

# IgA Nephropathy in a Patient with Tularemia: Causality or Coincidental Association?

Yasemin Çakır-Kıymaz<sup>1</sup> , Ertuğrul Keskin<sup>1</sup> , Şeyhmus Kaya<sup>2</sup> , Ferhan Candan<sup>3</sup> 

<sup>1</sup> Department of Infectious Diseases and Clinical Microbiology, Sivas Cumhuriyet University School of Medicine, Sivas, Türkiye

<sup>2</sup> Department of Pathology, Sivas Cumhuriyet University School of Medicine, Sivas, Türkiye

<sup>3</sup> Division of Nephrology, Department of Internal Diseases, Sivas Cumhuriyet University School of Medicine, Sivas, Türkiye

## ABSTRACT

Immunoglobulin A (IgA) nephropathy is the most common primary glomerulonephritis. Oropharyngeal tularemia is a zoonotic infection caused by *Francisella tularensis*. To the best of our knowledge, no previous report has documented *F. tularensis* as a potential cause of IgA nephropathy. Here, we describe a case of IgA nephropathy occurring in the context of oropharyngeal tularemia. A 47-year-old man developed dark-colored urine a few days after the onset of upper respiratory symptoms. Kidney biopsy confirmed IgA nephropathy in the setting of acute kidney injury. Treatment with prednisolone and cyclophosphamide, in combination with tularemia-specific therapy, led to clinical improvement. This case highlights a possible association between tularemia and IgA nephropathy, warranting further investigation into the underlying mechanisms.

**Keywords:** *Francisella tularensis*, IgA nephropathy, acute renal failure, glomerulonephritis, tularemia

## INTRODUCTION

Tularemia is a zoonotic infectious disease caused by *Francisella tularensis*, a Gram-negative intracellular coccobacillus (1). The oropharyngeal form of tularemia typically presents with fever, severe sore throat, exudative tonsillopharyngitis, and lymphadenopathy (2). Immunoglobulin A (IgA) nephropathy, the most common primary glomerulonephritis worldwide, is characterized by mesangial deposition of IgA, IgG, IgM, and C3 (3). Infections are known to contribute to the pathogenesis of IgA nephropathy (4). However, to date, no studies have reported *F. tularensis* as a cause of IgA nephropathy. We describe a case of IgA nephropathy occurring in a patient with oropharyngeal tularemia and no prior history of chronic disease.

### Corresponding Author:

Yasemin Çakır-Kıymaz

### E-mail:

yasemincakir2553@gmail.com

**Received:** July 3, 2025

**Accepted:** August 19, 2025

**Published:** December 15, 2025

### Suggested citation:

Çakır-Kıymaz Y, Keskin E, Kaya Ş, Candan F. IgA nephropathy in a patient with tularemia: Causality or coincidental association? Infect Dis Clin Microbiol. 2025;4:437-42.

**DOI:** 10.36519/idcm.2025.768

# A Rare Case of IgA Nephropathy During Tularemia Infection



## Background



Although tularemia-associated acute kidney injury has been previously reported, IgA nephropathy has never been documented in this context.

## Case report



47-year-old male with fever, tonsillitis, and dark urine.

- Creatinine: 3.36 mg/dL
- Urine protein: 68.8 mg/dL
- Tularemia MAT: Positive

## Pathology



Renal biopsy showed:

- Mesangial IgA (3+) and C3 (2+) deposition
- Mild mesangial proliferation
- Fibrin necrosis & partial crescents

## Diagnosis



IgA nephropathy occurring during oropharyngeal tularemia.

## Treatment & Outcome

- Antimicrobial therapy
- Corticosteroids
- Cyclophosphamide



Marked renal improvement

## Conclusion

This first reported case of IgA nephropathy during tularemia highlights the need to consider tularemia in the differential diagnosis of acute kidney injury following cryptic tonsillitis.

**IDCM**

DEC 2025 ISSUE, CASE REPORT: IgA Nephropathy in a Patient with Tularemia: Causality or Coincidental Association? / Yasemin Çakır-Kıymaz, Ertuğrul Keskin, Şeyhmus Kaya, Ferhan Candan / DOI: 10.36519/idcm.2025.768

Graphic Abstract

## CASE

A 47-year-old male with no prior chronic illness presented with chills and shivering. He was initially diagnosed with an upper respiratory tract infection and received symptomatic treatment. Due to persistent symptoms, he re-presented to the hospital, where clindamycin was prescribed. Shortly thereafter, he developed dark-colored urine and returned for further evaluation. On examination, his temperature was 38°C, pulse 70 beats/min, and blood pressure 130/80 mmHg. Oropharyngeal examination revealed right-sided cryptic tonsillitis. Laboratory investigations showed white blood cell (WBC) count of  $15.25 \times 10^3/\mu\text{L}$ , platelet (PLT) count of  $380 \times 10^3/\mu\text{L}$ , serum creatinine 3.36 mg/dL (reference: 0.7–1.2 mg/dL), and C-reactive protein (CRP) 129 mg/L (reference: 0–5 mg/L). Detailed laboratory results are presented in Tables 1 and 2.

The patient denied chronic medications, allergies, smoking, or illicit drug use. He was admitted with

a diagnosis of acute kidney injury (AKI). Blood and throat cultures, streptococcal antigen testing, and screenings for Epstein-Barr virus (EBV), cytomegalovirus (CMV), brucellosis, hepatitis, and human immunodeficiency virus (HIV) were performed. Amoxicillin-clavulanate (1 g orally every 12 hours) was initiated. Neck ultrasonography revealed bilateral cervical lymph nodes, with the largest one measuring 33×15 mm in the right Level 2 region.

Renal biopsy showed mild mesangial proliferation and fibrin necrosis in some glomeruli. Immunofluorescence staining demonstrated mesangial IgA deposition, confirming the diagnosis of IgA nephropathy (Figure 1). Persistent tonsillitis and epidemiological findings—including rural residence, agricultural occupation, and the presence of regional tularemia cases—prompted testing for tularemia. Both *Brucella* Rose Bengal and tularemia microagglutination tests (MATs) were ordered. Given his history and local outbreak, ciprofloxacin (400 mg IV daily) was initiated.

**Table 1.** Laboratory findings during hospitalization and treatment.

Laboratory findings	First admission	3rd day	10th day	Day 3 after prednisolone (CYC start)	CYC 1 dose	CYC 4 dose	CYC 6 dose	Reference value
White blood cells ( $10^3/\mu\text{L}$ )	15.25	11.76	9.41	18.07	15.03	15.7	14.17	4–10.5
Neutrophils (%)	76	70.8	54.5	82	77.6	74.5	78.9	40–75
Platelets ( $10^3/\mu\text{L}$ )	380	346	405	352	185	233	208	150–450
CRP (mg/L)	129	169	37	15	0.9	24	1.66	0–5
ESR (mm/h)	65	-	63	51	41	26	14	0–20
AST (IU/L)	57	48	19	11	14	10	12	0–40
ALT (IU/L)	36	34	26	21	22	23	34	0–40
Creatinine (mg/dL)	3.36	3.82	3.34	2.80	1.13	1.29	1.3	0.7–1.2
BUN (mg/dL)	41.5	43.0	43.4	57.4	34.9	33.9	28.0	6–20
Urine protein (mg/dL)	68.8	-	512	-	7.9	8.9	-	0–15
Albumin/creatinine (mg/g)	311	146	-	-	28.3	22	-	0–30
Urine creatinine (mg/dL)	120.3	53.8	32.2	-	60.1	62.1	-	-
<b>Urine test strip</b>								
Leucocytes	16	-	6	1	3	2	0	0–3
Erythrocytes	20	-	47	8	39	48	2	0–2
Protein	+	-	Negative	Negative	Negative	Negative	Negative	Negative
Hemoglobin	3+	-	3+	+	3+	3+	Negative	Negative
Glucose	Negative	-	Negative	Negative	Negative	Negative	Negative	Negative

**CYC:** Cyclophosphamide, **CRP:** C-reactive protein, **ESR:** Erythrocyte sedimentation rate, **AST:** Aspartate aminotransferase, **ALT:** Alanine aminotransferase, **BUN:** Blood urea nitrogen.

On the tenth day of hospitalization, prednisolone therapy began for IgA nephropathy. The patient received intravenous prednisolone (500 mg daily for three days), followed by cyclophosphamide. After six months of follow-up, proteinuria decreased to 98 mg/day (reference 0–140 mg/day), glomerular filtration rate (GFR) improved from 21 to 88 mL/min, and serum creatinine dropped from 3.3 to 1.1 mg/dL.

## DISCUSSION

Immunoglobulin (IgA) nephropathy is the most common form of primary autoimmune glomerulonephritis, characterized by the mesangial deposition of immune complexes containing abnormally glycosylated IgA1 antibodies (4). Various conditions, including autoimmune and gastrointestinal diseases,

malignancies, and infections, have been implicated in its pathogenesis (5). Infectious agents such as hepatitis B virus (HBV), hepatitis C virus (HCV), HIV, and several bacterial pathogens have been linked to the development of IgA nephropathy, and infection-related mechanisms are increasingly recognized as contributing factors (4,5).

Acute kidney injury has been reported in tularemia, with proposed mechanisms including acute tubular necrosis, interstitial nephritis, and glomerulonephritis (6–8). Tilley et al. (7) described a case of tularemia presenting with non-oliguric AKI that resolved after doxycycline therapy, while Kaiser et al. (8) reported four tularemia cases complicated by rhabdomyolysis-induced kidney failure. However, no previous reports have demonstrated direct

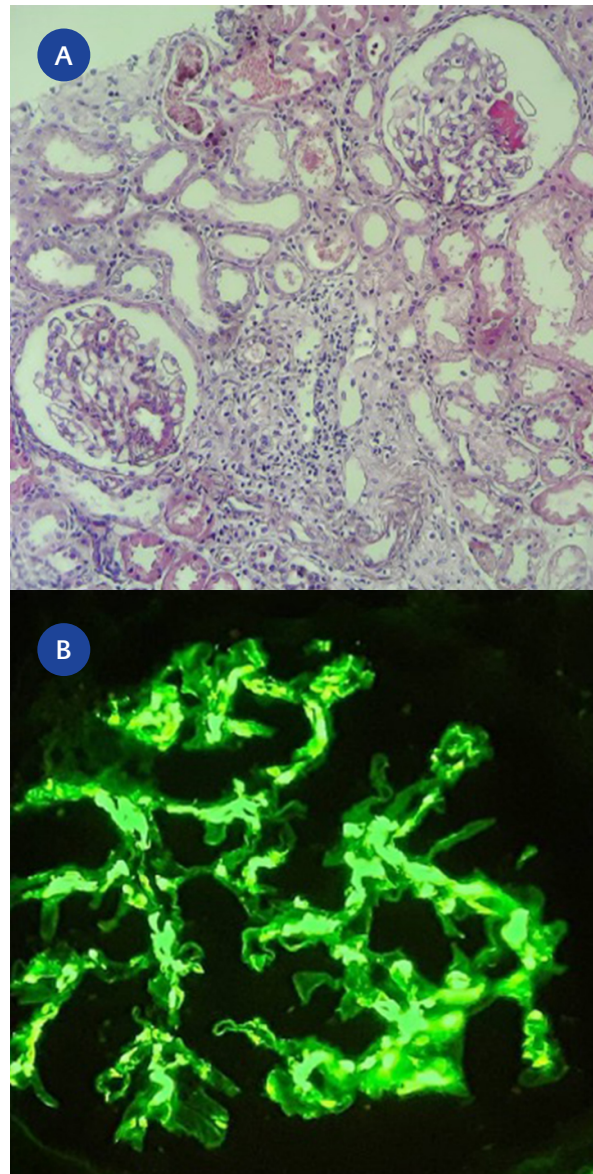
**Table 2.** Evaluation of diagnostic tests.

Laboratory findings	Results	Reference value
C3	165.4	90–180
C4	46.5	10–40
ANA	Negative	Negative
ASMA	Negative	Negative
Anti-dsDNA	Negative	Negative
Anti-CCP	Negative	Negative
AMA-M2	Negative	Negative
Anti-MPO (p-ANCA)	Negative	Negative
Anti-PR3 (c-ANCA)	Negative	Negative
Anti-GBM	Negative	Negative
Anti-Cardiolipin IgM	Negative	Negative
Anti-Cardiolipin IgG	Negative	Negative
Group A streptococcus antigen	Negative	Negative
ASO (IU/mL)	141	0–200
Anti-HCV	Negative	Negative
Anti-HIV	Negative	Negative
HBsAg	Negative	Negative
Tularemia MAT	Positive (1/160)	Negative

**ANA:** Anti-nuclear antibody, **ASMA:** Anti-smooth muscle antibody, **Anti-dsDNA:** Anti-double stranded DNA antibody, **Anti-CCP:** Anti-cyclic citrullinated peptide antibody, **AMA-M2:** Anti-mitochondrial M2 antibody, **Anti-MPO:** Anti-myeloperoxidase antibody, **Anti-PR3:** Anti-proteinase 3 antibody, **Anti-GBM:** Anti-glomerular basement membrane antibody, **ASO:** Anti-streptolysin O antibody, **HCV:** Hepatitis C virus, **HIV:** Human immunodeficiency virus, **HBsAg:** Hepatitis B surface antigen, **MAT:** Microagglutination test.

a causal relationship between *F. tularensis* infection and IgA nephropathy. In the present case, AKI developed shortly after cryptic tonsillitis, and no alternative cause was identified, suggesting a possible link between tularemia and the onset of IgA nephropathy.

Based on published data, a hypothetical model for the pathogenesis of IgA nephropathy has been proposed. In patients with IgA nephropathy, some IgA1 molecules produced by immunoglobulin-secreting cells have a galactose deficiency, and these molecules are recognized by anti-glycan IgG antibodies.



**Figure 1.** Kidney tissue, IgA nephropathy. Mild mesangial cell/matrix proliferation in the glomeruli, fibrin necrosis in the glomerulus (glomerulus at the 1 o'clock position), erythrocyte casts in the tubules, tubular injury, and areas of tubular atrophy/fibrosis (A, Hematoxylin and Eosin, ×100). Globally granular staining at 3+ intensity in the glomerulus with anti-IgA antibody (B, Immunofluorescence staining, ×200).

These complexes bind to mesangial cells, causing glomerular damage (9). It is known that the IgA accumulating in the glomerular mesangium in patients with IgA nephropathy is exclusive of the IgA1 subclass and that IgA produced by tonsil lymphocytes in these patients is predominantly polymeric

IgA1 (10). Serum IgA levels increase in about half of the patients with IgA nephropathy, and tonsillectomy reduces serum IgA levels, suggesting a relationship between the tonsils and IgA nephropathy (11). Given that oropharyngeal tularemia is also a form of tonsillopharyngitis, a similar mechanism may have led to the development of IgA nephropathy in this case.

IgA nephropathy is histologically characterized by the deposition of IgA in the mesangial region, mesangial cell proliferation, and expansion of the extracellular matrix within glomeruli. Complement C3 is almost invariably present, and C4 is frequently detected (12). In the present case, the diagnosis was established through biopsy, and no secondary etiology was identified. The kidney biopsy revealed diffusely global granular staining with anti-IgA antibodies in the mesangial/perimesangial areas at 3+ intensity, and anti-C3 antibodies stained at 2+ intensity. Immunohistochemically, there was no specific staining for C4d or amyloid A. Partial crescent formation of cellular nature was detected in five glomeruli. Chronic tubulointerstitial injury was patchy, with areas of atrophy and fibrosis (10–20%). Similarly, mild focal and segmental arterial and arteriolar sclerosis were observed.

The symptoms of IgA nephropathy range from asymptomatic hematuria to rapidly progressive glomerulonephritis. Without appropriate management, 30–40% of patients with IgA nephropathy progress to end-stage kidney disease (ESKD) within 20 years (13). Currently, no specific treatment exists to alter the production of immune complexes or prevent their mesangial accumulation in IgA

nephropathy. Thus, management primarily focuses on renin-angiotensin blockade, proteinuria reduction, and blood pressure control. The benefit of corticosteroid therapy compared to maximum supportive treatment with renin-angiotensin blockade remains controversial. The largest randomized controlled trial published in Italy demonstrated that corticosteroid therapy reduced proteinuria and prevented progression to ESKD over 10 years (14). A small single-center study of 38 high-risk patients with progressive IgA nephropathy, defined as a  $\geq 15\%$  increase in serum creatinine in the year preceding study entry, showed that treatment with prednisolone and cyclophosphamide for three months, followed by azathioprine, significantly reduced proteinuria and improved renal survival over a 5-year follow-up period (15).

In the present case, corticosteroid and cyclophosphamide therapy, combined with antimicrobial treatment for tularemia, resulted in substantial improvement in renal function and proteinuria. Serum creatinine decreased markedly following steroid therapy, and clinical recovery was maintained during outpatient follow-up.

## CONCLUSION

This is the first reported case of IgA nephropathy associated with tularemia. In endemic regions, tularemia should be considered in the differential diagnosis of AKI following cryptic tonsillitis. Further studies are warranted to clarify the potential immunopathogenic link between *F. tularensis* infection and IgA nephropathy.

**Ethical Approval:** N.A.

**Informed Consent:** Informed consent was obtained from the patient for publication.

**Peer-review:** Externally peer-reviewed

**Author Contributions:** Concept – Y.Ç.K.; Design – Y.Ç.K., E.K.; Supervision – F.C.; Materials – E.K., Ş.K.; Data Collection and/or Processing – E.K., Ş.K.; Analysis and/or Interpretation – Y.Ç.K.; Literature Review – F.C., Ş.K.; Writer – Y.Ç.K.; Critical Reviews – F.C.

**Conflict of Interest:** The authors declare no conflict of interest.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Scientific Presentation:** This case was presented as a poster at the 25th Turkish Congress of Clinical Microbiology and Infectious Diseases (KLİMİK 2025), held on 24–27 April 2025 in Antalya, Türkiye.



## REFERENCES

- 1 Çakır Kıymaz Y, Bolat S, Katırcı B, Aldemir Ö, Altunkaya I, Özcan MM, et al. Evaluation of the clinical characteristics, laboratory parameters, and antibiotic treatment in patients diagnosed with tularemia. *J Infect Chemother*. 2025;31(2):102546. [\[CrossRef\]](#)
- 2 Çakır Kıymaz Y, Bolat S, Katırcı B, Aldemir Ö, Altunkaya I, Mustafa Özcan M, et al. The great tularemia outbreak in Sivas: Evaluation of 205 cases. *Diagn Microbiol Infect Dis*. 2025;111(1):116585. [\[CrossRef\]](#)
- 3 Nihei Y, Kitamura D. Pathogenesis of IgA nephropathy as a tissue-specific autoimmune disease. *Int Immunol*. 2024;37(2):75-81. [\[CrossRef\]](#)
- 4 Suzuki H, Fan R, Zhang Z, Brown R, Hall S, Julian BA, et al. Aberrantly glycosylated IgA1 in IgA nephropathy patients is recognized by IgG antibodies with restricted heterogeneity. *J Clin Invest*. 2009;119(6):1668-77. [\[CrossRef\]](#)
- 5 Rollino C, Vischini G, Coppo R. IgA nephropathy and infections. *J Nephrol*. 2016;29(4):463-8. [\[CrossRef\]](#)
- 6 Lee HC, Horowitz E, Linder W. Treatment of tularemia with imipenem/cilastatin sodium. *South Med J*. 1991;84(10):1277-8. [\[CrossRef\]](#)
- 7 Tilley WS, Garman RW, Stone WJ. Tularemia complicated by acute renal failure. *South Med J*. 1983;76(2):273-4. [\[CrossRef\]](#)
- 8 Kaiser AB, Rieves D, Price AH, Gelfand MR, Parrish RE, Decker MD, et al. Tularemia and rhabdomyolysis. *JAMA*. 1985;253(2):241-3.
- 9 Novak J, Julian BA, Tomana M, Mestecky J. IgA glycosylation and IgA immune complexes in the pathogenesis of IgA nephropathy. *Semin Nephrol*. 2008;28(1):78-87. [\[CrossRef\]](#)
- 10 Xie Y, Chen X, Nishi S, Narita I, Gejyo F. Relationship between tonsils and IgA nephropathy as well as indications of tonsillectomy. *Kidney Int*. 2004;65(4):1135-44. [\[CrossRef\]](#)
- 11 Tomino Y, Sakai H; Special Study Group (IgA Nephropathy) on Progressive Glomerular Disease. Clinical guidelines for immunoglobulin A (IgA) nephropathy in Japan, second version. *Clin Exp Nephrol*. 2003;7(2):93-7. [\[CrossRef\]](#)
- 12 Roberts IS. Pathology of IgA nephropathy. *Nat Rev Nephrol*. 2014;10(8):445-54. [\[CrossRef\]](#)
- 13 Tota M, Baron V, Musial K, Derrough B, Konieczny A, Krajewska M, et al. Secondary IgA nephropathy and IgA-associated nephropathy: a systematic review of case reports. *J Clin Med*. 2023;12(7):2726. [\[CrossRef\]](#)
- 14 Pozzi C, Andrucci S, Del Vecchio L, Melis P, Fogazzi GB, Altieri P, et al. Corticosteroid effectiveness in IgA nephropathy: long-term results of a randomized, controlled trial. *J Am Soc Nephrol*. 2004;15(1):157-63. [\[CrossRef\]](#)
- 15 Ballardie FW, Roberts ISD. Controlled prospective trial of prednisolone and cytotoxics in progressive IgA nephropathy. *J Am Soc Nephrol*. 2002;13(1):142-8. [\[CrossRef\]](#)