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A Rare Cause of Retroperitoneal Fibrosis in Adults: H Syndrome Presenting After 35 Years- A Case Report

Türker Emre,[1]* Nazife Nur Özer Şensoy[2]

[1]Department of Nephrology, University of Health Sciences, Bursa City Training and Research Hospital, Bursa, Turkey
[2]Department of Nephrology, University of Health Sciences, Bursa City Training and Research Hospital, Bursa, Turkey

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Case Report

Introduction. Retroperitoneal fibrosis (RPF) is a rare fibro-inflammatory disorder that may cause urinary tract obstruction and renal failure. Although most RPF cases are IgG4-related, rare genetic conditions can also contribute to the disease. H syndrome, an autosomal recessive disorder caused by biallelic SLC29A3 mutations, usually presents in childhood with cutaneous, endocrine, and systemic manifestations; adult onset is exceptionally rare.
Case presentation. A 36-year-old woman was admitted to hospital with the complaint of nausea, vomiting, and oliguria. Laboratory tests showed urea 116 mg/dL, creatinine 5,8 mg/dL,. Non-contrast computed tomography imaging revealed bilateral hydronephrosis and a 2,5 cm retroperitoneal fibrotic mass encasing the abdominal aorta and iliac arteries. Extensive evaluation—including positron emission tomography, lymph-node histology, and autoimmune/IgG4 serology—found no evidence of malignancy, infection, or IgG4-related disease. Family history disclosed parental consanguinity and a brother with H syndrome. Next-generation sequencing identified a homozygous SLC29A3 (NM_018344.5):c.1339G > A (p.Glu447Lys) mutation, confirming H syndrome. Bilateral ureteral stenting and corticosteroid therapy led to full renal recovery (creatinine 0.7 mg/dL).
Conclusion. This case expands the clinical spectrum of H syndrome by documenting late-onset RPF without typical dermatologic or auditory signs. Recognition of familial risk and timely genetic testing were decisive for diagnosis. Early decompression and immunosuppression preserved renal function. Reporting such atypical presentations increases awareness of H syndrome as a rare genetic cause of RPF and supports comprehensive genetic evaluation in adults with unexplained retroperitoneal fibrosis.

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INTRODUCTION

Retroperitoneal fibrosis (RPF) is a rare disorder characterized by excessive fibrotic tissue and chronic inflammation in the retroperitoneal space, often leading to ureteral compression, hydronephrosis, acute kidney injury (AKI), and potentially irreversible renal failure.[1] Immunoglobulin G4 (IgG4)-related disease is the leading cause, accounting for approximately 70% of cases.[2] Secondary causes include autoimmune diseases, malignancies, infections, medications, and trauma.[3]

H syndrome is an autosomal recessive disorder caused by mutations in the *SLC29A3* gene, which encodes the human equilibrative nucleoside

transporter 3 (hENT3), essential for lysosomal function.[4] This multisystemic disorder presents with hypertrichosis, hyperpigmentation, hearing loss, hepatosplenomegaly, hyperglycemia, hypogonadism, hallux flexion contractures, and height reduction. Although typically diagnosed in childhood, adult-onset cases are exceptionally rare.[5,6]

The coexistence of H syndrome with RPF is an unusual clinical phenomenon. Here in, we present a rare case of adult-onset RPF associated with H syndrome, contributing to the limited literature on this rare association.[7]

CASE PRESENTATION

A 36-year-old female presented to the emergency department with the complaints of nausea, vomiting, and oliguria. The patient's medical history was unremarkable for prior renal issues; however, she reported nonspecific abdominal discomfort over the preceding months. Physical examination revealed mild abdominal tenderness without organomegaly. Laboratory findings at admission are summarized in Table 1. Serum urea was elevated at 116 mg/dL and creatinine at 5.8 mg/dL, with an estimated glomerular filtration rate (eGFR) of 9.5 mL/min/1.73 m².

Urinalysis indicated a urinary tract infection (UTI); urine culture revealed the presence of Escherichia coli (> 10^5 CFU/mL), which was susceptible to third-generation cephalosporins. The patient received intravenous ceftriaxone (2 g/day for 7 days), resulting in sterilization of urine cultures. The spot urine protein/creatinine ratio was 385 mg/g, excluding significant proteinuria. Abdominal ultrasonography disclosed bilateral hydronephrosis, with right and left kidney dimensions measuring 54x122 mm and 56x119 mm, respectively. Both kidneys exhibited increased parenchymal echogenicity, suggestive of chronic parenchymal injury. Computed tomography of the abdomen further revealed retroperitoneal fibrotic tissue encasing the abdominal aorta and iliac arteries, measuring up to 2,5 cm in thickness, along with para-aortic and para-caval lymphadenopathy, with lymph nodes up to one cm in size. Abdominal CT images demonstred retroperitoneal fibrosis and are presented in Figure 1. Given the radiological findings, the differential diagnosis included IgG4-related disease, malignancy, and other autoimmune conditions. Positron emission tomography imaging failed to demonstrate hypermetabolic lesions indicative of malignancy.

Histopathological evaluation of an excisional biopsy from an inguinal lymph node revealed reactive lymphoid hyperplasia without evidence of neoplasia. Immunohistochemical staining, including IgG4 and lymphoma markers (e.g., CD20, CD3, Ki-67), showed no abnormal plasma cell infiltration or evidence of lymphoproliferative

Table 1. Key Admission Laboratory Findings in a 36-Year-Old Woman with H Syndrome and Obstructive Nephropathy

Parameter	Value	Comment
Urea (mg/dL)	116	Markedly elevated
Creatinine (mg/dL)	5.8	Markedly elevated
eGFR (mL/min/1.73 m^2)	9.5	Severely reduced
Phosphorus (mg/dL)	4.9	Mildly elevated
CRP (mg/L)	13.4	Elevated
PTH (ng/L)	127	Elevated
Uric acid (mg/dL)	6.2	Mildly elevated
Ferritin (ng/L)	210	Elevated
Hemoglobin (g/dL)	6.9	Markedly reduced

The table lists only parameters that were outside the normal range. All other results—including albumin, total protein, calcium, liver enzymes, bilirubin, lactate dehydrogenase, white blood cells, platelets, and mean corpuscular volume—were within reference limits. Reference ranges: urea 12.8–42.8 mg/dL; creatinine 0.50–0.90 mg/dL; estimated glomerular filtration rate (eGFR) 60–120 mL/min/1.73 m²; phosphorus 2.5–4.5 mg/dL; C-reactive protein (CRP) 0–5 mg/L; parathyroid hormone (PTH) 15–65 ng/L; uric acid 2.4–5.7 mg/dL; ferritin 13–150 ng/L; hemoglobin 11.9–14.6 g/dL. Abbreviations: eGFR, estimated glomerular filtration rate; CRP, C-reactive protein; PTH, parathyroid hormone.

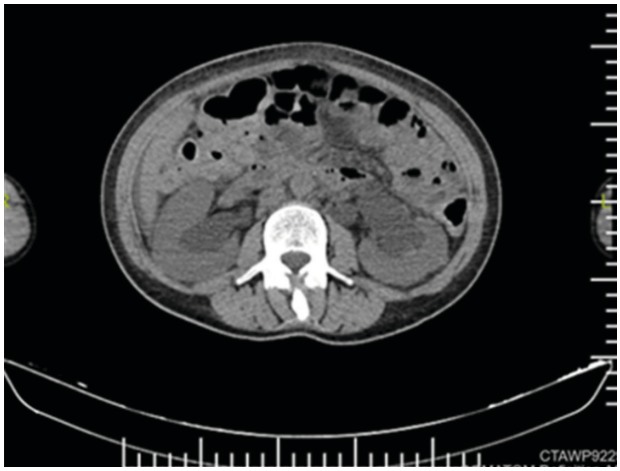

Figure 1. Abdominal CT Scan Showing Retroperitoneal Fibrosis
The abdominal CT scan reveals a fibrotic mass surrounding the retroperitoneal space, extending from the aorta to the iliac arteries and paravertebral area. The thickest region measures 2.5 cm. Bilateral hydronephrosis is present due to renal compression. Mildly enlarged lymph nodes are observed without malignancy, and abdominal organs appear normal.

Table 2. IgG Subclasses, Serologic and Autoimmune Markers at Presentation

Test	Value	Comment	Reference ranges
CA-15-3 (IU/mL)	40	Elevated	0 – 25
Reticulocytes (×10^9/L)	17.5	Low	33 – 101
IgG2 (g/dL)	1.58	Mildly low	1.69 – 7.86
IgA (g/dL)	4.67	Mildly elevated	0.7 – 4
Total IgG (g/L)	17.4	Mildly elevated	7 – 16
Serum free light chain κ (mg/L)	34.6	Elevated	6.7 – 22.4
Serum free light chain λ (mg/L)	44.3	Elevated	8.3 – 27
Serum amyloid A (mg/L)	4.62	Elevated	< 0.50

All other tumor, infectious, and autoimmune markers—including CA-125, CA-19-9, carcinoembryonic antigen (CEA), procalcitonin, antinuclear antibody (ANA), anti-dsDNA, anti-Sm/RNP, anti-ENA Scl70, anti-SSA, anti-SSB, rheumatoid factor, CCP, anti-cardiolipin IgG/M, PR3-ANCA, MPO-ANCA, lupus anticoagulant LA1/LA2, anti-phospholipid antibodies IgG/M, anti-GBM, HBsAg, anti-HBs, anti-HCV, and anti-HIV—were within normal limits or negative.
Abbreviations: ANA, antinuclear antibody; anti-dsDNA, anti-double-stranded DNA; CCP, cyclic citrullinated peptide; PR3-ANCA, proteinase-3 antineutrophil cytoplasmic antibody; MPO-ANCA, myeloperoxidase antineutrophil cytoplasmic antibody; anti-GBM, anti-glomerular basement membrane antibody; FLC, serum free light chain.

disorder. Serologic and autoimmune marker results are presented in Table 2, showing that IgG4 levels, autoimmune markers (antinuclear antibodies, rheumatoid factor), and inflammatory markers (C-reactive protein, erythrocyte sedimentation rate) were all within normal limits.

Formun AltıA detailed family history revealed parental consanguinity and a male sibling diagnosed with H syndrome during childhood, who exhibited sensorineural hearing loss, hyperpigmented skin lesions, and retroperitoneal fibrosis, with the cutaneous manifestations depicted in Figure 2. In light of these findings, genetic testing of the patient was performed using next-generation

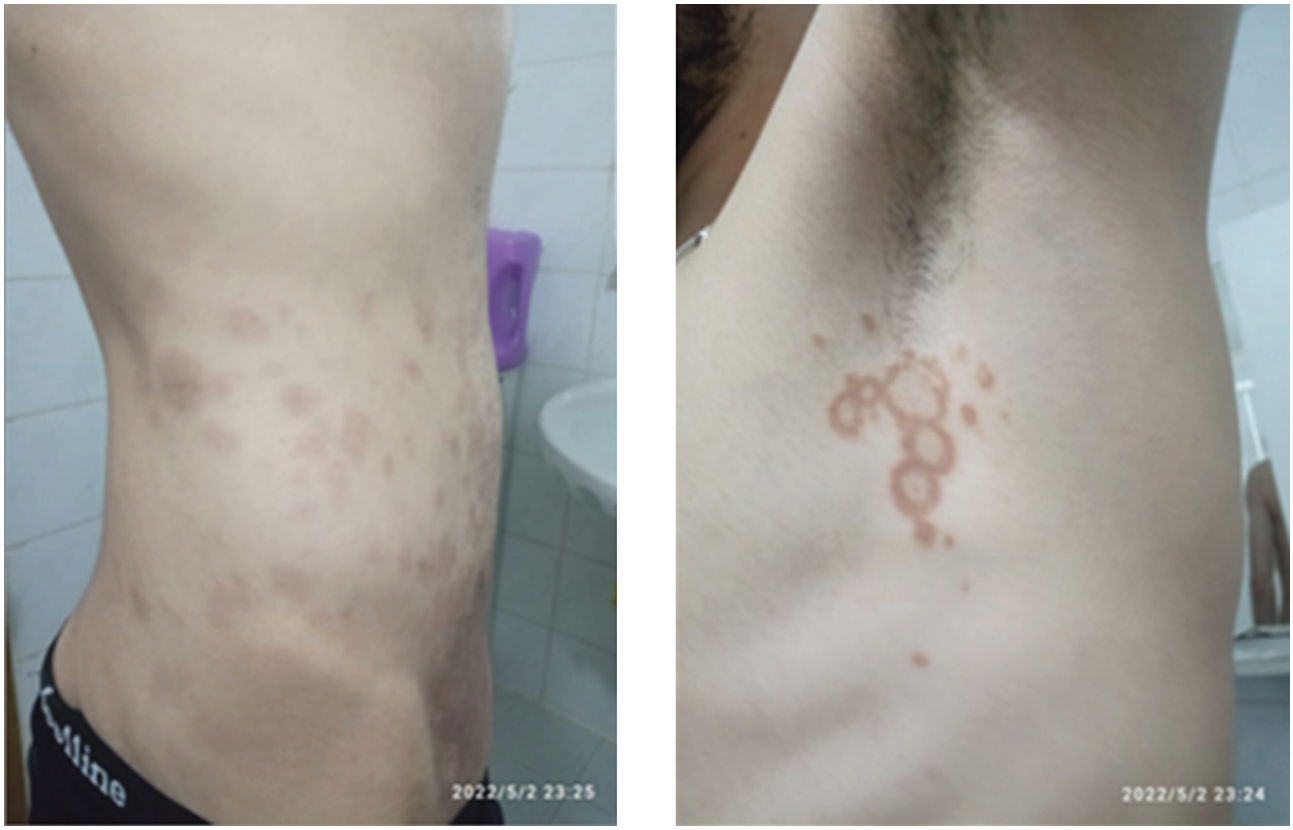

Figure 2. Cutaneous manifestations of the patient's sibling with H syndrome. Hyperpigmented and hypertrichotic plaques on the lower limb of the sibling, diagnosed clinically and genetically with H syndrome from the age of 2 years.

sequencing and identified a homozygous SLC29A3 (NM_018344.5):c.1339G > A (p.Glu447Lys) missense mutation, confirming the diagnosis of H syndrome.

The patient was underwent bilateral ureteral stenting to relieve the ureteral obstruction and was initiated on corticosteroid therapy (prednisolone 1 mg/kg/day). Over the subsequent weeks, renal function improved significantly, and creatinine levels decreased to 0,7 mg/dL. The patient was discharged in stable condition and scheduled for regular follow-up to monitor disease progression.

This single-patient case report did not require formal ethics committee approval according to our institutional policy. Written informed consent for publication of this case and all accompanying images was obtained from the patient.

DISCUSSION

Retroperitoneal fibrosis is most commonly associated with IgG4-related disease, malignancies, and autoimmune disorders.[1] However, RPF is a recognized manifestation of H syndrome, particularly in pediatric cases; nevertheless, its presentation in adulthood is extremely rare, as illustrated by this case. The delayed onset in this patient underscores the phenotypic heterogeneity of H syndrome and the potential influence of genetic, epigenetic, and environmental factors.[8] The literature on adult-onset H syndrome is limited, making this case an important contribution.

H syndrome is characterized by significant clinical variability, even among individuals with the same pathogenic mutation.[9] The absence of hallmark features such as hypertrichosis, hyperpigmentation, and hearing loss in this case complicates the diagnostic process. The discovery of familial consanguinity and the sibling's diagnosis were pivotal in guiding the diagnostic workup.

The pathophysiological mechanisms by which SLC29A3 mutations contribute to retroperitoneal fibrosis remain poorly understood.[9] The prevailing hypothesis suggests that chronic immune activation and inflammatory cell infiltration induce fibroblast proliferation and extracellular matrix deposition in the retroperitoneal space. Glucocorticoids, as administrated in this case, serve to attenuate the inflammatory response and mitigate fibrosis progression.[1]

The identification of an adult-onset, atypical presentation of H syndrome broadens the clinical spectrum of this disorder and emphasizes the importance of genetic testing in patients with unexplained retroperitoneal fibrosis, particularly when there is a positive family history. The rarity of adult-onset presentation further underscores the importance of documenting such cases to expand the current understanding within the medical literature.

Several pediatric cases of RPF associated with H syndrome have been reported, most of which presented in early life and exhibited typical cutaneous and systemic features.[10,11] In contrast, our patient developed RPF in adulthood, lacked hallmark features such as hypertrichosis and hearing loss, and experienced complete renal recovery after prompt decompression and corticosteroid therapy. These distinctions underscore the expanding phenotypic spectrum of H syndrome and highlight the importance of considering this diagnosis even in adults with unexplained RPF.

CONCLUSION

This case presents a rare instance of late-onset retroperitoneal fibrosis secondary to H syndrome, a genetic disorder predominantly identified in childhood. The absence of classical phenotypic features in this patient underscores the syndrome's clinical heterogeneity. The adult-onset presentation of H syndrome observed in this case represents an exceptionally rare occurrence in the literature. Early recognition and diagnosis of H syndrome in atypical cases are essential for timely intervention, renal function preservation, and appropriate genetic counseling. This report contributes to the expanding literature on H syndrome and its variable clinical manifestations, thereby enhancing diagnostic accuracy for future cases.

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CONFLICT OF INTEREST

None.

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*Correspondence to:
Türker Emre, MD
Department of Nephrology, Bursa City Training and Research Hospital, Bursa, Turkey.
ORCID ID: 0000-0003-3630-2169
Tel: +905333968110
E-mail: aturkeremre@yahoo.com

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