Clinical characteristics of acute lobar nephronia in renal allograft

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To the Editor: Acute lobar nephronia (ALN), also known as acute focal bacterial nephritis, is a severe form of upper urinary tract infection (UTI) that is characterized by the presence of an inflammatory mass lesion in the kidney without abscess formation. It is considered to be the midpoint between acute pyelonephritis and renal abscess.[1] ALN was first described in 1979 as a radiologic diagnosis in ten adults and two children.[2]

There are no useful laboratory biomarkers for ALN; therefore, its diagnosis depends mostly on imaging studies. The diagnostic criteria for ALN include: (1) a history of UTI, fever, chills, and pain around the affected kidney; and (2) a poorly defined striated or wedge-shaped lesion with decreased enhancement on computed tomography (CT) imaging.[3] In the acute stage, ALN is usually considered a severe form of pyelonephritis. In the chronic stage, irregular follow-up after transplantation may cause physicians to overlook pathological developments during the formation and disappearance of transplant scars. This could result in an initial diagnosis of unexplained renal masses in the transplant allograft. Furthermore, due to the widespread use of new immunosuppressant medications, the incidence of UTIs has increased. Consequently, it is essential to investigate the clinical characteristics and disease progression of ALN in transplant recipients to reduce the likelihood of missed or incorrect diagnoses, as well as inappropriate treatments.

We retrospectively reviewed patients who were initially diagnosed with UTI at Nanfang Hospital of Southern Medical University, between January 2005 and January 2021. Patients who met the diagnostic criteria for ALN were selected based on clinical presentation and CT radiological findings.[3] Data on patient demographics, transplant, and post-operative immunosuppression regimens, and the course of the upper UTI were collected to summarize the ALN clinical characteristics and disease progression in renal transplant allografts. This study was approved by the Ethics Committee of Nanfang Hospital of Southern Medical University (NFEC-2020-044). In addition, we conducted a literature search for ALN in renal allografts using the keywords "acute lobar nephronia [abstract/title]" or "acute focal bacterial nephritis [abstract/title]," and "renal transplant [abstract/title]" or "kidney transplant [abstract/title]" in PubMed. Eligible studies that were published between January 1, 1979 and January 31, 2021 were included without any language restrictions.

A total of 14 renal transplant recipients with ALN were included [Supplementary Table S1, http://links.lww.com/CM9/A945]. We identified eight patients (Cases 1–8) from our center by retrospectively reviewing 302 renal transplant patients with a diagnosis of UTI who received renal transplants (at our center) between January 2005 and January 2021. Additionally, six single case reports of ALN in renal transplant recipients were identified in the literature review (Cases 9–14). All six cases met the accepted diagnostic criteria for ALN based on the clinical presentation and radiological findings described in the original publications.

Renal transplantation in the 14 patients were performed over a period of 36 years (1985–2021). The male to female ratio was 1:6, and the median age at transplantation was 36.5 (range 17–65) years. Cadaveric donation accounted for 11/13 of cases (donor information was not provided in Case 14), whereas living relatives provided the remaining donations. Seven recipients (7/13, underlying diseases were not provided in Case 14) had diabetes, and three recipients (3/13) were hepatitis B virus carriers.

The median time of occurrence of ALN after transplantation was 49 (range 2–180) months. In the acute phase of

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disease presentation, 12/14 of the patients had hyperpyrexia and 10/14 had discomfort or tenderness in the renal allograft region. Laboratory findings revealed that 12/13 (Case 14 was excluded due to lack of information) of the patients had positive hemogram or infection indices including leukocyte count, neutrophil percentage, and C-reactive protein (CRP) levels. Abnormal leukocyte counts in the midstream urine were found in 12/13 (Cases 9 and 14 excluded) of the patients, and 7/14 of the patients had decreased renal allograft function. With the exception of four patients who had unidentified pathogens, we found that 10/13 (13 species) of the pathogenic microorganisms detected in the patients were gram-negative bacteria, such as *Escherichia coli, Klebsiella pneumoniae*, and *Proteus mirabilis*, and 3/13 (13 species) were gram-positive bacteria, including *Enterococcus faecalis* and *Staphylococcus aureus*.

Biopsies were performed in three of the eight patients from our center to rule out malignancies. Histopathological examination of renal tissue from patients with ALN showed dense acute and chronic inflammatory infiltrates in the renal parenchyma without evidence of neoplasia or renal allograft rejection. These results were similar to the pathological findings in two of the six published cases that reported biopsy findings.

The average duration of antibiotic maintenance therapy in the acute phase of the 14 cases was 15.6 ± 8.9 days. All eight patients from our center were administered intravenous or oral antibodies, and their urine white blood cell (WBC) counts became negative after 4.6 ± 3.0 days of the targeted antibiotic treatment. The patients were followed up once per month after transplantation, with a median follow-up duration of 72.5 (range 2–188) months. ALN recurred during follow-up in three cases (Cases 2, 3, and 4). Seven of the eight patients from our center showed chronic renal scar formation, which was detected using B-scan ultrasound, and two of those cases developed recurrence in the scar area with non-specific granulomatous changes confirmed by pathological diagnosis on biopsy. The renal function of six patients from our center recovered gradually after the use of targeted antibiotics (ABX), and the allografts have remained well functional so far (median duration 57 months, range 2–134 months). Allografts in Cases 3 and 7 were lost due to chronic rejection at 14 and 8 months, respectively, after developing ALN. In the six patients reported in the literature (Cases 9–14), the renal lesions gradually resolved between 2 weeks and 6 months, with the ultimate recovery of renal function. There were no available long-term follow-up data for those cases.

Based on the clinical presentation, we summarized and divided the ALN disease course after transplantation into three phases [Figure 1]. Phase I is the early stage of acute exacerbation of chronic UTI. The onset of the disease is insidious and recurrent, with no typical clinical signs or mild urination discomfort. Renal allograft imaging, hemogram, or infection indices often show no positive findings, and the presence of leukocytes in the urine may be the only finding. Phase II is the stage of acute suppurative infection. At this stage, misdiagnoses are common. Patients often have acute disease onset following strenuous physical activities and show typical symptoms of upper UTIs, such as rigors, hyperpyrexia, and discomfort in the region of the renal allograft. Laboratory findings include a significant increase in blood infection indices (eg, leukocyte count, neutrophil band cell count, and CRP level) and a decrease in renal allograft function. A positive culture for pathogenic microorganisms in blood and urine may be observed, with *E. coli, Klebsiella, Proteus,* and *Streptococcus* being the most common pathogens.[5] Pathogens may invade the renal parenchyma of the allograft by retrograde infection and could colonize the renal pelvis, which may lead to ALN. Additionally, pathogens may enter the systemic circulation. In this phase, radiological findings are most remarkable. Ultrasonography shows either hyperechoic or hypoechoic areas with unclear boundaries[3] inside the renal parenchyma of the allograft, mostly located in the upper pole (8/11 cases in our study; Figure 1C and 1G). CT images may show transverse striations or wedge-shaped non-homogeneous low-density shadows with poorly defined boundaries [Figure 1A and 1E] in or around the transplanted kidney [Figure 1E]. A moderate enhancement is observed after contrast-enhanced scanning [Figure 1A]. Positron emission tomography (PET)-CT imaging may indicate solid changes and hypermetabolic foci (5/6 in our study; Figure 1B and 1F). Histopathological examination of the renal tissue in ALN reveals suppurative changes in the renal parenchyma without evidence of neoplasia or renal allograft rejection. Secondary infections of other pathogenic microorganisms may form granulomas. Recurrent infection and a protracted course of the disease lead to renal allograft failure. Usually, the patient's clinical condition improves rapidly after the initiation of antibiotic treatment. In our patients, laboratory tests showed that blood infection indices decreased and urine WBC counts became negative, resulting in the recovery of renal function. However, infections may not resolve immediately, and fibrosis and scar tissue may also develop.

Phase III is the scar formation stage. In our patients, ultrasonography showed a slight echo-enhancement and hypoechogenic region with an indistinct margin and heterogeneous density. However, PET-CT examination at this stage showed no obvious abnormalities. Pathological biopsy results showed chronic tubulointerstitial damage and fibrotic changes. Generally, if patients have a poor response to antibiotic therapy, ALN lesions may gradually liquefy, form abscesses, and enter the stage of renal abscess possibly leading to allograft rupture. At this time, the condition is severe, and surgical interventions such as drainage must be applied.

In summary, ALN often presents as renal masses and may easily be misdiagnosed as renal cancer, resulting in allograft loss through nephrectomy. A diagnosis of ALN should be considered in patients who have had short-term anti-infective treatment without subsequent reduction of the focal lesions in renal allografts. After imaging, pathological diagnosis, and identifying the pathogenic microorganisms, a sufficient course of ABX should be administered to reduce recurrence and scar formation. In addition, regular follow-up and dynamic

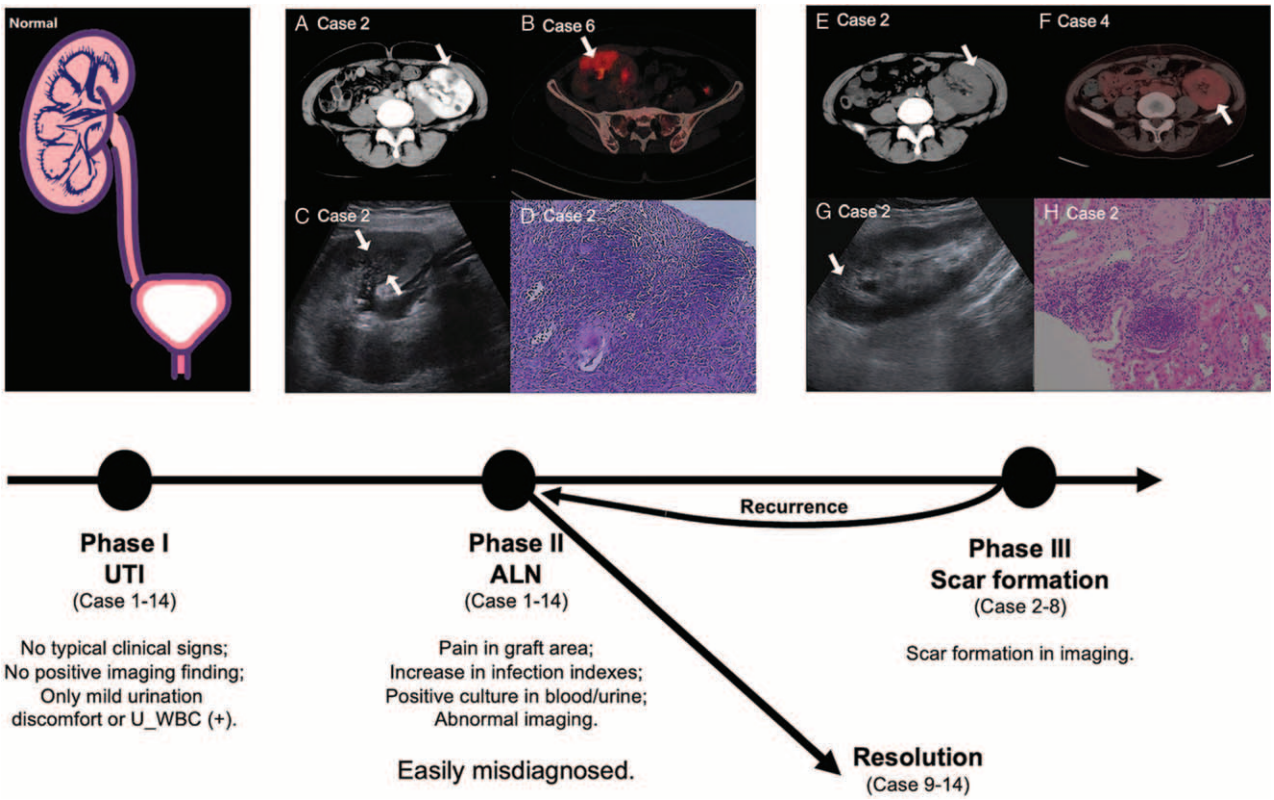

Figure 1: Diagram, imaging, and pathology results at different stages of lobar nephroma (A-H). Phase II: Acute infection. Ultrasonography (US) shows a heterogeneous liquid anecholc area mostly at the upper pole of the renal parenchyma with unclear borders, while some lesions appear as solid masses. CT reveals a heterogeneous hypodense mass in the renal allograft with ill-defined margins, and enhanced scanning shows moderate enhancement. PET-CT reveals a solid lesion and hypermetabolic foci. A pathological biopsy is beneficial to confirm the diagnosis, which presents as suppurative lesions and a proliferation of surrounding fibrous tissue without signs of oncogenesis or rejection. Phase III: Chronic scarring after infection. US shows increased echogenicity with an inner heterogeneous hypoechoic area and ill-defined margins. A CT image shows low-density shadows in and around the transplanted kidney. There are no apparent abnormalities in the PET-CT images. Hematoxylin and eosin staining (Original magnification × 100) demonstrates chronic tubulointerstitial injury and fibrosis. ALN: Acute lobar nephronia; CT: Computed tomography; PET: Positron emission tomography; UTI: Urinary tract infection.

monitoring using ultrasound should be performed to monitor changes in the infection focus.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

None.

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