

RITUXIMAB IN THE MANAGEMENT OF ADULTS' GLOMERULAR DISEASES

(A retrospective study about 15 cases)



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Introduction: Glomerular diseases are renal disorders resulting from damage to the glomerulus. Besides supportive care therapy, conventional immunosuppression plays a key role in their therapeutic strategy. Yet, its numerous severe adverse effects paved the way for more-targeted approaches, notably monoclonal antibodies (mAb), of which, Rituximab (RTX), an anti-CD20 mAb. Its use was initially approved in lymphoproliferative conditions and extended afterward to auto-immune, including renal, diseases. However, most of RTX's indications in Nephrology are "Off-Label". This study aims to highlight the increase of off-label indications of RTX in Nephrology and evaluate its efficacy in the management of different glomerular diseases.

Materials and methods:

This study is a monocentric retrospective cohort study conducted in the Nephrology department of the Hassan II University Hospital in Fez, Morocco. It included patients with a glomerular disease who received RTX during their follow-up at the department, with an age > 16 years old and regardless of their sex or medical history. The data collection and analysis started in January 2022 and lasted until December 2022, 3 months after the last administered dose of RTX.

Results:

15 patients are included in our study. The sex ratio is ≈ 0,67 (6:9). The mean age at the administration of RTX is ≈ 35,87 ± 19,07 [16 - 78] years old. The mean duration of the follow-up is ≈ 20,47 ± 25,39 [1-98] months. Before RTX's administration, the average values of the biochemical markers were as follows:

Protein in the urine (g/d) = 4,92 ± 3,36 [0,75-11];
Serum Albumin (g/L) = 27,8 ± 7,18 [18-39];
Serum Creatinine (mg/L) = 26,42 ± 24,55 [6-92];
e-GFR (mL/min/1,73m²) = 59,26 ± 49,23 [6-158].

8 patients had nephrotic syndrome or nephrotic-range proteinuria before RTX and 4 patients had microscopic hematuria. 8 patients had an e-GFR < 60 mL/min/1,73m².

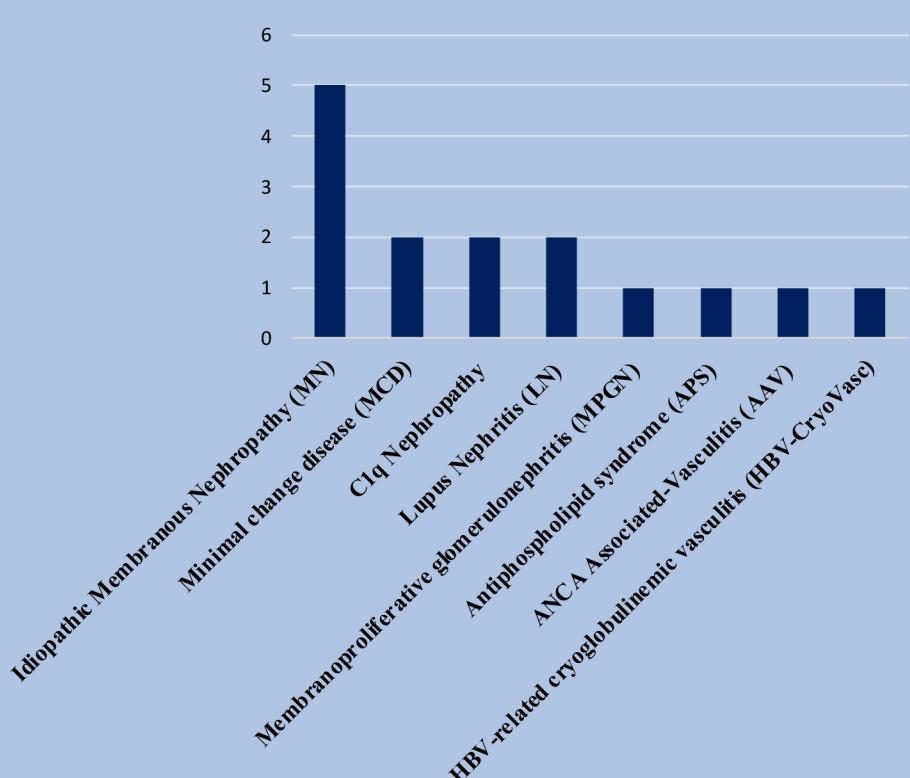
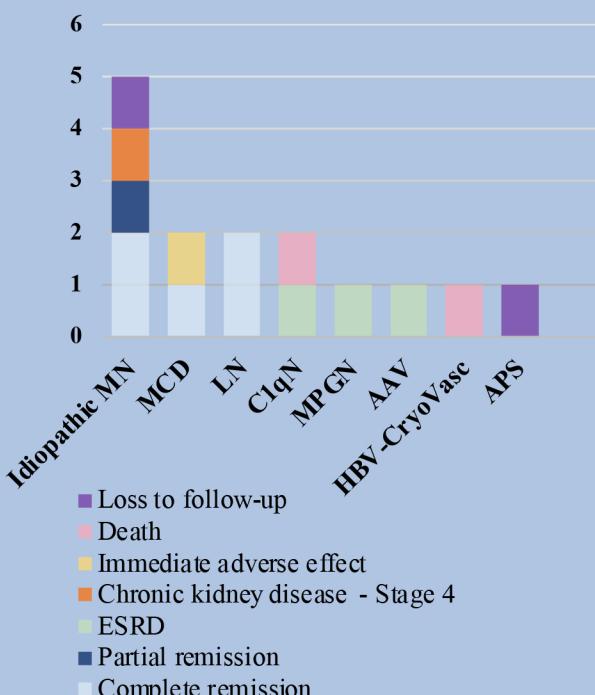
The indications of RTX covered the glomerular diseases shown in Graphic 1.

7 cases received the 2-infusion regimen (1g/week for 2 weeks) vs. 6 who received the 4-infusion regimen (375 mg/m²/week for 4 weeks). RTX was mostly prescribed as a 2nd or 3rd line therapy.

The data collected shows a total remission rate of 40%. 3 cases (20%) developed end-stage kidney disease (ESRD) requiring long-term hemodialysis (Graphic 2).

There was one case of infusion-related adverse effects (rash, shortness of breath, and excessive sweating) and 3 cases of infectious complications, of which 2 cases of death: 1 case of bacterial and tuberculous meningitis, associated with hypogammaglobulinemia and 1 case of septic shock due to multidrug-resistant urinary tract infection and skin infection.

The 3rd case of infectious adverse effects presented a urinary tract infection.



Graphic 1: Indications of RTX in the study.



Discussion:

The small number of included patients may be due to the little availability and the high cost of RTX. Yet, the prescription rate increased during the past few years. The main indication of RTX in our study was idiopathic MN. In comparison to studies conducted in the MENA region, there appears to be no significant discrepancy in terms of efficacy and safety [1][2][3].

Indications and recommendations: [4]

MN: KDIGO 2021 recommends the use of RTX as a therapeutic option in moderate to high-Risk MN, as a 1st line treatment, after relapse, or in a first resistance episode with stable e-GFR.

MCD: It is recommended as a 1st line treatment in steroid-dependent/frequently relapsing MCD or when glucocorticoid (GC) -sparing is necessary.

AAV: AAV is the only on-label indication of RTX. RTX is preferred in certain situations, such as in the pediatric population, patients concerned about their fertility, weakened elderly adults, relapsing AAV, AAV with PR3-ANCA, and the necessity of corticoid-sparing therapy. GC-RTX-Cyclophosphamide can be considered in severe renal disease.

LN: KDIGO recommends the use of RTX in active class III or IV +/- V for corticosteroid minimization or in refractory LN, and class V LN with nephrotic syndrome.

Immune-mediated MPGN: RTX is considered in decreased kidney function and active urinary sediment as a 2nd line therapy after a failure to Mycophenolate Mofetil.

Regarding the rest of the indications, the positive outcomes of RTX therapy are mostly reported through case reports/series, or retrospective/prospective studies.

Conclusion: In a time when conventional immunosuppression is the therapeutic milestone of glomerular diseases, mAbs bring hope into allowing a steroid-sparing and adverse-effect minimizing approach. This study aimed at bringing further evidence of the efficacy of RTX on glomerular injuries. Nevertheless, further controlled trials are mandatory to back up the safety and positive outcomes of B cell depletion and to establish a proper therapeutic strategy. The main goal is to get approval from medicine agencies for the On-Label use of RTX in Nephrology.

References:

- El Abdi A, Benbekha S, Bouattar T, Benamar L, Bayahia R, Ouzeddoun N. Le rituximab en néphrologie : expérience mono-centrique du service de néphrologie, dialyse et transplantation rénale du CHU de Rabat : à propos de 10 cas. Revue Marocaine de Néphrologie. 2021 Jun; 1(1):62-67.
- Tlili S, Mouna J, Gaidi H, Raja A, Soumaya C, Gouch R, et al. Le rituximab dans les néphropathies primitives de l'adulte. La Revue de Médecine Interne. 2021 Jun 1;42(1S):A134.
- AlSahow A, Al-Muhaiete A, Nawar H, AlHelal B, AlYousef A, Abdallah E, et al. Use of Rituximab as an off-Label medication in Glomerular Diseases: Clinical Perspective. Medical Principles and Practice. 2022 Jan 12;31(1).
- KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. In: Supplements to Kidney International, Official Journal of the International Society of Nephrology. 2021 Oct; 100(S1-S276).