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Original Article

Behçet's disease and renal failure

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Abstract

Background. The aims of this study were (i) to investigate the prevalence of Behçet's disease (BD) among dialysis patients in Turkey, (ii) to report the clinical characteristics of patients with BD and end-stage renal disease (ESRD), (iii) to evaluate the effect of ESRD on course and activity of BD and (iv) to analyse the published data about BD and renal failure.

Methods. A questionnaire investigating BD among dialysis patients was submitted to 350 dialysis centres and we obtained the data for 20 596 patients from 331 dialysis centres. We submitted a second questionnaire regarding clinical characteristics of the patients with BD and ESRD. The PubMed and Web of Science databases were used for the analysis of BD and renal failure.

Results. Fourteen patients with BD were determined and the prevalence of BD was 0.07% among 20 596 dialysis patients in Turkey. None of the patients has had a new manifestation of BD after initiation of haemodialysis treatment. The analysis of previous data about renal BD demonstrated 67 patients with renal failure.

Conclusions. The most common cause of renal failure in BD is amyloidosis. Routine urine analysis and measurement of serum creatinine and blood urea nitrogen levels are needed for early diagnosis. Vascular access-related problems are common and the activity of BD appears to decrease in patients with ESRD after initiation of haemodialysis.

Keywords: amyloidosis; Behçet's disease; cyclosporin; glomerulonephritis; renal failure

Introduction

Behçet's disease (BD) is a multisystem disorder characterized by vasculitis [1–3]. Renal problems in BD have been reviewed recently [4] and amyloidosis, glomerulonephritis and vascular involvement are the main causes of renal BD. The number of patients with BD and renal failure is limited and clinical characteristics of these patients have not been evaluated previously. The effect of uraemia on activity of BD is not known. The aims of this study are (i) to investigate the prevalence of BD among dialysis patients in Turkey, (ii) to report the clinical characteristics of patients with BD and end-stage renal disease (ESRD), (iii) to evaluate the effect of ESRD on course and activity of BD and (iv) to analyse the published data about BD and renal failure.

Subjects and methods

A questionnaire investigating BD among dialysis patients was submitted to 350 dialysis centres and we later contacted the physicians or nurses at the dialysis centres from whom we had not received a response. Finally, we obtained data for 20 596 patients (18 823 haemodialysis patients and 1773 peritoneal dialysis patients; ~90% of the dialysis patients in Turkey) from 331 dialysis centres. We submitted a second questionnaire regarding clinical characteristics of the patients with BD and ESRD to physicians of the related dialysis centre and talked to the physicians and the patients when necessary.

Five more patients have been reported to us from dialysis centres after their response to our first questionnaire. These five patients are not included in the analysis of prevalence, but available clinical data about these patients was evaluated. We were able to obtain the clinical characteristics of three out of the five patients and all five patients had died within a few weeks/months after the diagnosis of ESRD.

Literature review

We conducted a comprehensive review of the literature with an attempt to analyse cumulated data about renal failure in BD using the PubMed and Web of Science databases.

Results

Fourteen living patients with BD were determined on the day of filling in the first questionnaire. The

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prevalence of BD was 0.07% among 20 596 dialysis patients in Turkey. All patients fulfilled the diagnostic criteria of the International Study Group [5]. All patients were on haemodialysis. One patient had previously had a renal transplantation, but he began haemodialysis 1 year later. The specific medications that the patients were receiving were colchicine ($n=6$), steroids ($n=2$) and cyclosporin ($n=1$).

The mean age of these patients was 45 years (range: 27–64 years). Fifteen of the 17 (88%) patients were male. The mean duration of BD was 17 years (range: 4–39 years). The mean interval between the initial manifestation of BD and the diagnosis of renal disease was 12 years (range: 1–36 years). The mean duration of haemodialysis therapy was 54 months (range: 4 months–19 years). The causes of renal failure in our patients with BD and ESRD compared with the causes of 67 cases of BD-related renal failure (some of these are mild and transient) reported in the literature are presented in Table 1 [4,6–12]. The frequency of extrarenal manifestations in patients with BD and ESRD compared with one of the major studies conducted in Turkey [13] are shown in Table 2. Hypertension was present in five patients (29%). The presentation of renal disease was oedema/nephrotic syndrome in nine patients (53%) and hypertension/abdominal pain in one patient (6%). Renal disease was diagnosed incidentally (by routine urine analysis and measurement of serum creatinine and blood urea nitrogen levels) in seven patients (41%).

Table 1. Causes of ESRD among our patients with BD and literature review of causes of BD-related renal failure based on the diagnosis of the authors

Cause	Our patients (*n*)	Literature review (*n*)
Amyloidosis	9	29
Glomerulonephritis	–	21
Cyclosporin nephrotoxicity	1[a]	5[b]
Amyloidosis + cyclosporin nephrotoxicity	1[a]	–
Cyclosporin-related TTP/HUS	–	4
Renal artery aneurysm	–	2
Renal vein thrombosis	–	2[c]
Interstitial nephritis	–	2
Multiple aortic aneurysms	–	1
Renal artery stenosis (left) + small kidney (right)	1	–
Hydronephrosis (left) + aortic aneurysm	1	–
Diabetes mellitus	1[d]	–
Uncertain	3[e]	4
Total	17	67

[a]Clinical diagnosis.
[b]One of the patients also had glomerulonephritis.
[c]Both of the patients also had amyloidosis.
[d]The cause of renal failure was probably diabetes mellitus in this patient.
[e]Two of the patients received cyclosporin previously.
TTP, thrombotic thrombocytopenic purpura; HUS, haemolytic uraemic syndrome.

Table 2. The frequency (%) of extrarenal manifestations in patients with BD and ESRD compared with one of the major studies conducted in Turkey [13]

Clinical features	Our study ($n=17$)	Gurler *et al.* ($n=2147$)
Oral ulceration	100	100
Genital ulceration	94	88
Skin involvement	88	
Erythema nodosum		48
Papulopustular lesions		54
Ocular involvement	59	29
Arthritis/arthralgia	82	16
Vascular involvement	59	17
Gastrointestinal system involvement[a]	12	3
Central nervous system involvement	12	2

[a]Gastrointestinal system involvement other than amyloidosis.

Activity of BD after initiation of haemodialysis treatment

None of the patients has had a new manifestation of BD. Arthritis, an attack of uveitis and vascular involvement were the pre-existing manifestations of BD observed after the initiation of haemodialysis treatment in two patients. The frequency of oral and genital aphthous lesions has disappeared or decreased significantly after the initiation of haemodialysis treatment in nine patients. The oral and genital aphthous lesions were very rare in five patients prior to dialysis treatment and continued to be very rare. The duration of haemodialysis treatment was short in order to evaluate the influence of ESRD on the frequency of oral and genital aphthous lesions in the remaining three patients. Abnormal skin reactions or pustule formation at the entry sites of arteriovenous fistula needles were not observed.

Vascular access problems

Attempts were made to create an arteriovenous fistula in 15 patients and the first attempt was successful in six of these patients. Following other attempts, arteriovenous fistulas were created in 14 patients and vascular access was provided by internal jugular vein catheterization in one patient for 4 months because of two unsuccessful arteriovenous operations. Arteriovenous fistula operations were not performed in the remaining two patients who had died within a few weeks. Two patients had recurrent fistula thrombosis and one patient had excessive arterial dilatation. Temporary vascular catheters were inserted into femoral, subclavian or internal jugular veins in 14 patients. Seven patients did not have any temporary vascular access-related problem. Thrombosis and infection of the catheter were observed. One patient had subclavian vein thrombosis.

Discussion

BD is mainly seen in the Middle East and East Mediterranean regions, along the Silk Route and in

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Japan. The prevalence of BD among dialysis patients has not been investigated in these countries/regions and our study demonstrated a prevalence of 0.07% among 20 596 patients in Turkey. This sampling is, however, limited to only ESRD patients and may miss a significantly large population with lesser degrees of renal insufficiency and may also have unknowingly omitted those with ESRD and BD who have died. The death of five patients within a few weeks/months after the diagnosis of ESRD indicates that renal failure related to BD may be more common than had been recognized. Our study shows that amyloidosis is the leading cause of renal failure among dialysis patients having BD in Turkey. Amyloidosis and glomerulonephritis are the most common causes of BD-related renal failure among the cases reported previously. It should be kept in mind that the reviewed data only show the reported cases and these numbers do not reflect the exact frequency of underlying causes of renal failure among patients with BD.

Uraemia-related immunosuppression may cause amelioration of the activity of rheumatic diseases such as systemic lupus erythematosus [14]. Peces *et al.* [6] have reported the disappearance of oral and genital aphthous lesions at the uraemic stage and after the initiation of haemodialysis treatment in one patient. These two observations led us to evaluate the effect of uraemia on the activity of BD. Although the follow-up period before haemodialysis treatment was longer than that after initiation of haemodialysis treatment, the rarity of extrarenal manifestations, the absence of new lesions, the absence of pustule formation at the entry sites of arteriovenous fistula needles and the decreased frequency of oral and genital aphthous ulcerations indicate that ESRD may reduce the activity of BD. The possible mechanisms of the reduction of BD activity after initiation of haemodialysis treatment may be (i) depressed cellular and humoral immunity as a result of uraemia, (ii) the dialysis procedure itself or (iii) a natural course of BD. The retrospective nature of our study may have some disadvantages and limitations (such as unequal follow-up periods before and after initiation of haemodialysis treatment, inadequacy to detect new patients for evaluation and inability to investigate the incidence of BD-related renal failure), but to conduct a prospective study is difficult because only a minority of patients with BD develop ESRD and many patients die within a few weeks/months after the diagnosis of ESRD.

Because interventions, such as puncture of arteries for angiography or vascular surgery, lead to formation of further false aneurysms at the site of vascular interference or anastomosis [15], haemodialysis of patients with BD may carry some difficulties, such as failure of arteriovenous fistula or grafts and high risk of temporary vascular access-related problems. Experience of problems related to vascular access for haemodialysis is limited. Although early failure of arteriovenous fistula or graft was observed, long-term survival and patency of arteriovenous fistula or graft have also been reported [4]. The problems related to arteriovenous fistula or temporary vascular access are relatively common in our study. Magnetic resonance angiography can be used safely in the evaluation of the patients with vascular access problems [15]. In order to avoid complications related to temporary vascular access, early diagnosis of renal disease and appropriate management of renal failure is required.

The experience about renal transplantation and peritoneal dialysis in patients with BD has only been anecdotally reported [4]. Because of the common occurrence of vascular access problems, peritoneal dialysis may have some advantages. Management of renal failure with peritoneal dialysis has been reported in four patients [4,12]. Peritoneal dialysis was complicated by septic thrombosis of the catheter in one of these patients. Three cases with BD, ESRD and renal transplantation have been reported previously [4]. One patient had thrombi at the inferior vena cava and iliac veins and vein–vein anastomoses had been performed to the right ovarian vein, notably, an unusual place in renal transplantation. Short-term prognosis was favourable in the transplanted patients.

We conclude that the most common cause of renal failure in BD is amyloidosis. Patients receiving cyclosporin for treatment of BD require close monitoring. Routine urine analysis and measurement of serum creatinine and blood urea nitrogen levels are needed for early diagnosis. Although a control group is not available, in our experience, vascular access-related problems are common and the activity of BD appears to decrease in patients with ESRD after initiation of haemodialysis. In spite of some difficulties, haemodialysis and renal transplantation are safe treatment options in BD-related ESRD. Awareness of renal problems by physicians, especially rheumatologists, dermatologists and opthalmologists who are familiar with BD, may lead to determination of the exact prevalence and early diagnosis of renal failure in BD.

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Conflict of interest statement. None declared.

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