10.5152/turkjnephrol.2024.23620

Turkish Journal of Nephrology

Tubulointerstitial Nephritis Induced by Adalimumab

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Last revision received: November 10, 2023 **Accepted:** December 15, 2023 **Publication Date:** April 25, 2024

Cite this article as: Mahjoubi YS, Kaabi W, Lakhoua G, et al. Tubulointerstitial nephritis induced by adalimumab. *Turk J Nephrol.* 2024;33(3):301-302.

To the Editor,

Tumor necrosis factor alpha (TNFα) inhibitors effectively treat chronic inflammatory diseases. However, they are associated with potential adverse reactions, including kidney injury.[1,2] We present a case of acute tubulointerstitial nephritis (TIN) following adalimumab treatment.

A male aged 59 years with Crohn's disease was treated with adalimumab 40 mg subcutaneously every other 2 weeks. After 2 years, kidney function tests revealed an elevated level of creatinine of 1.7 mg/dL (range: 0.5-1 mg/dL) and urea of 123.72 mg/dL (range: 16.8-45 mg/dL). His estimated glomerular filtration rate (eGFR using Chronic Kidney Disease EPIdemiology (CKD-EPI)) was 47.6 mL/min/1.73 m2. Prior to initiating adalimumab, his kidney function was normal. Additional investigations, including a complete blood count, urinalysis, complement levels, immunological tests, viral serologies, and kidney ultrasound, revealed no abnormalities. A kidney biopsy showed tubular injury and interstitial inflammation characterized by the presence of lymphocytes, plasma cells, and eosinophils. Adalimumab was stopped, and he received a short course of combination therapy with cyclophosphamide and prednisolone (the exact doses and administration regimen were unknown). A partial improvement in the creatinine level was noted within a month, which decreased to 1.5 mg/dL, and the urea level dropped to 65.46 mg/dL, accompanied by an eGFR of 53.7 mL/min/1.73 m^2. The patient's kidney function had completely recovered after 3 months. Informed consent was obtained from the patient who agreed to take part in the study.

The role of adalimumab in the development of TIN in our case was valued as plausible according to the updated French method because of a compatible chronology (compatible delay of onset and improvement of kidney function after drug cessation) and the evocative semiology (absence of other possible causes).[3]

Tubulointerstitial nephritis is caused by drugs in more than 75% of cases, mainly antibiotics, non-steroidal anti-inflammatory drugs, and diuretics.[1,2] Physical examinations and further investigations ruled out systemic diseases in this patient. Additionally, the patient was treated with adalimumab exclusively; he did not use any other drug or self-medications.

Moreover, our patient's disease remained in remission for years, and a rapid response was observed after drug withdrawal. Therefore, Crohn's disease as a cause of TIN was excluded. Among previously reported cases, the onset delay ranged from 2 months to 9 years.[1,2,4,5] Our patient developed kidney injury after a 2-year treatment. Similarly to our case, the recovery of previous reported cases required at least 2-3 months.[1,2,4,5] The difficulty of

the management of anti-TNFα-associated TIN is that there are few alternative options for the control of the underlying disease. Three patients were switched to another class of medication,[1,4] 1 patient was switched to a different TNFα inhibitor in the literature[2] and in a single case, a successful rechallenge was reported.[5]

Drug-induced TIN should be considered in patients treated with TNFα inhibitors and hence kidney functions should be monitored regularly.

Informed Consent: Informed consent was obtained from the patient who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.Y.S.; Design – M.Y.S., W.K.; Supervision – W.K., A.Z.; Resources – R.D., S.E.A.; Materials – R.D., S.E.A.; Analysis and/or Interpretation – M.Y.S., W.K.; Literature Search – M.Y.S.; Writing Manuscript – M.Y.S., W.K.; Critical Review – L.G., I.A.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

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