Clin. Lab. 2026;72:XXX-XXX

CASE REPORT

Alpha Thalassemia-Related Diabetic Nephropathy

Fan Wu, Bingqing Liu, Zhengjie Wang

Department of Nephrology, The Affiliated Hospital of Putian University, Putian, China

SUMMARY

Background: **Thalassemia, an autosomal recessive hematologic disorder, causes renal dysfunction via chronic hypoxia, anemia, iron overload, and iron chelating agents. This case showed severe tubulointerstitial lesions with diabetic nephropathy.**
Methods: **Comprehensive diagnostic evaluation included targeted laboratory investigations, renal imaging studies, percutaneous renal biopsy, and thalassemia genetic testing to elucidate etiological mechanisms.**
Results: **Laboratory findings confirmed microcytic hypochromic anemia with renal impairment. Imaging studies revealed pulmonary embolism, splenomegaly, and lower extremity deep vein thrombosis. Genetic analysis identified α-thalassemia. Renal histopathology demonstrated stage III diabetic nephropathy with severe tubulointerstitial fibrosis and tubular atrophy.**
Conclusions: **Refractory anemia with renal dysfunction requires thalassemia exclusion. The cause of renal injury in thalassemia needs to be confirmed by renal biopsy.**
(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250742)

Correspondence:
Haishan Xu
Department of Nephrology
The Affiliated Hospital of Putian University
351100 Putian
China
Phone: +86 594 6738101
Fax: +86 594 2330980
Email: 13656997838@139.com

Case Report accepted July 21, 2025

KEYWORDS

alpha-thalassemia, diabetic nephropathy, renal insufficiency

INTRODUCTION

Thalassemia refers to a group of hereditary hemolytic anemias, in which mutations or deletions of the globin gene lead to varying degrees of suppression of α or β globin synthesis. Thalassemia poses a significant disease burden globally, with 5% to 20% of the world population carrying one or more α-thalassemia mutations, and approximately 1.5% carrying one or more β-thalassemia mutations [1]. The prevalence of α-thalassemia and β-thalassemia in China was 7.88% and 2.21%, respectively, with the disease mainly distributed in South China. In addition, the most common α-globin and β-globin gene mutations were -SEA and CD41/42, respectively [2].
Recent studies have identified the impact of thalassemia on the kidneys, where chronic hypoxia, long-term anemia, iron overload, and iron chelating agents are the main causes of tubular dysfunction and glomerular filtration abnormalities [3]. However, to our knowledge,

diabetes nephropathy is rarely reported in patients with thalassemia. This report describes the first case of diabetes nephropathy associated with α-thalassemia.

CASE PRESENTATION

A 75-year-old female with a decade-long history of diabetes mellitus and seven years of hypertension was admitted to our respiratory department three years ago due to progressive dyspnea and cough, where diagnostic imaging revealed bilateral acute pulmonary embolism on pulmonary CTA (Figure 1A, B), concurrent right lower extremity deep vein thrombosis on color Doppler ultrasound (Figure 1C), and splenomegaly with splenic infarction on MRI (Figure 1D). Laboratory investigations at the time showed normal urinalysis, creatinine 36 μmol/L, and glomerular filtration rate (GFR) indicating hyperfiltration (174 mL/minute/1.73 m^2). At the same time, hemoglobin was found to be 74 g/L, suggesting microcytic hypochromic anemia, yet no further workup was pursued to elucidate the etiology of her anemia.

In March 2025, the patient was admitted to the Department of Gastroenterology due to poor appetite and emaciation. The electronic gastroscopy indicated reflux esophagitis and chronic atrophic gastritis. The complete blood count revealed hypochromic microcytic anemia. She had hyperferritinemia of 538.50 ng/mL. An ultrasonogram showed splenomegaly, normal sized kidneys with no evidence of obstructive uropathy. Further examination showed creatinine 188 μmol/L, urine protein 2+, and ACR 927.6 mg/g. All the other biochemical investigations (viral serology and immunological analyses) were normal. Based on the above examination, it was considered that poor appetite may be related to renal disease, so the nephrology department was consulted. Because of the patient's high blood pressure and previous history of thromboembolism, roxadustat was selected to promote hematopoiesis. Anemia was not improved after treatment, and renal function deteriorated progressively. However, Hb was constantly under the normal reference range, which could not be explained by the iron deficiency anemia. The patient was diagnosed with α-thalassemia based on the results of our genetic tests showing the deletion of -SEA gene. Capillary electrophoresis showed hemoglobin A2 (alternative adult hemoglobin made of alpha- and delta-globin chains) was decreased to 1.6%. As there were no signs of diabetic retinopathy upon further fundus examination, we performed a renal biopsy to clarify the cause of renal insufficiency. The results indicated diabetic nephropathy and severe chronic renal tubular interstitial lesions, with positive staining of renal tubular epithelial cells in the cytoplasm using Prussian blue (Figure 2). Based on the consultation with the hematology department, rotercept was given to treat thalassemia, and finerenone was given to treat diabetic nephropathy. One month later, HB 76 g/L, creatinine 99.3 μmol/L, and urine protein + were reexamined.

DISCUSSION

Thalassemia is a hereditary hematologic disorder caused by defective synthesis of α- or β-globin chains that constitute human hemoglobin. In α-thalassemia, reduced production of α-globin chains results in impaired hemoglobin synthesis, peripheral hemolysis, and ineffective erythropoiesis [4]. Clinical manifestations include anemia, pulmonary arterial hypertension, splenomegaly, iron overload, and growth retardation [4]. Patients with thalassemia develop chronic hemolysis accompanied by associated endothelial injury, platelet activation, and alterations in thrombomodulin, which collectively contribute to a hypercoagulable state [5,6]. Many patients with thalassemia develop splenomegaly due to increased erythrocyte destruction by the reticuloendothelial system (particularly in the spleen) and heightened extramedullary hematopoiesis (EMH) activity [7]. The aforementioned mechanisms can explain the patient's development of pulmonary embolism, lower extremity deep vein thrombosis, and splenomegaly three years prior.

Although thalassemia may present with multisystem complications including cardiopulmonary disorders, endocrine organ diseases, liver impairment, and thromboses in various vascular beds, renal involvement has received relatively limited attention. Multiple factors may contribute to renal pathology in thalassemia patients, including iron overload, chronic anemia, hypoxia, acquired Fanconi syndrome, inappropriate iron chelation therapy, nephrotoxic medications, infectious agents, post-splenectomy state, and nephrolithiasis [3]. Diabetic nephropathy is typically not considered a major contributor to renal dysfunction in thalassemia patients, as renal biopsies are rarely performed, leading to missed definitive diagnoses of kidney disease. In this patient, in addition to diabetic nephropathy, iron staining was positive in the cytoplasm of renal tubular epithelial cells. Renal tubular cells subjected to iron overload release cytokines and growth factors, inducing interstitial injury that may result in tubulointerstitial scarring and glomerulosclerosis [8].

Renal biopsy provides valuable information regarding iron deposition in the kidneys. However, due to its invasive nature, this procedure may not be feasible for many thalassemia patients. Even without regular red blood cell transfusions, thalassemia patients frequently develop iron overload secondary to increased intestinal iron absorption, which can lead to severe organ damage. Moreover, because their hematological parameters may resemble those of iron-deficiency anemia, thalassemia patients risk misdiagnosis and subsequent iatrogenic iron accumulation from inappropriate supplementation. Multiple analogous studies demonstrate that excessive iron deposition induces reactive oxygen species (ROS) production, thereby exacerbating renal cellular injury. Chronic anemia promotes hypoxic damage to the renal tubulointerstitium and peritubular capillaries. Over time, apoptosis and mesenchymal-to-epithelial transi-

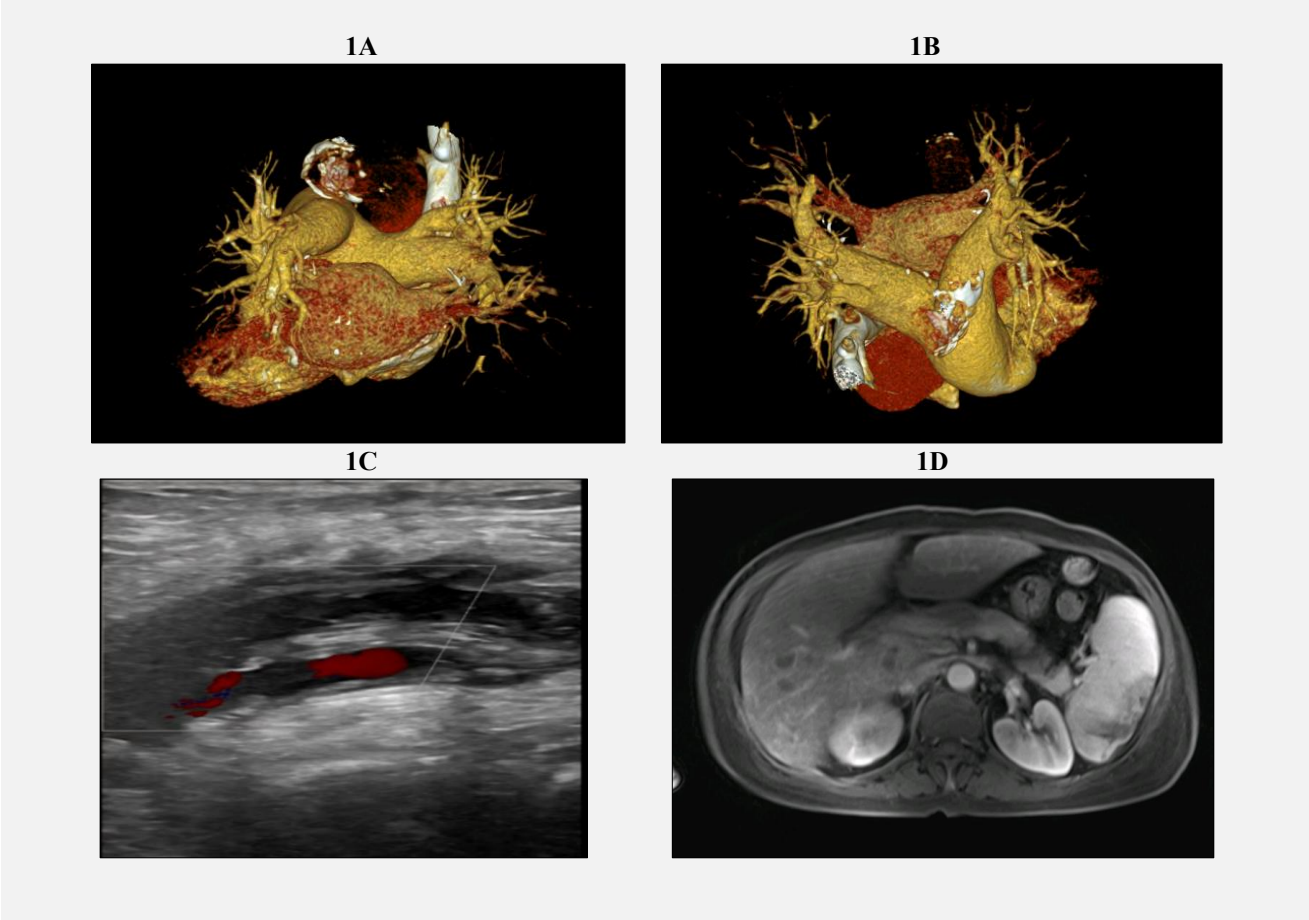

Figure 1. Pulmonary artery CTA (Figure 1A - B). Vascular ultrasonography (Figure 1C). Abdominal Magnetic Resonance Imaging (Figure 1D).

tion (MET) contribute to progressive loss of normal renal function. Reduced systemic vascular resistance and resultant hyperdynamic circulation lead to glomerular capillary wall stretching and endothelial injury, further accelerating renal deterioration [9,10]. This provides an explanation for the severe chronic tubulointerstitial lesions observed in the patient.

Three years prior, the patient exhibited hyperfiltration (eGFR 174 mL/minute/1.73 m²), which may be associated with early-stage diabetic nephropathy. Similarly, renal hyperfiltration and albuminuria are common findings in thalassemia patients. This hyperfiltration likely represents a consequence of chronic anemia, analogous to observations in young children with sickle cell anemia [11]. Chronic anemia is thought to reduce systemic vascular resistance leading to hyperdynamic circulation and subsequent increased renal plasma flow and GFR [12]. Glomerular hyperfiltration appears to be deleterious to the mesangial compartment, causing it to increase matrix volume and cellularity, initiating a sclerotic process [13,14]. In the long-term, such modifications may theoretically lead to a progressive decline in GFR through the typical pathway of hyperfiltration-albuminuria-progressive renal damage. Interestingly, emerging evidence suggests that thalassemia and excessive heme iron intake independently elevate diabetes risk. Pancreatic iron overload alters ROS generation, disrupts hypoxia-inducible factor-1α (HIF-1α) stabilization, and impairs adenosine triphosphate (ATP) synthesis, thereby compromising β-cell function and viability [15]. These findings imply a potential pathophysiological link between the patient's thalassemia and diabetes development.

It should be noted that this follow-up period remains relatively short, rendering it insufficient for evaluating the long-term efficacy of the treatment. This is one of the limitations of the present study.

CONCLUSION

This report represents the first documented case of α-thalassemia complicated by diabetic nephropathy. Without proactive screening protocols, healthcare providers

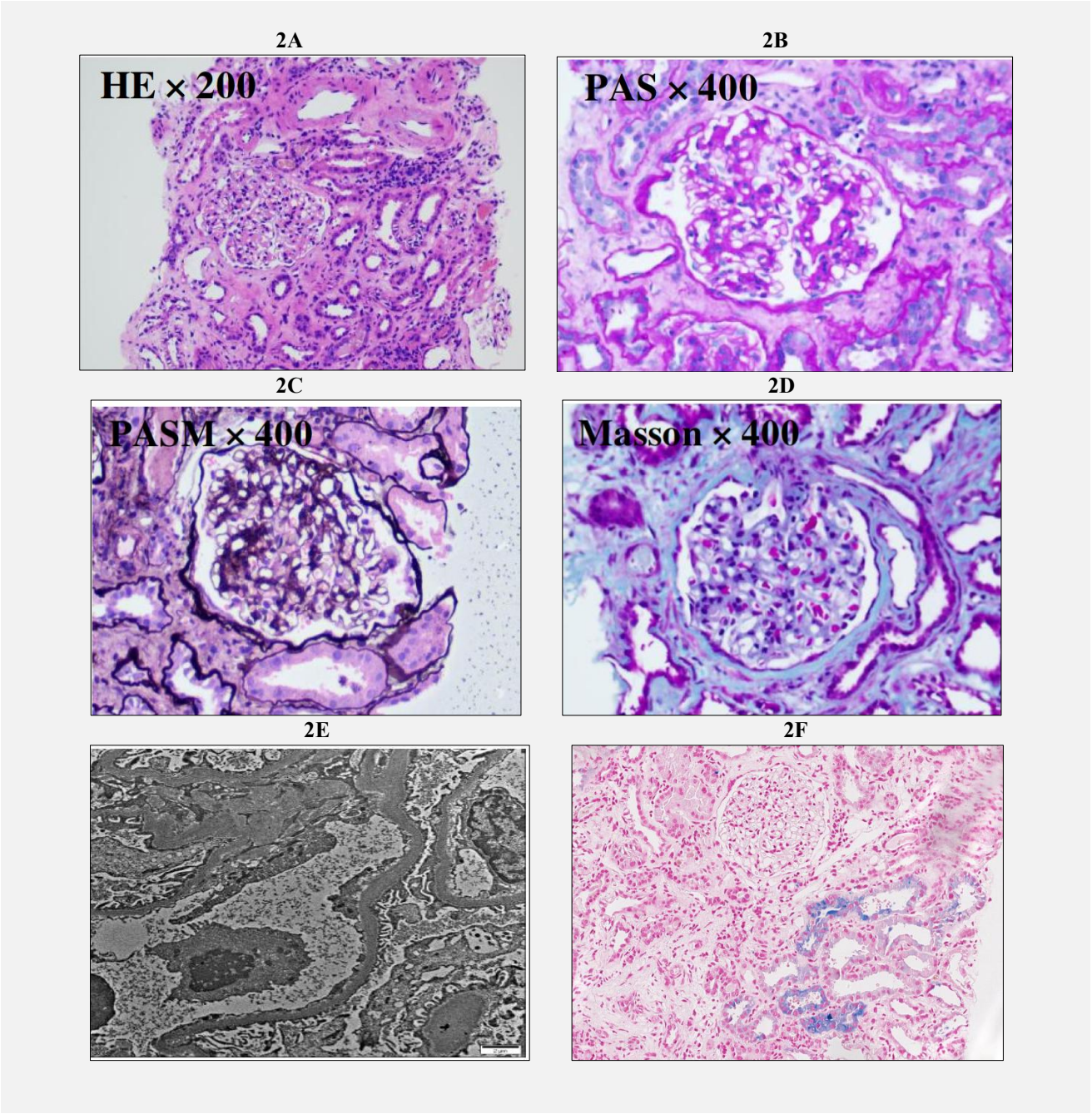

Figure 2. Hematoxylin-eosin (Figure 2A). Periodic Acid-Schiff (Figure 2B). Periodic Acid-Silver Methenamine (Figure 2C). Masson's trichrome (Figure 2D). Electron microscopic image (Figure 2E). Prussian blue staining (Figure 2F).

may overlook renal dysfunction in thalassemia patients, underscoring the necessity for regular monitoring to enable early detection of renal impairment and timely implementation of appropriate therapeutic interventions. When renal disease coexists with anemia, particularly in the context of renal insufficiency, thalassemia is prone to misdiagnosis or underdiagnosis, even in high-prevalence regions. Moreover, timely renal biopsy remains essential for definitive diagnosis to retard disease progression.

Financial Support:
This research was sponsored by a grant from the Natural Science Foundation of Fujian Province (No. 2025J 011522).

Declaration of Interest:
No conflicts of interest exist in this article.

References:

1. Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. Bull World Health Organ 2008 Jun;86(6):480-7. (PMID: 18568278)

2. Lai K, Huang G, Su L, He Y. The prevalence of thalassemia in mainland China: evidence from epidemiological surveys. Sci Rep 2017 Apr 19;7(1):920. (PMID: 28424478)

3. Demosthenous C, Vlachaki E, Apostolou C, et al. Beta-thalassemia: renal complications and mechanisms: a narrative review. Hematology 2019 Dec;24(1):426-38. (PMID: 30947625)

4. Musallam KM, Rivella S, Vichinsky E, Rachmilewitz EA. Non-transfusion-dependent thalassemias. Haematologica 2013 Jun;98 (6):833-44. (PMID: 23729725)

5. Cappellini MD, Musallam KM, Poggiali E, Taher AT. Hypercoagulability in non-transfusion-dependent thalassemia. Blood Rev 2012 Apr;26 Suppl 1:S20-3. (PMID: 22631037)

6. Chansai S, Fucharoen S, Fucharoen G, Jetsrisuparb A, Chumpia W. Elevations of Thrombotic Biomarkers in Hemoglobin H Disease. Acta Haematol 2018;139(1):47-51. (PMID: 29402840)

7. Rivella S. Ineffective erythropoiesis and thalassemias. Curr Opin Hematol 2009 May;16(3):187-94. (PMID: 19318943)

8. Alfrey AC. Role of iron and oxygen radicals in the progression of chronic renal failure. Am J Kidney Dis 1994 Feb;23(2):183-7. (PMID: 8311072)

9. Landing BH, Gonick HC, Nadorra RL, et al. Renal lesions and clinical findings in thalassemia major and other chronic anemias with hemosiderosis. Pediatr Pathol 1989;9(5):479-500. (PMID: 2813197)

10. Nangaku M. Chronic hypoxia and tubulointerstitial injury: a final common pathway to end-stage renal failure. J Am Soc Nephrol 2006 Jan;17(1):17-25. (PMID: 16291837)

11. Groothoff JW, Metry E, Deesker L, et al. Clinical practice recommendations for primary hyperoxaluria: an expert consensus statement from ERKNet and OxalEurope. Nat Rev Nephrol 2023 Mar;19(3):194-211. (PMID: 36604599)

12. Davis LE, Hohimer AR. Hemodynamics and organ blood flow in fetal sheep subjected to chronic anemia. Am J Physiol 1991 Dec; 261(6 Pt 2):R1542-8. (PMID: 1750577)

13. Lafferty HM, Anderson S, Brenner BM. Anemia: a potent modulator of renal hemodynamics in models of progressive renal disease. Am J Kidney Dis 1991 May;17(5 Suppl 1):2-7. (PMID: 2024667)

14. Hostetter TH. Hyperfiltration and glomerulosclerosis. Semin Nephrol 2003 Mar;23(2):194-9. (PMID: 12704579)

15. Wang X, Fang X, Wang F. Pleiotropic actions of iron balance in diabetes mellitus. Rev Endocr Metab Disord 2015 Mar;16(1):15-23. (PMID: 25520048)