Case of the Month

Case of the month from Lillebaelt hospital, University Hospital of South Denmark, Denmark: Renacidin® – still a useful adjunct to endoscopic surgery for complex renal struvite stone disease

Louise Faurholt Øbro, Susanne Sloth Osther, Palle Jørn Sloth Osther and Helene Jung
Department of Urology, Vejle Hospital – A Part of Lillebaelt Hospital, University Hospital of Southern Denmark, Vejle, Denmark

Introduction

Renal infection stones constitute a particular treatment challenge because of the combination of large stone burden and associated UTI with urease-producing bacteria. As small residual fragments are thought to represent a 'nidus' of stone re-growth, it is of utmost importance to render patients with infection stones completely stone-free [1]. Because of the soft 'matrix' constitution of struvite (magnesium ammonium phosphate) stones, complete endoscopic removal may be impossible, especially in difficult anatomical circumstances.

Renacidin® is a citrate- and magnesium-containing chemolytic agent that was used to prevent and dissolve renal struvite and apatite stones in the 1960s. As a result of severe adverse events, the use of Renacidin was banned by the US Food and Drug Administration in 1963 and not reapproved until 1990 [2]. It was concluded that the Renacidin mortalities observed after renal stone dissolution were attributable to increased intrarenal pressure and obstructed ureteric catheters rather than to drug toxicity [3]. After the banning of the drug, Nemoy and Stamey proposed a protocol for Renacidin irrigation, describing preparation measures in terms of laboratory studies, contraindications and irrigation settings [4]. Acknowledgement of the crucial necessity of sterile renal urine prior to treatment and sufficient renal drainage facilitated the resumed approval of Renacidin in 1990 [2]. However, after renewed popularity in the 1990s, the use of Renacidin ceased again after a decade, as the shortcomings of the treatment seemed to outweigh its advantages. The Renacidin treatment regimen requires extensive planning and collaboration with several other departments such as infective diseases, nephrology, radiology, pharmacy and the intensive care unit (ICU). The patient should be prepared for potentially long hospital stays under 1:1 observation at the ICU. Thus, the procedure is costly and time-consuming and is moreover in strong competition with increasing technological improvements that allow for more complex cases to be treated endourologically. However, in very selected cases, Renacidin chemolysis in combination with endourology may be the only option to render a patient with struvite stones stone-free.

We present our experience of a challenging case and the restart of a Renacidin irrigation programme to treat renal struvite stones.

Case Presentation

This case report outlines the treatment regimen in a patient with severe, recurrent, hitherto treatment-refractory struvite stones using a combination of endourological surgery and intraluminal lavage with Renacidin.

In 2020, a 52-year-old woman was referred to the Department of Urology, Vejle Hospital, part of Lillebaelt Hospital, Denmark, for a second opinion after several failed attempts to render the patient stone-free. CT, laboratory analyses and stone analysis documented bilateral struvite stones, recurrent UTI (Proteus mirabilis and Pseudomonas aeruginosa) and renal impairment (creatinine 150–220 mmol/L) due to recurrent obstructive renal calculi. Four ureteroscopic procedures had been performed (right kidney), but stones were not sufficiently cleared due to their soft matrix composition, and significant stone burdens re-occurred on a monthly basis. The patient presented with flank pain, renal obstruction and urinary infection at the Emergency Department several times a month and was on indefinite sick leave due to kidney stone disease.

Initially, we scheduled the patient for endourological treatment (endoscopic combined intrarenal surgery [ECIRS]) in order to clear the stone burden on the right side. Endoscopic view revealed solid struvite calculi and soft matrix stones occluding the entire collecting system including the ureter on the right side (Fig. 1A,B). The soft and obstructive matrix was not visible on CT, hence, the stone burden was even greater than anticipated based on preoperative imaging. Moreover, two of the anterior calyces containing larger, solid stones were not accessible with endourological tools due to very narrow calyx necks. Trilogy (EMS, Nyon, Switzerland)
was used in an attempt to remove the matrix by a combination of ballistic energy and suction, as the stone material was resistant to laser treatment.

After 5 months and three ECIRS procedures it became clear that the patient would not become stone-free, as new, large stone burdens continued to recur within very short time periods. Accordingly, we requested the Danish Health Authorities for permission to use Renacidin for chemolysis in this special case, as Renacidin is not an approved drug in Denmark. After approval by the relevant authorities, meticulous informed consent to proceed with chemolytic treatment was obtained from the patient.

Treatment Approach

Table 1 shows the treatment protocol. Two Ch. 12 nephrostomy tubes (Rüsch, Teleflex Medical), one in the upper pole and one in the lower pole, and a JJ stent (Polaris 5/26) were inserted into the right kidney 5 days prior to treatment. A bladder catheter drained the bladder. Intravenous piperacillin/ tazocin 2 g three times daily was administered beginning 24 h before Renacidin infusion started.

The patient was monitored on a 1:1 staff to patient ratio at the ICU. Laboratory analyses including blood count, calcium, magnesium, phosphate, creatinine, potassium, sodium and urine culture were performed. A CT was performed 24 h prior to initiation of Renacidin treatment.

Irrigation was initiated with saline 60 mL/h through the upper pole nephrostomy tube. When 20 min of saline irrigation was tolerated without flank pain, Renacidin irrigation could begin. Renacidin 60 mL/h was administered through the upper pole nephrostomy tube, increasing to 120 mL/h if no flank pain or fever was reported. Outflow was monitored in the lower pole nephrostomy tube and in the bladder catheter. Careful inspection and measurement of the outflow of irrigant and urine was carried out every 10 min throughout the procedure. Laboratory analyses were repeated twice daily, with special attention to magnesium and phosphate levels. The patient was observed for flank pain, and heart rate, blood pressure and body temperature were monitored every hour. Renacidin irrigation was conducted for 8 h daily on 7 days. A urine culture was performed every second day.

Results

After 7 days of Renacidin irrigation, a CT scan and a ureteroscopy was performed. On ureteroscopic view, the matrix that previously occluded the entire collecting system was found to be totally cleared from the system and no solid calculi could be visualized. On CT, a few small solid stones (<10% of initial stone burden) were left behind in one of the occluded, anterior calyces that was not endoscopically accessible. Hydronephrosis had decreased significantly (Fig. 2A,B). Creatinine level decreased after treatment to <100 mmol/L. There were no complications to the treatment. The patient is currently 10 months from treatment and still no stones or signs of obstruction have recurred in the right kidney. A renogram shows increased renal function on the right side and creatinine level remains normal. There have been no UTIs since the end of Renacidin treatment. The patient now awaits treatment on the contralateral kidney.

Discussion

Renacidin irrigation in combination with endourology proved to be an effective agent for the treatment of severe, otherwise
treatment-refractory struvite stones. The treatment protocol requires a large set-up, good patient compliance and intensive observation during treatment. Other authors report treatment duration of up to 71 days to clear bilateral stones [5] and also advocate for vigilant monitoring and multidisciplinary collaboration for a safe and efficient outcome.

Table 1 Treatment protocol.

| Preoperatively | Treatment protocol | Contraindications and requirements |
|----------------|--------------------|-----------------------------------|
| 1. Laboratory studies: blood count, metabolic panel, calcium, uric acid, magnesium, phosphate, creatinine, urine culture | 1. Initiate irrigation with saline 60 mL/h through nephrostomy tube 1 (upper pole) | Stop Renacidin irrigation in case of: (see below) |
| 2. Stone analysis (infrared spectroscopy) | 2. Observe that inflow equals outflow + expected diuresis in nephrostomy tube 2 (lower pole) | Flank pain |
| 3. CT urography | 3. Observe the patient for flank pain | Fever |
| 4. PCNL and/or URS to clear as much of the stone burden as possible endoscopically prior to irrigation treatment. | 4. After 30 min, if no flank pain, and inflow = outflow, initiate Renacidin irrigation 60 mL/h | Increased plasma magnesium |
| 5. Insert two nephrostomy tubes, preferably one in the upper pole and one in the lower pole, one JJ catheter and a bladder catheter prior to treatment to secure optimal drainage | 5. Observe for flank pain and outflow | Objective measures indicating acute UTI |
| 6. Prepare the patient for long-lasting treatment – up to 20 days. Obtain informed consent | 6. If no flank pain and inflow = outflow, increase Renacidin irrigation to 120 mL/h | Nephrostomy tube leakage |
| 7. Establish collaboration with key stakeholders from nursing, pharmacy, nephrology and ICUs | 7. Continue intensive observation for flank pain and diuresis | No treatment effect after 7 days of irrigation |
| | 8. Monitor heart rate, blood pressure, temperature × 1-2/ h | |
| | 9. Daily laboratory tests: creatinine, magnesium, phosphate, sodium, calcium, potassium, blood count, urine culture | |
| | 10. Irrigate with Renacidine 8–10 h daily | |
| | 11. Continue irrigation 7–20 days or until patient is rendered stone-free | |
| | 12. CT once a week to assess stone burden | |
| | 13. Prophylactic intravenous antibiotic according to previous urine culture to be administered intravenously on a daily basis throughout the irrigation period | |

ICU, intensive care unit; PCNL, percutaneous nephrolithotomy; URS, ureterorenoscopy.

Fig. 2 (A) CT showing right kidney prior to Renacidin® treatment. A JJ stent has been inserted. (B) CT showing the right kidney after treatment with Renacidin.
Acknowledgement
Open access funding enabled and organized by ProjektDEAL.

Disclosure of Interests
None to declare.

Patient Consent
The authors received and archived patient consent for image recording and publication in advance of the image recording procedures and publication.

References
1 Tiselius HG, Hellgren E, Andersson A et al. Minimally invasive treatment of infection staghorn stones with shock wave lithotripsy and chemolysis. Scand J Urol Nephrol 1999; 33: 286–90
2 Gonzalez RD, Whiting BM, Canales BK. The history of kidney stone dissolution therapy: 50 years of optimism and frustration with renacidin. J Endourol 2012; 26: 110–8
3 Auerbach S, Mainwaring R, Schwarz F. Renal and ureteral damage following clinical use of Renacidin. JAMA 1963; 183: 61–3
4 Nemoy NJ, Stamey TA. Surgical, bacteriological and biochemical management of “infection stones”. JAMA 1971; 215: 1470–6
5 Parkhomenko E, Williams V, Kurtz M. Stone dissolution: Current safe and effective use of Renacidin. Videourology 2021; 35. https://doi.org/10.1089/vid.2021.0016

Correspondence: Helene Jung, Department of Urology, Vejle Hospital – Part of Lillebaelt Hospital, University Hospital of Southern Denmark, Jomsborgvej 8, 5000 Odense C, Denmark.
e-mail: helene.jung@rsyd.dk

Abbreviations: ECIRS, endoscopic combined intrarenal surgery; ICU, intensive care unit.