspondence: Jarosław Sak, Department of Ethics and Human Philosophy, Medical University of Lublin, ul. Staszica 4/6, 20-059 Lublin
E-mail: jareksak@tlen.pl

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Table 1. Disease history of primary amyloidosis 1995–2007

	May 1995	May 1998	October 1999	January 2007
Age	19	22	23	30
Blood pressure	120/70		130/100, 145/105	
Proteinuria	up to 10,0g/day	up to 7g/day		
Renal function	Normal	Dysfunction	End-stage renal dysfunction	End-stage renal dysfunction
Creatinin level	0.7 mg%	1.7 mg%		
IgG level (normal range: 850–1350 mg/dl)	1500 mg/dl	2300 mg/dl	1755 mg/dl	
IgA level (normal range: 160–330 mg/dl)	460 mg/dl		615 mg/dl	
IgM level(normal range: 95–165 mg/dl)	500 mg/dl		207 mg/dl	
Total protein level	4.6 g/L	4.8 g/L	7.9 g/L	
Renal biopsy	failed	typical features of amyloidosis		
Treatment	3 pulses of methylprednisolone (3×1 g)	pulses of cyclophosphamide 0,4 g/month	Peritoneal dialysis (started)	Haemodialysis (started)

Huge anaemia (Hgb 7.6g/l) necessitated the performance of marrow biopsy, in which amyloid deposits were found. The treatment was changed to orally administered melphalan (6 mg/24h) and prednisone (0.8 mg/kg) for 7 days every month. This treatment was performed from April 2000–2001. The same schema was then given every 2 months until April 2002.

In October 1999, because of ESRD, a Tenckhoff catheter was inserted into the patient's peritoneal cavity and PD treatment started. Initially, continuous ambulatory peritoneal dialysis (CAPD) was performed, but because of dialysate leak into the abdominal wall this was changed to automatic peritoneal dialysis (APD). Despite supplementation of epoietin and iron, secondary anaemia (Hgb level 8.7g/l) was observed. In the subsequent marrow biopsy, progressive marrow injury was observed. In order to improve marrow function, the patient was given prednisone 20 mg/day. Total protein level was 7.9g/l; albumin 3,38 g/l. Immunoglobulin levels reduced to the values: IgG -1755 mg/dl (n. 700–1600 mg/dl), IgA-615 mg/dl (n.70–400 mg/dl), and IgM-207 mg/dl (20–230 mg/dl), respectively. Improvement was observed in peripheral blood (Hgb 10.9g/l) and general clinical status of the patient.

At the beginning of the disease the patient revealed normal values of blood pressure (120/70mmHg), and when PD was started, blood pressure was 130/100 to 145/105 mmHg. In January 2007, because of a massive peritonitis, peritoneal dialysis was stopped. After 87 months of peritoneal dialysis treatment the patient was transferred to haemodialysis.

DISCUSSION

Systemic amyloidosis results in extracellular deposition of fibrillar protein in vital organs, leading to their injury and even finally insufficiency. It results in a poor diagnosis, especially for patients with primary amyloidosis (AL) [3, 8, 9].

Renal involvement is frequent in both types of amyloidosis, and can affect up to 75% of cases.[3]. Long-time survival is rather rare. Esteve et al. found that survival time in AL patients was shorter than in those with secondary amyloidosis (AA): 58% and 19% at 12 and 24 month vs 55% and 44%, respectively [3]. Bollée et al. also observed that median survival in AL dialyzed patients was only 26 months [9]. A long-term survival of patients with primary amyloidosis

was described by Kyle et al., who observed 10 years or more survival in 4.7% of 810 patients with AL [10]. Kumar et al., when examined the trends in overall survival in patients with primary amyloidosis, during the period 1977–2006 found significant improvement in survival time [11]. There is no doubt, that one of factors improving survival in amyloidosis is better and earlier treatment.

Standard treatment for primary amyloidosis consists of orally given melphalan with prednisone [8]. In the presented case, after the first failed renal biopsy, the patient was treated by being given pulses of methylprednisolone, followed by oral prednisone. When the next renal biopsy was performed in the then 23-year-old patient and the diagnosis of primary amyloidosis established, she was given colchicine orally (0.5 mg/day), and cyclophosphamide intravenously as a pulse (400 mg) every month. Deterioration in renal function was the reason for starting PD. Because of significant anaemia, marrow biopsy was performed, which found amyloid deposits. Orally given melphalan with prednisone was introduced. As described by Gertz et al., the median time from diagnosis to starting dialysis was 13.8 months [12]. The patient started peritoneal dialysis 53 months after proteinuria occurred, and 17 months after amyloidosis was confirmed in renal biopsy.

A newly- established method of AL treatment is using a high-dose of melphalan given intravenously, followed by autologous stem cell transplantation [4, 8]. A crucial question in such patients remains: when and whether to perform renal transplant? [4]. Furthermore, this type of treatment can be offered only to patients with a good general status and with limited cardiac involvement [8]. Unfortunately, the patient in the presented case was disqualified from renal transplant.

Kidney involvement in amyloidosis, as described above, usually leads to ESRD, which needs RRT. It is a matter of interest, which method of RRT is better for the patients: haemodialysis or peritoneal dialysis? Already in the late 1970s, Stone et al. used PD to treat patients with amyloidosis who needed RRT. They demonstrated that paraproteins were removed in dialysate [13]. The improvement in electrophoresis of serum proteins and decrease in immunoglobulin serum levels was also noticed in the presented case. On the other hand, Moroni et al. found no differences in survival rates between patients treated with HD versus those treated with PD, although patients younger than 45 years had a longer survival time [14]. The same authors found an intra-dialytic hypotension as the most common complication of HD,

while in PD patients the most common complication was peritonitis. [14]. This is consistent with the observation in the current case: the female lost the possibility to be treated by PD because of peritonitis. Esteve et al. found that mean the survival time of 12 and 24 months after the start of dialysis was 30% and 5%, respectively [9]. Gude et al. have also described a case of short-time PD treatment in primary amyloidosis [7]. The female patient in the current case survived on peritoneal dialysis for 87 months in a general quite well state. No other such long survival time on PD in a patient with primary amyloidosis has been found. It is believed that the lowering of immunoglobulin levels in blood and normalization of total protein in serum resulted in the removal, with dialysate, of pathological polyclonal proteins. This effect also probably sustained cardio-circulatory sufficiency of the patient and significantly prolonged her survival.

CONCLUSION

According to the results obtained, peritoneal dialysis is an effective and recommended method of treatment in patients suffering from primary amyloidosis. Peritoneal dialysis should be the first choice therapy in ESRD patients; contrary to haemodialysis, peritoneal dialysis removes pathological proteins and allows the avoidance of intra-dialytic hypotension. Moreover, peritoneal dialysis is a safe method which markedly prolongs the patient's survival, mainly in those with no possibility to undergo renal transplantation.

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