Do Kidney Biopsies Help Us Understand Loin Pain Hematuria Syndrome?

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INTRODUCTION

Loin pain-hematuria syndrome (LPHS) first described in 1967, is a complex and poorly understood rare disease that predominantly affects young women. Patients with LPHS experience extreme flank pain along with hematuria in the absence of a primary kidney pathology. Due to inadequate understanding of the pathophysiology of LPHS, the goal of management has been limited to symptomatic relief and pain management. While it is uncertain if the source of pain and hematuria are interrelated, there is consensus that hematuria is glomerular in origin.

Objective: To evaluate the correlation of glomerular basement membrane (GBM) alterations with hematuria and pain for the 14 LPHS patients.

METHODOLOGY

Kidney biopsies: 14 LPHS patients

EHR was reviewed for :
Demographic data - sex, age, ethnicity, weight, height
Renal markers - urine blood & protein, serum creatinine
Comorbidities – diabetes, hypertension

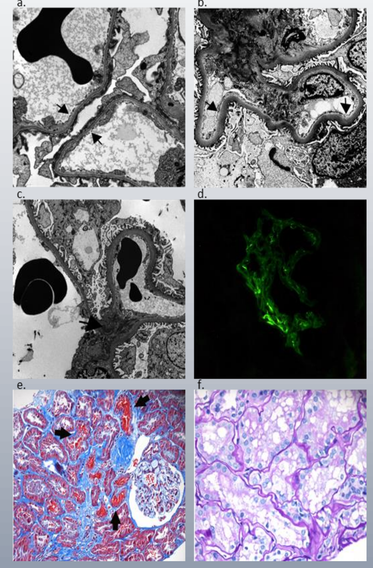
A single pathologist evaluated biopsy under light microscopy, immunofluorescence microscopy, and electron microscopy.

RESULTS

Table 1: Patient Characteristics

Baseline characteristics	(N=14)
Age (year), median (IQR)	37 (33.5-43.25)
Sex (female), N (%)	14/14 (100%)
Ethnicity Caucasian, N (%) Aboriginal, N (%) South Asian, N (%)	 11/14 (78.6%) 2/14 (14.3%) 1/14 (7.1%)
BMI (kg/m^2), median (IQR)	31.75 (26.1-38.2)
Location of pain (unilateral), N (%)	10/14(71.4.%)
Duration of LPHS (years), median (IQR)	6 (4.0-10.0)
Age of onset (year), median (IQR)	30 (24.7-38.5)
Morphine milligram equivalent (mg), median (IQR)	48 (19.0-136.0)
Number of pain medications, median (IQR)	3 (2.0-3.0)
eGFR (mL/min/1.73m^2) using CKD-EPI, median (IQR)	109 (90.5-120.5)
Urea (mmol/L), median (IQR)	4.6 (4.0-5.7)
Creatinine (µmol/L), median (IQR)	64 (54.7-69.2)
ACR (<3.0 mg/mmoL), N (%)	14/14 (100%)
Proteinuria (urine analysis), N (%)	Negative 14/14 (100%)
Macrohematuria, N (%)	11/14 (78.6%)
Hypertension, N (%)	3/14 (21.4%)
Diabetes, N (%)	2/14 (14.3%)
Kidney stones, N (%)	8/14 (57.1%)
Family history of kidney stones, N (%)	2/14 (14.3%)
Current smoker, N (%)	4/14 (28.6%)
Association of pain with hematuria (self-reported), N (%)	8/14 (57.1%)

Kidney Biopsy Outcomes



Histological Findings:

- 3/14 had normal GBM
- 3/14 had thin GBM[a]
- 6/14 had thick GBM[b]
- 1/14 had IgA nephropathy[c,d]
- 1/14 Insufficient biopsy
- 10/14 positive for RBC ± casts[e]
- 7/14 stained positive for C3
- 4/14 positive for arteriolar hyalinosis
- 5/14 patients had endothelial injury[f]

Hematuria and GBM:

Normal GBM - microhematuria
Abnormal GBM - gross hematuria

Pain:

No interstitial edema observed in any of the biopsies

CONCLUSIONS

- While renal histology can help verify if hematuria is glomerular in origin, it is limited in its capacity to ascertain the cause of hematuria.
- Genetic and proteomic studies are needed to identify genes/pathways involved in LPHS pathology, moving from histopathology to identification of molecular mechanisms underlying LPHS etiology.

LIMITATIONS

Small sample size conducted in a single center, which limits generalizability of the study.
We categorized patients as having an abnormal GBM, even if focal GBM abnormality exists. Our intent was to better understand RBC egression through GBM and not necessarily to diagnose collagenopathy spectrum of diseases.