Renal Manifestations in 2007 Korean Patients with Behçet’s Disease

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Purpose: Behçet’s disease (BD) theoretically affects all sizes and types of blood vessels and results in multi-organ involvement. However, renal BD has not been fully characterized, though the kidneys are histologically rich in blood vessels. Materials and Methods: A total of 2007 patients who fulfilled the diagnostic criteria for BD were enrolled in this study. We reviewed the medical records and test results of the BD patients and used univariate and multivariate logistic regression analyses to determine the clinical significance of renal involvement in BD. Results: Among the 2007 BD patients, we noted hematuria in 412 (20.5%) and proteinuria in 29 (1.4%). Univariate analysis showed that the BD patients with hematuria were predominantly female and older, had higher erythrocyte sedimentation rates (ESRs), and more frequently presented with genital ulcerations. BD patients with proteinuria had higher ESR levels compared to BD patients without proteinuria. In the multivariate analysis, age, sex, and ESR were found to be significantly associated with hematuria in BD patients, whereas only ESR was associated with proteinuria in BD patients. We also found that IgA nephropathy was the most common pathologic diagnosis in 12 renal BD patients who underwent renal biopsies. Conclusion: We suggest that routine urinalysis and serum renal function tests be performed for the early detection of renal BD, especially in older female BD patients with recurrent hematuria, high ESR levels, and frequent genital ulcers, as well as in BD patients with proteinuria and high ESR levels.

Key Words: Behçet’s disease, renal involvement, hematuria, proteinuria, IgA nephropathy

INTRODUCTION

Behçet’s disease (BD) theoretically affects all sizes and types of blood vessels and results in multi-organ involvement. Renal BD has not been fully characterized, although kidneys are histologically rich in blood vessels and receive approximately...
20% of the cardiac output. The main causes of renal BD reportedly include AA type amyloidosis, glomerulonephritis, renal vascular involvement, and interstitial nephritis. The clinical manifestations of renal BD range from asymptomatic hematuria and/or proteinuria to end-stage renal disease. Akpolat, et al. have demonstrated that renal involvement in BD seems to be more frequent than has been reported, and most renal BD patients have an indolent disease course. Histopathologically, minor glomerular changes and microscopic vascular disease are most commonly observed in renal BD patients with a mild clinical course.

In this study, we retrospectively reviewed the clinical characteristics of 2007 Korean BD patients and analyzed the results of their urinalyses. Herein we also discuss the findings of light microscopy, immunofluorescence tests, and electron microscopy in 12 BD patients who underwent renal biopsy.

**MATERIALS AND METHODS**

Two thousand and seven patients (584 males and 1423 females (1 : 2.4); median age, 42 years; age ranging, 13 to 82 years) who were registered at the BD Specialty Clinic of Severance Hospital between January 2009 and December 2010 and fulfilled the diagnostic criteria for BD were enrolled in this study. The criteria used for BD diagnosis are outlined by the International Study Group for BD. A diagnosis of hematuria was made on the basis of microscopic examination of urine sediment, with a count of five erythrocytes/high power field (1 field, 400× magnification) appearing more than two times in one year or three times in six months considered positive. Among the 2007 BD patients, 12 patients underwent renal biopsies, and two nephrologists made the diagnosis of renal disease through biopsy confirmation, taking into account the findings of light microscopy, immunofluorescence tests, and electron microscopy.

Patient medical records were reviewed in order to investigate the clinical characteristics of BD, the results of the urinalyses, and other laboratory test results. Lab tests included complete blood count, blood glucose level, renal and liver function tests, erythrocyte sedimentation rate (ESR; normal range, ≤0.8 mg/dL), C-reactive protein (CRP; normal range, ≤20 mm/hour), anti-streptolysin O titer, rheumatoid factor, antinuclear antibodies, sexually transmitted infection work-up, and HLA B51 genotype. Additionally, patients with hematuria and/or proteinuria underwent intravenous pyelogram, ultrasonographic examination of the abdomen and pelvis, cytologic examination of the urine, and lab tests including complement levels and the quantitative evaluation of serum immunoglobulins.

Chi-square tests, Fisher’s exact tests, and Mann-Whitney U tests were applied to assess differences between the clinical features of BD patients with hematuria and/or proteinuria and those with normal urinalyses. The strength of associations among urinary abnormalities, demographics, clinical symptoms, and laboratory characteristics are expressed as odds ratios (ORs) and 95% confidence intervals (CI). Logistic regression models were used, and variables with \( p \leq 0.15 \) in the univariate analysis were included in the multivariate analysis. All analyses were performed using SAS software version 9.1.3 (SAS Institute Inc., Cary, NC, USA). Differences were considered statistically significant when the \( p \)-value was less than 0.05.

**RESULTS**

**Clinical characteristics of 2007 BD patients**

Among the 2007 patients, the following symptoms were observed in descending order of frequency: recurrent oral ulcers in all 2007 patients (100%), genital ulcers in 1688 patients (84.1%), cutaneous involvement in 1579 patients (78.7%), arthritis in 1057 patients (52.7%), and ocular involvement in 682 patients (34.0%) (Table 1). Gastrointestinal system involvement was noted in 218 patients (10.9%), central nervous system involvement in 50 patients (2.5%), a positive pathergy test in 47 patients (2.3%), and epididymitis in 27 patients (1.4%). Positive HLA B51 genotype was identified in 271 patients (13.5%).

**BD patients with renal manifestations**

Among the 2007 BD patients, hematuria was seen in 412 patients [20.5%; 48 males and 364 females (1 : 7.6), with a median age of 48 years and ages ranging from 17 to 76 years] and proteinuria in 29 patients [1.4%; 11 males and 18 females (1 : 1.6), with a median age of 42 years and ages ranging from 23 to 74 years]. Five of the 2007 BD patients were found to have both hematuria and proteinuria. The following symptoms were observed in descending order of frequency in the 412 BD patients with hematuria (Table 1): recurrent oral ulcers in all 412 patients (100%), genital ulcers in 362 patients (87.9%), cutaneous involvement in 322 patients (78.2%), arthritis in 231 patients (56.1%), and ocular
involvement in 135 patients (32.8%). Gastrointestinal system involvement was noted in 45 patients (10.9%), vascular system involvement in 17 patients (4.1%), central nervous system involvement in 8 patients (1.9%), and epididymitis in 3 patients (0.7%). Positive HLA B51 genotype was identified in 56 patients (13.6%) and 14 patients (3.4%) had a positive pathergy test.

Using chi-square tests, Fisher’s exact tests, and Mann-Whitney U tests, hematuria was found to be more frequent in female BD patients (<0.0001) and BD patients with higher ESR (<0.0001), CRP (<0.0001), and anti-streptolysin O titer (ASO) (p=0.040) levels. Also, BD patients with hematuria more frequently experienced genital symptoms (p=0.019).

Among the 29 BD patients with proteinuria, the following symptoms were observed in descending order of frequency (Table 2): recurrent oral ulcers in all 29 patients (100%), genital ulcers in 24 patients (82.8%), cutaneous involvement in 23 patients (79.3%), arthritis in 11 patients (37.9%), and ocular involvement in 5 patients (17.2%). Vascular involvement was noted in 3 patients (10.3%), a positive pathergy test in 2 patients (13.8%), gastrointestinal system involvement in 1 patient (3.5%), and epididymitis in 1 patient (3.5%). No patient experienced central nervous system involvement. Positive HLA B51 genotype was identified in 4 patients (13.8%).

Univariate analysis
The univariate analysis (Table 2 and 3) showed that BD patients with hematuria were predominantly female (OR, 3.84; 95% CI, 2.79-5.28; p<0.001), older (OR, 1.01; 95% CI, 1.00-1.02; p=0.03), had higher ESR levels (OR, 1.02; 95% CI, 1.01-1.02; p<0.001), and more frequently experienced genital ulcerations (OR, 1.47; 95% CI, 1.06-2.03; p=0.02) compared with BD patients without hematuria. BD patients with proteinuria had higher ESR levels (OR, 1.03; 95% CI, 1.02-1.04; p<0.001) compared to BD patients without proteinuria. However, no association was found between proteinuria in BD patients and sex (p=0.30), age (p=0.24), or genital ulceration (p=0.84).

Multivariate analysis
The variables with a p-value <0.15 in the univariate comparisons of BD patients with and without hematuria (Table 3) as well as BD patients with and without proteinuria (Table 2) were considered for inclusion in the multivariate

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Table 1. Comparison of Demographic Characteristics, Symptoms, and Laboratory Findings of BD Patients Grouped According to the Presence of Hematuria

| 2007 BD patients | BD patients with hematuria, n (%) | BD patients without hematuria, n (%) | p value |
|------------------|---------------------------------|-------------------------------------|---------|
| Age*             | 47 (13-82)                      | 48 (17-76)                          | 0.059   |
| Sex              |                                 |                                     |<0.0001 |
| Male             | 584 (29.1)                      | 48 (11.7)                           | 536 (33.6) |
| Female           | 1423 (70.9)                     | 364 (88.3)                          | 1059 (66.4) |
| Oral ulcers      | 2007 (100)                      | 412 (100)                           | 1595 (100) |
| Genital ulcers   | 1688 (84.1)                     | 362 (87.9)                          | 1326 (83.13) |
| Skin lesions     | 1579 (78.7)                     | 322 (78.9)                          | 1257 (78.8) |
| Eye lesions      | 682 (34.0)                      | 135 (32.8)                          | 547 (34.3) |
| Arthritis        | 1057 (52.7)                     | 231 (56.1)                          | 826 (51.8) |
| GI involvement   | 218 (10.9)                      | 45 (10.9)                           | 173 (10.9) |
| Vascular involvement | 88 (4.4)             | 17 (4.1)                            | 71 (4.5) |
| CNS involvement | 50 (2.5)                        | 8 (1.9)                             | 42 (2.6) |
| Epididymitis     | 27 (1.4)                        | 3 (0.7)                             | 24 (1.5) |
| Positive pathergy test | 47 (2.3)             | 12 (2.9)                            | 35 (2.2) |
| Positive HLA-B51 | 271 (13.5)                      | 56 (13.6)                           | 214 (13.4) |
| ASO*             | 47.7 (0-491)                    | 49.3 (0-410.9)                      | 46.8 (0-491) |
| ESR (mm/hour)*   | 16 (0-120)                      | 22 (2-120)                          | 14 (0-120) |
| CRP (mg/dL)*     | 0.3 (0-33.5)                    | 0.3 (0.1-33.5)                      | 0.2 (0-19.7) |

Gl, gastrointestinal system; CNS, central nervous system; ASO, anti-streptolysin O titer; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BD, Behçet’s disease.

*Data are presented as median values (minimum-maximum).
analyses. In comparing BD patients with and without hematuria, multivariate analyses were performed including the following variables: age ($p=0.03$), sex ($p=0.001$), genital ulcers ($p=0.02$), arthritis ($p=0.12$), ESR ($p<0.001$), and CRP ($p=0.12$). Among these factors, age (OR, 1.01; 95% CI, 1.00-1.02; $p=0.034$), sex (OR, 3.60; 95% CI, 2.60-4.98; $p<0.001$) and ESR (OR, 1.01; 95% CI, 1.01-1.02; $p=0.001$) were found to be significantly associated with hematuria in

Table 2. Univariate and Multivariate Comparisons of BD Patients with and without Proteinuria

|                  | BD patients with proteinuria, n (%) | BD patients without proteinuria, n (%) | Univariate OR (95% CI) | $p$ value | Multivariate OR (95% CI) | $p$ value |
|------------------|------------------------------------|----------------------------------------|------------------------|-----------|-------------------------|-----------|
| Age*             | 42 (23-74)                         | 47 (13-82)                             | 0.98 (0.95-1.01)       | 0.24      | 1.01 (1.00-1.02)        | 0.034     |
| Sex              |                                    |                                        |                        |           |                         |           |
| Male             | 11 (37.9)                          | 573 (29.0)                             | 0.67 (0.31-1.42)       | 0.30      |                         |           |
| Female           | 18 (62.1)                          | 1405 (71.0)                            |                        |           |                         |           |
| Oral ulcers      | 29 (100)                           | 1978 (100)                             |                        |           |                         |           |
| Genital ulcers   | 24 (82.8)                          | 1664 (84.1)                            | 0.90 (0.34-2.39)       | 0.84      |                         |           |
| Skin lesions     | 23 (79.3)                          | 1556 (78.7)                            | 1.04 (0.42-2.57)       | 0.93      |                         |           |
| Eye lesions      | 5 (17.2)                           | 677 (34.2)                             | 0.40 (0.15-1.05)       | 0.06      | 0.40 (0.15-1.07)        | 0.067     |
| Arthritis        | 11 (37.9)                          | 1046 (52.9)                            | 0.55 (0.26-1.16)       | 0.12      | 0.53 (0.25-1.13)        | 0.10      |
| GI involvement   | 1 (3.5)                            | 217 (11.0)                             | 0.29 (0.04-2.14)       | 0.23      |                         |           |
| Vascular involvement | 3 (10.3)                       | 85 (4.3)                               | 2.57 (0.76-8.66)       | 0.13      | 1.87 (0.51-6.79)        | 0.34      |
| CNS involvement  | 0 (0)                              | 50 (2.53)                              | 0.94 (0.00-5.42)       | 0.96      |                         |           |
| Epididymitis     | 1 (3.5)                            | 26 (1.3)                               | 2.68 (0.35-20.45)      | 0.34      |                         |           |
| Positive pathergy test | 2 (6.9)                  | 45 (2.3)                               | 3.18 (0.73-13.8)       | 0.12      | 2.86 (0.63-12.97)       | 0.17      |
| Positive HLA-B51 | 4 (13.8)                           | 267 (13.5)                             | 1.03 (0.35-2.97)       | 0.96      |                         |           |
| ASO*             | 1 (0.0-2.0)                        | 4 (1.0-5.4)                             |                        |           |                         |           |
| ESR (mm/hour)*   | 0.2 (0-33.5)                       | 1.0 (0.0-120)                          | 1.00 (1.00-100)        | 0.97      |                         |           |
| CRP (mg/dL)*     | 1.0 (0.1-25.1)                     | 1.0 (0.2-33.5)                         | 1.00 (1.00-100)        | 0.95      |                         |           |

GI, gastrointestinal system; CNS, central nervous system; ASO, anti-streptolysin O titer; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BD, Behçet’s disease; OR, odds ratio; CI, confidence intervals.

*Data are presented as median values (minimum-maximum).
†$p<0.0001$; $p<0.15$ (numbers in bold) were considered for inclusion in the multivariate analyses.

Table 3. Univariate and Multivariate Comparisons of BD Patients with and without Hematuria

|                  | Univariate OR (95% CI) | $p$ value | Multivariate OR (95% CI) | $p$ value |
|------------------|------------------------|-----------|-------------------------|-----------|
| Age (yrs)        | 1.01 (1.00-1.02)       | 0.03      | 1.01 (1.00-1.02)        | 0.034     |
| Sex              | 3.84 (2.79-5.28)       | <0.001    | 3.60 (2.60-4.98)        | <0.001    |
| Genital ulcers   | 1.47 (1.06-2.03)       | 0.02      | 1.18 (0.84-1.65)        | 0.34      |
| Skin lesions     | 0.96 (0.74-1.25)       | 0.77      |                         |           |
| Eye lesions      | 0.93 (0.74-1.18)       | 0.56      |                         |           |
| Arthritis        | 1.19 (0.96-1.48)       | 0.12      | 1.10 (0.88-1.38)        | 0.42      |
| GI involvement   | 1.01 (0.71-1.43)       | 0.97      |                         |           |
| Vascular involvement | 0.92 (0.54-1.59)       | 0.77      |                         |           |
| CNS involvement  | 0.73 (0.34-1.57)       | 0.42      |                         |           |
| Epididymitis     | 0.48 (0.14-1.60)       | 0.23      |                         |           |
| Positive pathergy test | 1.34 (0.69-2.60)       | 0.39      |                         |           |
| Positive HLA-B51 | 1.04 (0.76-1.42)       | 0.82      |                         |           |
| ASO              | 1.00 (1.00-1.00)       | 0.51      |                         |           |
| ESR (mm/hour)    | 1.02 (1.01-1.02)       | <0.001    | 1.01 (1.01-1.02)        | <0.001    |
| CRP (mg/dL)      | 1.01 (1.01-1.02)       | 0.12      | 1.01 (0.99-1.02)        | 0.34      |

GI, gastrointestinal system; CNS, central nervous system; ASO, anti-streptolysin O titer; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BD, Behçet’s disease; OR, odds ratio; CI, confidence intervals.

Variables with $p<0.15$ (numbers in bold) on univariate analysis were considered for inclusion in the multivariate analyses.
BD patients. However, neither genital ulcers (OR, 1.18; 95% CI, 0.84-1.65; \(p=0.34\)) nor arthritis (OR, 1.10; 95% CI, 0.88-1.38; \(p=0.42\)) was significantly associated with hematuria in BD patients on multivariate analysis.

In comparing BD patients with and without proteinuria, multivariate analyses were performed and included the following variables: eye lesions (OR=0.064), arthritis (OR=0.12), vascular involvement (OR=0.13), positive pathergy test (OR=0.12), and ESR (OR=0.001). Only ESR (OR, 1.03; 95% CI, 1.02-1.04; \(p<0.001\)) was associated with proteinuria in BD patients. Eye lesions (OR, 0.40; 95% CI, 0.15-1.07; \(p=0.067\)), arthritis (OR, 0.53; 95% CI, 0.25-1.13; \(p=0.10\)), vascular involvement (OR, 1.87; 95% CI, 0.51-6.79; \(p=0.34\)), and a positive pathergy test (OR, 2.86; 95% CI, 0.63-12.97; \(p=0.17\)) did not show any significant association.

**Results of kidney biopsies**

Among the 2007 BD patients, 12 patients [two males and ten females (1:5), with a median age of 48.5 years and ages ranging from 28 to 68 years] underwent renal biopsy (Table 4). All 12 patients (100%) experienced recurrent oral ulcers, 11 patients (91.7%) had genital ulcers, 10 patients (83.3%) had cutaneous involvement (erythema nodosum-like skin lesions in 6 patients, papulopustular lesions in 5 patients, and 1 had both types of skin lesions), 7 patients (58.3%) had arthritis, and 3 patients (25%) had ocular involvement. A positive pathergy test was found in 2 patients (16.7%), vascular involvement in 1 patient (8.3%), and gastrointestinal system involvement in 1 patient (8.3%). No patient experienced central nervous system involvement or epididymitis. Positive HLA B51 genotype was noted in 3 patients (25%).

The median age at BD onset of the 12 BD patients was 37 (range: 19-54) years (Table 4). The median duration between BD onset and kidney biopsy was 10.5 (range: 7-18) years. The following pathologic findings were observed in descending order of frequency in 12 BD patients (Table 5): IgA nephropathy in 8 patients (66.7%), mild arteriosclerosis in 3 patients (25%), minor glomerular changes in 3 patients (25%), crescentic glomerulonephritis in 1 patient (8.3%), and diabetic diffuse and nodular glomerulosclerosis in 1 patient (8.3%). All 3 BD patients with mild arteriosclerosis also had pathologic findings of IgA nephropathy. Seven of the 12 BD patients (58.3%) had no specific symptoms suggestive of BD renal involvement or any other kind of kidney problems (Table 6), whereas generalized edema was noted in 2 patients (16.7%), general weakness or frequent dizziness in 2 patients (16.7%), and foamy urine in 1 patient (8.3%).

Systemic therapies were provided to the 12 BD patients

### Table 4. Clinical Features of 12 Patients with Behçet’s Disease (BD) Who Underwent Kidney Biopsy

| Clinical findings | Patients with BD |
|-------------------|------------------|
| Sex               | F F F F F M F M F |
| Age (yrs)         | 68 37 61 56 47 45 49 50 48 47 53 28 |
| Age at BD onset (yrs) | 54 22 48 37 37 33 30 38 27 40 44 19 |
| Period between BD onset and the kidney biopsy (yrs) | 9 14 10 12 9 11 13 11 18 7 10 9 |
| Oral ulcers       | + + + + + + + + + + + + |
| Genital ulcers    | + + + + + + + + + + + + |
| EN-like lesions   | + - - - + + + + + - - - |
| Pseudofolliculitis| - + - - - - - - + - |
| Eye lesions       | - - - - - - - - - - - |
| Vascular involvement | - - - - - + - - - - - - |
| Arthritis         | - - + + + + + + + + + + |
| CNS involvement   | - - - - - - - - - - - - |
| GI involvement    | - - + + - - - - - - - - |
| Epididymitis      | - - - - - - - - - - - - |
| Pathergy test     | - + - - - - - - - - - + |
| HLA-B51 genotyping| - - - - - + - - - - - - |
| Proteinuria       | + + + + + + + + + + + + |
| Hematuria         | - + + + + + + + + + + |
| BUN/Cr elevation  | + + + + - - - - - - - |

EN, erythema nodosum; CNS, central nervous system; GI, gastrointestinal system; +, present; -, absent.
and their treatment responses are summarized in Table 6. Ten (83.3%) of the 12 BD patients had stable renal disease, 1 patient (8.3%) experienced disease progression and eventually died despite systemic prednisolone and colchicine treatment and hemodialysis, and 1 patient (8.3%) experienced disease progression despite treatment with systemic furosemide, hydrochlorothiazide, losartan potassium, and thiocytic acid.

### DISCUSSION

Since Oshima, et al." first reported hematuria and proteinuria associated with BD, AA-type amyloidosis, glomerulonephritis, and renal vascular disease have been accepted as renal manifestations of BD. According to a previous report, the types of renal involvement among 253 cases of BD patients were determined to be amyloidosis (n=108; 42.7%), glomerulonephritis (n=88; 34.8%), renal macroscopic/microscopic vascular disease (n=55; 21.7%), and interstitial nephritis (n=5; 2.0%). The authors suggested that BD patients with vascular involvement have a high risk of amyloidosis, which is the most common cause of renal failure in BD patients. Also, routine urinalysis and measurement of serum creatinine level have been proposed for early diagnosis of renal BD. In addition, Kavala, et al." reported that 16.1% (n=34) of BD patients (n=211) were revealed to have renal involvement as microalbuminuria in 11.1% (n=22) and proteinuria in 5.6% (n=12). The authors described that central nervous system involvement and disease duration of ≥10 years was significantly associated with the risk of microalbuminuria.

In the present study, we retrospectively reviewed the medical records of a total of 2007 BD patients and analyzed the

| Pt. No. | Pathologic findings                                      | Immunofluorescence tests                  |
|---------|----------------------------------------------------------|------------------------------------------|
| 1       | Crescentic glomerulonephritis and early IgA nephropathy   | IgG, IgA, C3, and fibrinogen             |
| 2       | Diabetic diffuse and nodular glomerulosclerosis           | IgG, IgA, C3, lambda, and fibrinogen     |
| 3       | Glomerular minor change with focal mild tubular atrophy and interstitial fibrosis | IgG and IgM                             |
| 4       | IgA nephropathy, subclass V                               | IgG, IgA, C3, and fibrinogen             |
| 5       | IgA nephropathy, subclass III and mild arteriosclerosis  | IgG, IgA, C3, kappa, lambda, and fibrinogen |
| 6       | IgA nephropathy, subclass III and mild arteriosclerosis  | IgG, IgM, IgA, C3, C4, lambda, and fibrinogen |
| 7       | IgA nephropathy, subclass I                               | IgA and C3                              |
| 8       | IgA nephropathy, subclass III and mild arteriosclerosis  | IgA, C3, lambda, fibrinogen              |
| 9       | Minor glomerular change                                   |                                          |
| 10      | Minor glomerular change                                   | C3 and fibrinogen                        |
| 11      | IgA nephropathy, subclass II                              | IgG, IgA, IgM, C3, C4, C1q, and fibrinogen |
| 12      | IgA nephropathy, subclass IV                              | IgG, IgA, IgM, C3, C4, C1q, and fibrinogen |

| Pt. No. | Clinical manifestations | Therapy                                      | Response                  |
|---------|------------------------|----------------------------------------------|---------------------------|
| 1       | Generalized edema      | Prednisolone, colchicine, hemodialysis        | Progressed, death         |
| 2       | Generalized edema      | Furosemide, hydrochlorothiazide, losartan potassium, thiocytic acid | Progressing               |
| 3       | Frequent dizziness     | Prednisolone, colchicine, azathioprine, mesalazine, potassium chloride | Stationary                |
| 4       | Asymptomatic           | Furosemide, hydrochlorothiazide, losartan potassium, thiocytic acid, polystyrene sulfonate calcium | Stationary                |
| 5       | Asymptomatic           | Prednisolone, colchicine, rebamipide, furosemide, olmesartan medoxomil, nisoldipine, sulodexine | Stationary                |
| 6       | Asymptomatic           | Prednisolone, colchicine                     | Stationary                |
| 7       | Asymptomatic           | Colchicine                                   | Stationary                |
| 8       | Asymptomatic           | Prednisolone, cyclophosphamide               | Stationary                |
| 9       | Foamy urine            | Prednisolone, colchicine                     | Stationary                |
| 10      | General weakness       | Colchicine, rebamipide                       | Stationary                |
| 11      | Asymptomatic           | Colchicine, rebamipide                       | Stationary                |
| 12      | Asymptomatic           | Prednisolone, colchicine, rebamipide, aceclofenac | Stationary                |

**Table 5. Immunohistopathologic Features of 12 Patients with Behçet’s Disease (BD) Who Underwent Kidney Biopsy**

**Table 6. Clinical Manifestations and Treatment Responses of 12 Patients with Behçet’s Disease (BD) Who Underwent Kidney Biopsy**
patients’ data using univariate and multivariate logistic regression analyses to determine the clinical significance of renal involvement in BD. Among the 2007 BD patients, hematuria was identified in 412 patients (20.5%) while proteinuria was noted in 29 patients (1.4%). The univariate analysis showed that the BD patients with hematuria were predominantly female and older, had higher ESR levels, and more frequently experienced genital ulcerations compared to BD patients without hematuria. BD patients with proteinuria had higher ESR levels compared to BD patients without proteinuria. Multivariate analysis revealed that age, sex, and ESR were significantly associated with hematuria in BD patients, whereas only ESR was associated with proteinuria in BD patients. Male gender has been considered a risk factor for all types of renal involvement in BD patients. Male ratio of BD patients might contribute to the marked female predominance in cases of hematuria.

Many types of glomerulonephritis have been reported to be associated with BD, however, the exact pathogenesis remains unclear. The suggested pathogenesis of glomerulonephritis in BD patients includes the deposition of immune complexes, IgA, and anti-neutrophilic cytoplasmic antibodies. Cumulative analyses by Akpolat, et al. demonstrated that only 6 (6.8%) of 88 BD patients with pathology-proven glomerulonephritis had IgA nephropathy. Our study demonstrated that IgA nephropathy was the most common pathologic findings among 12 BD patients who underwent renal biopsies. IgA nephropathy is the most common form of glomerulonephritis, with a prevalence ranging from 10% in North American renal biopsies to 30-40% in the Asian-Pacific area.

Several types of glomerular lesions can be found in BD and these lesions are probably the most common manifestation of renal disease observed in BD patients. Although current treatment options for renal BD are not evidence-based, corticosteroids, colchicine, azathioprine, and cyclophosphamide have been used for the treatment of glomerular lesions in BD. In our study, a majority of the 12 BD patients who underwent renal biopsies had indolent courses of renal diseases with systemic colchicine treatment with or without concomitant corticosteroids and azathioprine. It has been suggested that colchicine may prevent extracellular matrix and amyloid accumulation as well as various renal injuries via its anti-inflammatory action, which occurs through the inhibition of enhanced monocyte chemotactic protein-1 and intercellular adhesion molecule-1 expression. However, routine administration of colchicine for BD patients with hematuria, proteinuria, or biopsy-proven glomerular lesions requires further investigation.

In this study, we analyzed risk factors associated with hematuria and proteinuria in 2007 Korean BD patients and demonstrated that IgA nephropathy was the most common pathologic diagnosis in 12 renal BD patients who underwent renal biopsies. Our study group previously reported the clinical characteristics of 30 BD patients diagnosed with aneurysms or pseudoaneurysms in major arterial systems. One patient with multiple saccular aneurysms of the renal arteries was already included in the previous report; therefore, this patient was excluded in the present study. The high prevalence of hematuria or IgA nephropathy in BD patients may be the result of regional differences in the manifestations of BD or coincidental findings of BD and hematuria or IgA nephropathy. Based on our data, we recommend routine urinalysis and serum renal function tests as well as early consultation with a nephrologist for the diagnosis of renal BD, especially in older female patients with hematuria, high ESR levels, and frequent genital ulcers or BD patients with proteinuria and high ESR levels.

In addition, we believe that our data can be effectively used as a clinical reference for further investigations into the pathogenetic similarities and differences between BD and IgA nephropathy in the Asian-Pacific BD population.

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