Renal Data from the Arab World

Acute Interstitial Nephritis in the Military Hospital of Morocco: Clinical Features and Renal Outcomes

Yassir Zajjari¹, Dina Montasser¹, Aya Sobhi¹, Taoufiq Aatif¹, Mounia Azizi¹, Ahmed Alayoud², Driss El Kabbaj¹

¹Department of Nephrology-Dialysis, Military Hospital Mohammed V, Rabat, ²Department of Nephrology-Dialysis, Military Hospital Mohammed V, Agadir, Morocco

ABSTRACT. Acute interstitial nephritis (AIN) is a common cause of acute kidney injury, possibly with increasing incidence over recent years; therefore, epidemiological studies provide important information for clinical practice and investigations. The aim of this retrospective study was to describe the clinical features and outcome of patients with biopsy-proven AIN in a region of Morocco. All native renal biopsies (January 2008 to December 2017) on adults were reviewed, but only AIN cases were analyzed. Of the 407 renal biopsies performed in this period, 30 patients were included. The mean age of the patients was 47.1 ± 16.7 years; female gender was preponderant (60%). At the time of biopsy, the serum creatinine level was 33.9 ± 11.8 mg/L. The classic triad of fever, skin rash, and eosinophilia occurred in three (10%) patients. The common causes of AIN were drugs in 13 (43.3%) patients followed by autoimmune diseases in 11 (33.3%) patients. At six months postbiopsy, 26.7%, 33.3%, and 40% had partial, complete, and no recovery, respectively. In this study, a good outcome was associated with autoimmune diseases (P = 0.02) and with a higher intensity of interstitial edema (P = 0.01). However, a presence of a granuloma (P = 0.04), a higher percentage of interstitial fibrosis (P < 0.01), and glomerulonephritis (P = 0.01) were associated with no recovery and steroids seem to have no effect in the recovery (P = 0.14). This information provides a contribution toward understanding the epidemiology of acute renal failure in Africa, with implications in planning future prospective studies.

Introduction

Acute interstitial nephritis (AIN) is a relatively frequent cause of reversible acute kidney injury (AKI). It was described first by Councilman in 1898, as specific kidney injury characterized by an interstitial inflammatory cell infiltrate.¹ Since that time, several cases have been described.²⁻⁵ The clinical features of AIN are nonspecific and mimic acute tubular necrosis; therefore, renal biopsy is still gold standard for diagnosis.⁶⁻⁷ It represents 1%–3% of all the renal...
biopsies performed and in those biopsied for unexplained AKI, AIN was found in up to 27%.6-11

AIN is frequently induced by drugs, whereas the other causes included autoimmune diseases, infections, herbal remedies, and neoplastic conditions.12,13

A few studies on the clinical features and outcomes of patients with AIN were reported and the literature was limited to case reports or series on general patterns of renal diseases.13 In Morocco, a descriptive review conducted at our center found that AIN represents 10% of all the renal biopsies between January 2008 and December 2012 but did not report of renal outcome.14 Therefore, the aim of this study was to describe the clinical features, causes, and histological characteristics as well as treatment and outcome of patients with biopsy proven AIN. We also identified the factors associated with renal recovery in our patients.

Materials and Methods

This retrospective study included all cases of renal biopsy-proven AIN between January 2008 and December 2017 at the Military Hospital Mohammed V, Rabat, Morocco.

Two cores of renal tissue were obtained: one was sent for light microscopy and the other for immunofluorescence studies. For light microscopy sections were stained using hematoxylin and eosin, periodic acid–Schiff, Masson’s trichrome, and Jones silver stains.

The diagnosis of AIN was based on the presence of an inflammatory cell infiltrates of varying composition and interstitial edema with or without interstitial fibrosis.

We excluded patients younger than 16 years, patients with glomerulonephritis or primary vascular disease, renal transplant graft biopsies and all patients with less than six months of follow-up from initial admission.

We recorded the following data for each patient: age, gender, presence of fever, uveitis, arthralgia, skin rash, eosinophilia, 24-h urinary proteinuria excretion, hematuria, leukocyturia, serum creatinine (baseline value if reported and at the time of renal biopsy), estimated glomerular filtration rate (eGFR), the need for renal replacement therapy (RRT), and histopathological findings.

Eosinophilia was defined as eosinophils: 5 × 10^9/L and the eGFR was calculated using the modified diet in renal disease study equation.

Interstitial edema and infiltration were classified according to the area of the cortex occupied by the edema and cellular infiltrate as mild (10%–30%), moderate (31%–60%) and severe (61%–100%). The nature of cellular infiltrate was composed of eosinophils, lymphocytes, plasma cells, and monocytes. We also reviewed the percentage of glomerulosclerosis, tubular atrophy, and fibrosis as well as the presence of granuloma.

The data on the presumed etiological factor of the AIN were identified by the nephrologist. According to clinical features, cause, and the renal biopsy data, the decision to use steroid treatment had been taken by the nephrologist.

We followed patients for at least six months after renal biopsy and we monitored renal function during this period. Based on the last serum creatinine available within six months, response was classified as complete, partial or nonresponder. Thus, we defined complete recovery as improvement in serum creatinine level to within 25% of its baseline (or a eGFR ≥60 mL/min/1.73 m^2 if its baseline was not available); partial recovery as a ≥50% decrease in serum creatinine level from its value at the time of biopsy, but not reaching 25% of baseline value; and no recovery as not meeting criteria for complete or partial recovery or remaining on RRT.

Ethical approval for this study was provided by the Institutional Ethical Committee of our hospital.

Statistical Analysis

Statistical analysis was carried using the Statistical Package for the Social Sciences version 19 (IBM Corp., Armonk, NY, USA). Numerical data were expressed as a mean ± standard deviation and categorical data in percentage and numerical values. P < 0.05 was considered to be statistically significant.
Results

General and clinical data

Over the 10-year period, 30 cases of AIN were included in this study, constituting 7.3% of all native renal biopsies performed on this period (n = 407). Furthermore, AIN was the most common cause of unexplained acute renal failure (ARF) (30% of all biopsies performed for unexplained ARF).

Among the 30 patients with AIN, 18 (60%) were female, 12 (40%) were male, with an average age of 47.1 ± 14.6 (range 19–78) years at the time of renal biopsy. Baseline serum creatinine levels were available for 13 patients (the mean was 10.4 ± 6.1) and two (6.6%) patients had chronic kidney disease as defined by baseline eGFR 60 mL/min/1.73 m² for at least three months. The classic triad of fever, skin rash, and eosinophilia occurred in three (10%) patients and five (16.7%) patients had uveitis. There was a need of RRT at presentation in only one (3.3%) patient. The demographic, clinical, and laboratory characteristics of the patients are listed in Table 1.

Causes of acute interstitial nephritis

The common causes of AIN in our study were drugs in 13 (43.3%) patients followed by autoimmune diseases in 11 (33.3%) patients.

The most common culprit drugs were non-steroidal anti-inflammatory drug (NSAID) (23.3%) followed by antibiotics (10%), proton pump inhibitor (PPI) (3.3%), allopurinol (3.3%), and pemetrexed (3.3%). The antibiotics implicated were cotrimoxazole, amoxicillin, and ciprofloxacin. Pemetrexed is an antifolate agent approved for the treatment of non-small cell lung cancer.

Of autoimmune diseases, sarcoidosis was the most common etiology (16.7%) followed by Sjogren syndrome (10%), mixed connective tissue disease (6.7%), and tubulointerstitial nephritis and uveitis syndrome (3.3%).

In one patient, tuberculosis was the causative agent, the other causes included herbal remedies and malignancy conditions (6.7%). The etiology was unknown in only one patient who was dependent RRT at the time of renal biopsy. The causes of AIN in this study are listed in Table 2.

Histologic findings

On histological examination, interstitial edema and infiltration were identified in all patients. Interstitial infiltration was moderate in 21 (70%) patients, whereas the remaining patients had severe infiltration; whereas interstitial edema was moderate in 16 (53.3%) patients, while the remaining patients had mild edema. Table 3 summarizes the histologic characteristics of the patients with AIN.

Treatment and renal outcomes

Overall, 20 (66.6%) patients were treated with steroids, while the remaining were treated

| Characteristics | Value |
|-----------------|-------|
| Age (years±SD)  | 47.1±14.6 |
| Gender, n (%)    |       |
| Female           | 18 (60) |
| Male             | 12 (40) |
| Arthralgia, n (%)| 9 (30) |
| Skin rash, n (%) | 10 (33.3) |
| Fever, n (%)     | 6 (20) |
| Eosinophilia, n (%)| 7 (23.3) |
| Proteinuria (g/24 h±SD) | 0.8±0.2 |
| Microhematuria, n (%) | 5 (16.7) |
| Leukocyturia, n (%) | 27 (90) |
| Serum creatinine at biopsy (mg/L±SD) | 33.9±11.8 |
| eGFR at biopsy (mL/min/1.73 m²±SD) | 20.2±7 |

SD: Standard deviation; eGFR: estimated glomerular filtration rate.
by conservatively care. At six months, of the 20 patients who received steroids, seven (35%) patients achieved complete recovery and seven (35%) patients achieved partial recovery regardless of the cause. However, corticoids treatment did not significantly impact on recovery ($P = 0.14$).

One patient required RRT at the time of renal biopsy and did not recover after six months of follow-up, thus continuing RRT.

At six months postbiopsy, of the 30 patients with AIN, 26.7%, 33.3%, and 40% had partial, complete, and no recovery, respectively. We have compared the clinical and histological features of those patients who recovered completely or partially and those who did not recover (Table 4).

In this study, a good outcome was associated with autoimmune diseases ($P = 0.02$) and with a higher intensity of interstitial edema ($P = 0.01$). However, the presence of a granuloma ($P = 0.04$), a higher percentage of interstitial fibrosis ($P = 0.01$) and glomerulosclerosis ($P < 0.01$) were associated with no recovery (Table 4).

**Discussion**

The present study summarizes the 10-year experience with renal biopsy-proven AIN at our center. It is the first report in Morocco and North Africa showing the clinical features and

---

**Table 2. Etiology of acute interstitial nephritis.**

| Etiologic factor                  | n (%) |
|-----------------------------------|-------|
| Drugs                             | 13 (43.3) |
| NSAID                             | 7 (23.3) |
| Antibiotics                       | 3 (10) |
| PPIs                              | 1 (3.3) |
| Allopurinol                       | 1 (3.3) |
| Pemetrexed                        | 1 (3.3) |
| Autoimmune                        | 11 (36.6) |
| Sarcoidosis                       | 5 (16.7) |
| Sjogren syndrome                  | 3 (10) |
| Mixed connective tissue disease   | 2 (6.7) |
| TINU syndrome                     | 1 (3.3) |
| Cutaneous T-cell lymphoma          | 1 (3.3) |
| Infections                        | 1 (3.3) |
| Herbal remedy                     | 1 (3.3) |
| Unknown                           | 1 (3.3) |

NSAID: Nonsteroidal anti-inflammatory drug, PPIs: Proton-pump inhibitors, TINU: Tubulointerstitial nephritis and uveitis.

---

**Table 3. Histologic characteristics of the patients.**

| Characteristics                          | Value        |
|------------------------------------------|--------------|
| Interstitial edema, n (%)                |              |
| Mild                                     | 14 (46.7)    |
| Moderate                                 | 16 (53.3)    |
| Severe                                   | Nil          |
| Interstitial infiltration, n (%)         |              |
| Mild                                     | Nil          |
| Moderate                                 | 21 (70)      |
| Severe                                   | 9 (30)       |
| Presence of granuloma n (%)              | 9 (30)       |
| % of interstitial fibrosis (mean±SD)     | 25.6±13.5    |
| % of glomerulosclerosis (mean±SD)        | 19.5±13.6    |

SD: Standard deviation.
outcomes of AIN.

AIN occurred in 7.3% of all native renal biopsies, this prevalence is higher than other studies.\textsuperscript{12,13} This difference may be explicated by differences of racial characteristics, indications of renal biopsy for unexplained ARF and relative reluctance to biopsy in cases with suspicions of clinical diagnosis or patients whose renal recovery was achieved after withdrawal of the culprit drug. Hence, comparison with different data in order to draw accurate conclusions is difficult.

The typical signs of AIN are fever, rash, and eosinophilia with symptoms of ARF.\textsuperscript{11,15,16} Michel et al showed that less than 30% of patients had classic triad of AIN (fever, rash, and eosinophilia) in their biopsy series.\textsuperscript{17} In another study done by Effa et al this triad occurred in only 1.9% of patients.\textsuperscript{13} In our study, the classic triad of AIN was described in 10% of patients and all patients had modest proteinuria and renal failure but there was a need of RRT at presentation in only one patient.

In our study, drugs were the most common cause of AIN followed by autoimmune diseases. This is similar to that reported in many studies worldwide.\textsuperscript{12,18-21} The findings of several studies are compared in Table 5.

The etiology of AIN is changing with prevalent medication use. The most common culprit drugs in our study were NSAID (23.3%) followed by antibiotics (10 %) while the most frequent autoimmune causes described were sarcoidosis (16.7%) followed by Sjogren’s syndrome (10%). These findings were similar to several studies where drugs were the most prevalent cause of AIN (Table 5). Thus, based on our results of a relatively small number of infectious causes and a large number of autoimmune diseases, we showed that this data may reflect the etiopathogenicity of AIN in North Africa. However, further larger studies over longer time periods are required to confirm this trend.

Muriithi et al showed that the cause of AIN had no impact on recovery at six months.\textsuperscript{12} In contrast, in our study, a good outcome (renal recovery) was associated with autoimmune diseases ($P = 0.02$). We speculate that our sample was not large enough to obtain similar results.

The treatment of AIN is empiric, withdrawing

| Table 4. Characteristics and outcome of patients with acute interstitial nephritis. |
|---------------------------------|-----------------|-----------------|---|
| **Characteristics**             | **Recovery (n=18)** | **No recovery (n=12)** | **P** |
| Age (years) (mean±SD)           | 46.8±14.9        | 47.5±14.8        | 0.89 |
| Gender, n (%)                   |                  |                  | 0.45 |
| Female                          | 12 (66.7)        | 6 (33.3)         |      |
| Male                            | 6 (50)           | 6 (50)           |      |
| Eosinophilia, n (%)             | 5 (71.4)         | 2 (28.6)         | 0.67 |
| Serum creatinine at biopsy (mean±SD) | 31.8±11.7       | 37.1±11.6        | 0.24 |
| Autoimmune disease induced AIN, n (%) | 10 (90.1)        | 1 (9.9)          | 0.02 |
| Drug induced AIN, n (%)         | 6 (46.2)         | 7 (53.8)         | 0.17 |
| Interstitial edema, n (%)       |                  |                  | 0.01 |
| Mild                            | 5 (35.7)         | 9 (64.3)         |      |
| Moderate                        | 13 (81.2)        | 3 (18.8)         |      |
| Severe                          | Nil              | Nil              |      |
| Interstitial infiltration, n (%)|                  |                  | 0.7  |
| Mild                            | Nil              | Nil              |      |
| Moderate                        | 12 (57.1)        | 9 (42.9)         |      |
| Severe                          | 6 (66.7)         | 3 (33.3)         |      |
| % of interstitial fibrosis (mean±SD) | 16.6±8.4         | 39.1±6.6         | 0.01 |
| Presence of granuloma n (%)     | 8 (88.9)         | 1 (11.1)         | 0.04 |
| % of glomerulosclerosis (mean±SD) | 10.5±7.8         | 32.9±8.1         | 0.01 |
| Steroid therapy                 | 14 (70)          | 6 (30)           | 0.14 |

AIN: Acute interstitial nephritis, SD: Standard deviation.
| Studies                  | Year | Country    | Number of patients | Causes of AIN                      | Proportion of dependence RRT at time of renal biopsy | Proportion steroid treated | Outcome                                                                 |
|-------------------------|------|------------|--------------------|-----------------------------------|-----------------------------------------------------|----------------------------|------------------------------------------------------------------------|
| Bhaumik et al²²          | 1996 | India      | 19                 | 100% drug induced                 | 69% RRT dependent                                   | 31.5%                      | No effect of steroid therapy on the extent of renal recovery at last follow-up |
| Clarkson et al¹¹         | 2004 | Ireland    | 60                 | 92% drug induced                  | 58% RRT dependent                                   | 60%                        | No difference in serum creatinine at 1 year                               |
| Gonzalez et al²³        | 2008 | Spain      | 61                 | 100% drug induced                 | 23% RRT dependent                                   | 85%                        | Higher serum creatinine at last follow-up in those not steroid treated   |
| Raza et al²⁰            | 2012 | England    | 49                 | 67% drug induced 12.2% autoimmune diseases | 22.4% RRT dependent                               | 75%                        | Greater improvement in creatinine in steroid-treated patients at last follow-up |
| Muriithi et al¹²        | 2014 | USA        | 133                | 71% drug induced 16.9% autoimmune diseases | 22.4% RRT dependent                               | 86%                        | Within drug induced-AIN group, no difference in the recovery of renal function within the first 6 months in steroid-treated group |
| Valluri et al²¹         | 2015 | Scotland   | 171                | 73% drug induced 16.9% autoimmune diseases | 19% RRT dependent                                  | 63%                        | Within drug induced-AIN group, no difference in the recovery of renal function within the first 6 months in steroid-treated group |
| Effa et al¹³            | 2017 | South Africa | 54              | 70.4% drug induced 14.8% infections | 33.9% RRT dependent                                | 35.2%                      | Steroid did not influence renal recovery at 90-day postrenal biopsy     |
| Prendecki et al¹⁸       | 2017 | England    | 187                | 25% drug induced 14% autoimmune diseases | 12.3% RRT dependent                               | 84.5%                      | Greater improvement in creatinine in steroid-treated patients at 24 months |
| Wilson et al¹⁹          | 2017 | Australia  | 40                 | 40% drug induced 17.5% autoimmune diseases | 5% RRT dependent                                   | 57.5%                      | Steroid did not influence renal recovery at 90-day postrenal biopsy     |
| Our study               | 2019 | Morocco    | 30                 | 43.3% drug induced 36.6% autoimmune diseases | 3.3% RRT dependent                                 | 66.6%                      | Steroid did not significantly impact on recovery at 6 months postrenal biopsy |

AIN: Acute interstitial nephritis, RRT: Renal replacement therapy.
the culprit drug and treating the causative agent are the most effective intervention.\textsuperscript{12} Effect of steroid therapy in AIN remains unclear. In fact, several studies questioned the effectiveness of steroids, which have shown conflicting results. (Table 5) In the current study, we found that steroids did not significantly impact on renal recovery ($P = 0.14$). Similar results were reported by other studies (Table 5). In contrast, one Spanish study found that there was the good recovery of kidney functions after treatment with steroids and have established the importance of early start of steroids for renal recovery and to avoid the evolution of interstitial cellular infiltrates to interstitial fibrosis.\textsuperscript{23}

In another study, Raza et al. showed a greater proportion of renal recovery in steroid-group. However, no association was found between the degree of renal recovery and delay in starting steroids.\textsuperscript{20}

The data about histological examination which provides important information about the renal outcome of AIN are few and conflicting.\textsuperscript{22} Bhaumik et al showed that the presence of interstitial fibrosis and tubular atrophy were associated with poor prognosis; however, the severity and type of infiltrates did not affect the renal outcome.\textsuperscript{22} In contrast, Buysen et al. found no correlation between interstitial fibrosis, tubular atrophy and interstitial edema, infiltration and clinical course.\textsuperscript{24}

In this study, a good outcome was associated with higher intensity of interstitial edema ($P = 0.01$). However, a higher percentage of interstitial fibrosis ($P = 0.01$) and glomerulosclerosis ($P = 0.01$) were associated with no recovery. Thus, interstitial fibrosis and glomerulosclerosis are signs of chronicity, so it is understandable that the presence of these may be a factor in no renal recovery.

The current study found that the presence of a granuloma was associated with no renal recovery ($P = 0.04$). Similar results were also reported in another study reported by Singer et al.\textsuperscript{25}

**Limitation of study**

There were some biases in the current study. First, our study included a small sample size due to the fact that renal biopsy was not indicated systematically in AKI. Hence, our results do not clearly describe the spectrum of AIN. Second, this was a retrospective study and indications for corticosteroids in the management of drug-related AIN were not standardized. Therefore, large prospective regional studies are needed for further definition of clinical features of AIN, indications of corticosteroids and the factors of renal prognosis.

**Conclusion**

In this study, AIN is identified in a relative minority of all renal biopsies. It is frequently associated with the prescription of drugs and autoimmune diseases. A good outcome was associated with autoimmune diseases and with higher severity of interstitial edema. However, the presence of a granuloma, a higher percentage of interstitial fibrosis and glomerulosclerosis were associated with no recovery and steroids seem to have no effect in the recovery. This information provides a contribution toward understanding the epidemiology of AKI in Africa, with possible implications for the planning of future prospective studies.

**Conflict of interest:** None declared.

**References**

1. Councilman WT. Acute interstitial nephritis. J Exp Med 1898;3:393-420.
2. Galpin JE, Shinaberger JH, Stanley TM, et al. Acute interstitial nephritis due to methicillin. Am J Med 1978;65:756-65.
3. Lo WK, Rolston KV, Rubenstein EB, Bodey GP. Ciprofloxacin-induced nephrotoxicity in patients with cancer. Arch Intern Med 1993;153:1258-62.
4. Abu-Romeh SH, Huraib SO, Quadri MK, et al. Rifampicin-induced acute renal failure: A case report. Saudi J Kidney Dis Transpl 1996;7:401-3.
5. Aatif T, Fatih J, El Annaz H, Qamooss O. Allopurinol-induced drug reactions with eosinophilia and systemic symptoms syndrome with interstitial nephritis. Indian J Nephrol
6. Kodner CM, Kudrimoti A. Diagnosis and management of acute interstitial nephritis. Am Fam Physician 2003;67:2527-34.

7. Wilson DM, Turner DR, Cameron JS, Oggy CS, Brown CB, Chantler C. Value of renal biopsy in acute intrinsic renal failure. Br Med J 1976;2:459-61.

8. Cameron JS. Allergic interstitial nephritis: Clinical features and pathogenesis. Q J Med 1988;66:97-115.

9. Rossert J. Drug-induced acute interstitial nephritis. Kidney Int 2001;60:804-17.

10. Farrington K, Levison DA, Greenwood RN, Cattell WR, Baker LR. Renal biopsy in patients with unexplained renal impairment and normal kidney size. Q J Med 1989;70:221-33.

11. Clarkson MR, Giblin L, O'Connell FP, et al. Acute interstitial nephritis: Clinical features and response to corticosteroid therapy. Nephrol Dial Transplant 2004;19:2778-83.

12. Muriithi AK, Leung N, Valeri AM, et al. Biopsy-proven acute interstitial nephritis, 1993-2011: A case series. Am J Kidney Dis 2014;64:558-66.

13. Effa EE, Ekrikpo UE, Borkum M, Rayner BL, Heering P, Okpechi IG. Clinical profile and outcome of patients with biopsy-proven acute interstitial nephritis in cape town: A 10-year review. Clin Nephrol 2017;88:97-104.

14. Zajjar Y, Aatif T, Bahadi A, Hassani K, El Kabbaj D, Benyahia M. Kidney biopsy in the military hospital of morocco: Complications and histopathological findings. Saudi J Kidney Dis Transpl 2015;26:1044-9.

15. Praga M, González E. Acute interstitial nephritis. Kidney Int 2010;77:956-61.

16. Praga M, Sevillano A, Auñón P, González E. Changes in the aetiology, clinical presentation and management of acute interstitial nephritis, an increasingly common cause of acute kidney injury. Nephrol Dial Transplant 2015;30:1472-9.

17. Michel DM, Kelly CJ. Acute interstitial nephritis. J Am Soc Nephrol 1998;9:506-15.

18. Prenderg W, Tanna A, Salama AD, et al. Long-term outcome in biopsy-proven acute interstitial nephritis treated with steroids. Clin Kidney J 2017;10:233-9.

19. Wilson GJ, Kark AL, Francis LP, Hoy W, Healy HG, Mallett AJ. The increasing rates of acute interstitial nephritis in Australia: A single centre case series. BMC Nephrol 2017; 18:329.

20. Raza MN, Hadid M, Keen CE, Bingham C, Salmon AH. Acute tubulointerstitial nephritis, treatment with steroid and impact on renal outcomes. Nephrology (Carlton) 2012;17:748-53.

21. Valluri A, Hetherington L, Mcquarrie E, et al. Acute tubulointerstitial nephritis in scotland. QJM 2015;108:527-32.

22. Bhaumik SK, Kher V, Arora P, et al. Evaluation of clinical and histological prognostic markers in drug-induced acute interstitial nephritis. Ren Fail 1996;18:97-104.

23. González E, Gutiérrez E, Galeano C, et al. Early steroid treatment improves the recovery of renal function in patients with drug-induced acute interstitial nephritis. Kidney Int 2008; 73:940-6.

24. Buysen JG, Houthoff HJ, Krediet RT, Arisz L. Acute interstitial nephritis: A clinical and morphological study in 27 patients. Nephrol Dial Transplant 1990;5:94-9.

25. Singer DR, Simpson JG, Catto GR, Johnston AW. Drug hypersensitivity causing granulomatous interstitial nephritis. Am J Kidney Dis 1988;11:357-9.

Date of manuscript receipt: 1 January 2019.

Date of final acceptance: 30 January 2019.