CMJ. 2025;47(2):45-47
DOI: 10.7197/cmj.1662807

Cumhuriyet Medical Journal

| cmj.cumhuriyet.edu.tr | Founded: 2004 Available online, ISSN:1305-0028 Publisher: Sivas Cumhuriyet Üniversitesi

# False Positive Hepatitis A IgM in Membranous Nephropathy: A Treatment Dilemma

**Taha Enes Çetin[1,a,*], Ali Karataş[2,b], Gülçin Telli Dizman[3,c], Ömer Faruk Akçay[1,d], Özant Helvacı[1,e]**

[1] *Department of Nephrology, Gazi University, Ankara, Türkiye*
[2] *Department of Gastroenterology, Gazi University, Ankara, Türkiye*
[3] *Department of Infectious Diseases and Clinical Microbiology, Hacettepe University, Ankara, Türkiye*

**Corresponding author*

**Case Report**

*History*

*Received:* 21/03/2025
*Accepted:* 16/05/2025



**ABSTRACT**

Membranous nephropathy (MN) is a leading cause of nephrotic syndrome in adults, and is frequently associated with autoantibodies against M-type phospholipase A2 receptor (PLA2R). Immunosuppressive regimen, such as rituximab and calcineurin inhibitors, are recommended for high-risk patients. This case report discusses a 74-year-old female with anti-PLA2R-positive MN, whose treatment was delayed due to a false-positive hepatitis A virus (HAV)-IgM result. Despite asymptomatic presentation and normal liver function, concerns about potential viral reactivation complicated clinical decisions. After a month of monitoring, immunosuppressive treatment was initiated, and the patient's proteinuria achieved remission. This case underscores the importance of thorough evaluation of serological results, especially in cases where viral markers could influence critical treatment decisions. The risk of delaying MN treatment must be balanced against the potential dangers of initiating therapy under uncertain viral infection status.

***Keywords:*** Membranous nephropathy (MN), Anti-PLA2R, Hepatitis A virus (HAV), Immunosuppressive therapy

# Membranöz Nefropatide Yanlış Pozitif Hepatit A IgM: Tedavi Sürecinde Bir Kararsızlık

**Olgu Sunumu**

*Süreç*

*Geliş:* 21/03/2025
*Kabul:* 16/05/2025



**ÖZ**

Membranöz nefropati (MN), erişkinlerde nefrotik sendromun yaygın bir nedenidir ve çoğunlukla M-tipi fosfolipaz A2 reseptörüne (PLA2R) karşı gelişen antikorlarla ilişkilidir. Yüksek riskli MN vakalarında immünosupresif tedavi önerilmekte olup, tedavi öncesi viral enfeksiyonların değerlendirilmesi önemlidir. Hepatit A virüsü (HAV) enfeksiyonu, genellikle akut ve kendini sınırlayan hepatit ile ilişkilidir ve anti-HAV IgM pozitifliği aktif enfeksiyon göstergesi olarak kabul edilir. Ancak nadiren yanlış pozitif sonuçlar tedavi sürecini karmaşıklaştırabilir. Bu çalışmada, anti-PLA2R pozitif MN tanısı konulan ve yanlış pozitif anti-HAV IgM sonucu nedeniyle tedavi süreci geciken 74 yaşındaki bir kadın hasta sunulmaktadır. Hasta, nefrotik düzeyde proteinüri ile başvurdu ve böbrek biyopsisi ile MN tanısı doğrulandı. Yüksek anti-PLA2R titresi nedeniyle immünosupresif tedavi planlandı ancak hepatit taramasında anti-HAV IgM pozitifliği saptandı. Hastanın karaciğer enzimleri normal ve hepatit semptomları olmamasına rağmen, tedavi ertelendi. Farklı merkezlerde yapılan testler pozitifliği doğruladı ancak bir aylık izlemde hepatit gelişmemesi üzerine yanlış pozitiflik düşünüldü. Rituksimab ve ardından kalsinörin inhibitörü tedavisi başlatıldı. Tedavi süresince hepatit bulgusu gözlenmedi ve hasta remisyona girdi. On sekiz aylık takipte remisyon devam etti ancak anti-HAV IgM pozitifliği sürdü. Bu olgu, MN tedavisinde viral serolojilerin dikkatli değerlendirilmesi gerektiğini ve yanlış pozitif sonuçların tedavi kararlarını etkileyebileceğini göstermektedir.

***Anahtar Kelimeler:*** Membranöz nefropati (MN), Anti-fosfolipaz A2 reseptörü (Anti-PLA2R), Hepatit A virüsü (HAV), İmmünsüpresif tedavi

[a] *tahaenes23@gmail.com* *0000-0003-2125-5881*
[b] *akaratas85@hotmail.com* *0000-0002-2464-1975*
[c] *gulcin.telli@hacettepe.edu.tr* *0000-0001-8195-3345*
[d] *omerfaruk_akcay@yahoo.com* *0000-0001-6587-4938*
[e] *drozant@hotmail.com* *0000-0002-1382-2439*

*How to Cite:* Çetin TE, Karataş A, Telli Dizman G, Akçay ÖF, Helvacı Ö. False Positive Hepatitis A IgM in Membranous Nephropathy: A Treatment Dilemma, Cumhuriyet Medical Journal. 2025;47(2): 45-47

## Introduction

Membranous nephropathy (MN) is a common cause of nephrotic syndrome in adults, characterized by thickening of the glomerular capillary walls due to immune complex deposition. The majority of primary MN cases are associated with antibodies against the M- type phospholipase A2 receptor (PLA2R), which serve as a key diagnostic and prognostic marker.[1-3] Immunosuppressive therapy, including rituximab and calcineurin inhibitors, is often employed in high-risk MN cases to prevent disease progression.[4-5]

Hepatitis A virus (HAV) is a widespread infectious agent known for causing acute, self- limiting hepatitis, with HAV-IgM typically indicating active infection. However, in rare instances, HAV-IgM can yield false positive results, complicating clinical decisions, particularly when immunosuppression is considered.[6-9] The use of immunosuppressive agents in patients with viral infections carries significant risks, including viral reactivation and liver failure, as documented with hepatitis B virus.[9] Risk of fulminant hepatitis is unknown during course of HAV.

This case report presents a unique challenge in the management of a 74-year-old female with anti-PLA2R positive MN who exhibited a false positive HAV-IgM result complicating treatment process.

## Case Presentation

A 74-year-old female presented with complaints of leg swelling, leading to the detection of nephrotic-level proteinuria. The albumin was at 2.8 g/dL, the creatinine was 0.83 mg/dL, and the estimated glomerular filtration rate was 63 mL/min/1.73 m². Her 24-hour urine protein excretion was 8.6 g/day. Due to the delay in receiving the anti-PLA2R test results at our center, a renal biopsy was performed to diagnose the cause of her nephrotic-level proteinuria. The biopsy confirmed membranous nephropathy, and the anti-PLA2R test returned a high-titer positive result of 427 RU/mL, which further supported the diagnosis and advocated for a worse prognosis.

Before initiating immunosuppressive therapy for primary membranous nephropathy, routine hepatitis screening revealed a positive HAV ıgG and anti-HAV IgM result. The patient, however, remained asymptomatic with normal liver enzyme levels, including AST at 26 U/L, ALT at 21 U/L, ALP at 96 U/L, GGT at 243 U/L, total bilirubin at 0.35 mg/dL, and direct bilirubin at <0.10 mg/dL. Given the known risks associated with immunosuppression in patients with hepatitis, such as the potential for fulminant hepatitis B reactivation and death [9], the patient was referred to the gastoenterology department for further evaluation.

After assessing the risk, the gastroenterology team recommended delaying immunosuppressive therapy until the anti-HAV IgM result became negative. Subsequent hepatitis tests, conducted at external centers using General Biological's Corporation (company, ELISA) and ClearTest kits (company, ELISA), confirmed the initial positive results.

Immunological tests for autoimmune diseases were reviewed, and no significant pathology was detected. Additionally, serological tests for other viral antigens that could potentially cause heterologous reactions—including Epstein-Barr virus IgM (EBV IgM), cytomegalovirus IgM (CMV IgM), hepatitis C virus IgM (HCV IgM), and parvovirus B19 IgM—were performed, all of which yielded negative results. Monoclonal gammopathy was excluded. Due to the persistent positive anti-HAV IgM results, treatment initiation was delayed. However, after more than one month of follow-up without any signs or symptoms of hepatitis, a false positive result was suspected. In this case, following consultation with the gastroenterology department, liver biopsy was not considered necessary due to the absence of clinical or laboratory signs of hepatitis and the suspicion of a false-positive serological result. Therefore, a non-invasive monitoring approach was preferred. Consequently, the patient was treated with intravenous rituximab at an initial dose of 1 gram and and a further 1gram dose 14 days later. With this treatment, the patient was evaluated as non-responsive due to less than a 50% reduction in proteinuria at the 6-month follow-up, and a calcineurin inhibitor was subsequently added to the treatment regimen. Throughout the treatment, the patient was closely monitored, and no signs of hepatitis were observed. Eventually, her proteinuria achieved remission. After 18 months of follow-up she remains in remission, however she is still Anti-HAV IgM positive.

## Discussion

Membranous nephropathy (MN) is a leading cause of idiopathic nephrotic syndrome, particularly in the non-diabetic white population. Approximately 80% of cases are primary, with one-third undergoing spontaneous remission, one-third progressing to end-stage renal disease (ESRD), and the remaining one-third manifesting as chronic kidney disease.[1]

Immunosuppressive therapy is a key component of treatment for high-risk MN patients, and anti-PLA2R titers are used to assess disease activity and predict response to therapy.[3]

Our case had KDIGO high risk MN. Furthermore, the high-titer anti-PLA2R positivity decreased the likelihood of spontaneous remission.[3] However, the unexpected positive HAV-IgM result complicated the treatment approach. HAV is generally associated with acute, self-limiting hepatitis, with HAV-IgM typically persisting for 3 to 6 months.[6-8] While rare, false positive HAV-IgM results have been reported, potentially due to factors such as cross- reactive antibodies, polyclonal B cell activation, or subclinical viral reactivation.[10]

In our patient, the persistently positive HAV-IgM result led to a delay in initiating immunosuppression, despite the absence of clinical symptoms or abnormal liver function

tests. This case underscores the importance of carefully evaluating serological results in the context of the patient's overall clinical picture. The potential risks associated with delaying treatment in MN, such as progression to ESRD, must be weighed against the risks of initiating immunosuppression in the presence of a potential active viral infection.[9]

The literature documents cases of false positive HAV-IgM results in other conditions, such as autoimmune events and diuretic therapy.[11-12] Landry, reported a 78-year-old patient with positive HAV-IgM following diuretic therapy for heart failure, but the patient continued to be monitored without any clinical symptoms.[13] Our patient had received diuretic treatment for hypervolemia at an external facility, and we postulate this treatment might have caused false antibody positivity.

Ultimately, in the absence of clinical and laboratory signs of hepatitis, we carried on with immunosuppressive therapy, leading to remission of proteinuria without any hepatic complications. This case emphasizes the need for a cautious and individualized approach in managing complex cases where viral serologies may confound treatment decisions.

This case study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

## References


1. Couser, W. G. Primary membranous nephropathy. Clin. J. Am. Soc. Nephrol. 12, 983– 997 (2017).
2. Debiec, H. et al. Antenatal membranous glomerulonephritis due to anti-neutral endopeptidase antibodies. N. Engl. J. Med. 346, 2053–2060 (2002)
3. Beck, L. H. et al. M-type phospholipase A2 receptor as target antigen in idiopathic membranous nephropathy. N. Engl. J. Med. 361, 11–21 (2009).
4. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int. 100, S1–S276 (2021)
5. van de Logt, A. E. et al. Immunological remission in PLA2R-antibody-associated membranous nephropathy: cyclophosphamide versus rituximab. Kidney Int. 93, 1016– 1017 (2018).
6. Lemon SM , Ott JJ , Van Damme P , Shouval D . Type A viral hepatitis: a summary and update on the molecular virology, epidemiology, pathogenesis and prevention. J Hepatol. 2017 Sep 5;68:167–84.
7. Bower WA , Nainan OV , Han X , Margolis HS . Duration of viremia in hepatitis A virus infection. J Infect Dis. 2000 Jul;182(1):12–7.
8. Cohen JI , Feinstone S , Purcell RH . Hepatitis A virus infection in a chimpanzee: duration of viremia and detection of virus in saliva and throat swabs. J Infect Dis. 1989 Nov;160(5):887–90.
9. Martin ST, Cardwell SM, Nailor MD, et al. Hepatitis B Reactivationand Rituximab: A New Boxed Warning and Considerations for Solid Organ Transplantation. Am J Transplant. 2014;14:788–96.
10. Sustained false-positive results for hepatitis A virus immunoglobulin M: A case report and literature review Youwen Tan and Li Chen
11. Tennant E , Post JJ . Production of false-positive immunoglobulin M antibodies to hepatitis A virus in autoimmune events. J Infect Dis. 2016 Jan 15;213(2):324–5.Centers for Disease Control and Prevention positive test results for acute hepatitis A virus infection among persons with no recent history of acute hepatitis—United States, 2002-2004. MMWR Morb Mortal Wkly Rep 2005; 54:453–6.
12. Landry ML. Immunoglobulin M for Acute Infection: True or False? Clin Vaccine Immunol. 2016 Jul;23(7):540–5.
13. Landry ML. Immunoglobulin M for Acute Infection: True or False? Clin Vaccine Immunol. 2016 Jul;23(7):540–5