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Loin Pain Hematuria Syndrome

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Loin pain hematuria syndrome is a rare disease with a prevalence of ~0.012%. The most prominent clinical features include periods of severe intermittent or persistent unilateral or bilateral loin pain accompanied by either microscopic or gross hematuria. Patients with loin pain hematuria syndrome initially present with hematuria, flank pain, or most often both hematuria and flank pain. Kidney biopsies from patients with loin pain hematuria typically reveal only minor pathologic abnormalities. Further, loin pain hematuria syndrome is not associated with loss of kidney function or urinary tract infections. Loin pain hematuria syndrome–associated hematuria and pain are postulated to be linked to vascular disease of the kidney, coagulopathy, renal vasospasm with microinfarction, hypersensitivity, complement activation on arterioles, venocalyceal fistula, abnormal ureteral peristalsis, and intratubular deposition of calcium or uric acid microcrystals. Many patients with loin pain hematuria syndrome also meet criteria for a somatoform disorder, and analgesic medications, including narcotics, commonly are used to treat loin pain hematuria syndrome–associated pain. Interventional treatments include renal denervation, kidney autotransplantation, and nephrectomy; however, these methods should be used only as a last resort when less invasive measures have been tried unsuccessfully. In this review article, we discuss and critique current clinical practices related to loin pain hematuria syndrome pathophysiology, diagnosis, treatment, and prognosis.
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INDEX WORDS: Loin pain hematuria syndrome (LPHS); loin pain; hematuria; renal autotransplantation; renal denervation.

CASE PRESENTATION

A 26-year-old woman whose recent medical history was notable for a left pelvic kidney that became partially obstructed during an otherwise uneventful pregnancy underwent surgical consultation for elevation of her pelvic kidney (Fig 1). During the physical examination by the surgeon, she described her ongoing struggle with constant severe pain in her right lower back that radiated into her groin. For the right-sided back pain, she had variably required intravenous morphine, oxycodone, and oxycodone/acetaminophen, and she indicated that it was very difficult for her to play with her child and perform activities of daily living. Her right lower back and groin pain first started at 16 years of age after a high school track meet and was accompanied by an episode of hematuria at that time. Subsequently, she had experienced episodes of hematuria at irregular intervals, often independent of pain exacerbations. The patient provided accurate descriptions of her pain episodes, and a psychiatric consultation concluded that she was truthful about her efforts to avoid pain medications and she was not experiencing mental problems. A diagnosis of right-sided loin pain hematuria syndrome was made.

INTRODUCTION

Loin pain hematuria syndrome is a rare clinical entity that was described first in 1967 by Little et al.[1] The most predominant clinical feature is periods of severe unilateral, or less often bilateral, loin (flank) pain that commonly radiates toward the abdominal area, medial thigh, or groin.[2,3] The duration of pain may range from hours to constant persistent pain. Pain episodes often are associated with dysuria, vomiting, and low-grade fever, but they are not associated with a urinary tract infection.[4] The pain may be accompanied by intermittent microscopic or gross hematuria.[4,5] Initially, presentation typically includes both hematuria and flank pain, although sometimes one symptom may precede the other[2] (Box 1).

With fewer than 500 cases of loin pain hematuria syndrome reported in the literature to date, a multifactorial model, which would examine biological, psychological, and social factors, has not been effectively applied to this condition.[6] Due to the limited number of case reports, the complex nature of the disorder, and inconsistencies in its clinical presentation, including underlying kidney pathology, loin pain hematuria syndrome remains a poorly understood syndrome that may not represent a discrete disease.[7]

EPIDEMIOLOGY

Little is known regarding the epidemiology of loin pain hematuria syndrome. It is an extremely rare disease with a prevalence of ~0.012%.[8] Nearly 100 cases have been reported from Ohio in the United

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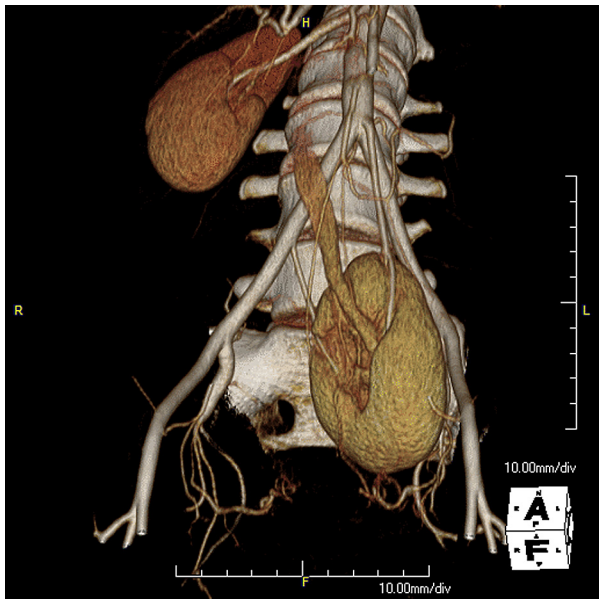

Figure 1. Computed tomographic scan shows the abnormal positioning of the left pelvic kidney, which did not contribute to the patient's diagnosis of loin pain hematuria syndrome.

States, and other cases have been reported in Great Britain, Australia, and Canada.[6] In contrast, a study from Montreal, Canada, questioned the clinical diagnosis of loin pain hematuria syndrome based on a lack of reported cases during a 10-year period.[6]

The initial report of loin pain hematuria syndrome was published in 1967, diagnosed in 3 women based primarily on the observation that their symptoms could not be explained by any other diagnostic assessment.[1] Fourteen years later, loin pain hematuria syndrome first was described in men.[9] Although recent studies report relatively higher percentages of men with loin pain hematuria syndrome, 70% of patients with loin pain hematuria syndrome in the 3 largest studies published to date were women.[9-11] Most patients with loin pain hematuria syndrome develop symptoms in their late 20s, but symptom onset is reported between 10 and 60 years of age.[2,7]

PATHOPHYSIOLOGY

Overview of Pathogenesis

The cause of loin pain hematuria syndrome remains poorly understood. Case reports and case series have shown variable findings ranging from overtly normal[12,13] to substantial abnormalities in kidney pathology, complement activation, thrombotic factors, and other potentially pathogenic processes. Accordingly, a defined pathologic basis for loin pain hematuria syndrome remains undetermined.[14] Although no causal links have been established, it is postulated that loin pain hematuria syndrome–associated hematuria and pain may be associated with vascular disease of the kidney, coagulopathy, renal vasospasm with microinfarction, hypersensitivity, complement activation on arterioles, venocalyceal fistula, abnormal ureteral peristalsis, intratubular deposition of calcium or uric acid microcrystals, or psychopathology, whereas a direct link between loin pain hematuria syndrome and immunoglobulin A (IgA) nephropathy remains tenuous.[3,12,15-19]

Box 1. Clinical Manifestations of Loin Pain Hematuria Syndrome

Hematuria

- Dysmorphic red blood cells (primarily acanthocytes), indicating a glomerular origin, are seen on urine smears
- Hematuria can be microscopic, but most loin pain hematuria syndrome patients have experienced at least 1 episode of gross hematuria
- Episodes of gross hematuria are almost always accompanied by worsening pain and usually last a few days, but gross hematuria and pain can persist for weeks to months
- Between episodes of gross hematuria, urinalysis typically shows microscopic hematuria; however, sometimes the hematuria clears up but the pain persists[2,13]

Kidney function

- Mean serum creatinine levels were reported at 0.9 mg/dL (80 μmol/L)
- Renal hypertension was reported to occur in 18% of loin pain hematuria syndrome patients (n = 33)
- Protein excretion was reported to be above the upper limit of normal of 150 mg/d in 32% of loin pain hematuria syndrome patients, but was >500 mg/d in only 6% of loin pain hematuria syndrome patients, with a maximum level of 1,635 mg/d (n = 34)[13]

Loin pain

- Loin pain is described as burning or throbbing, localized at the costovertebral angles, and made worse by a gentle punch
- Pain may radiate to the abdomen, inguinal area, or medial thigh
- Pain may be unilateral or, less often, bilateral, although the majority of loin pain hematuria syndrome patients eventually develop bilateral pain
- Pain is induced or exacerbated by exercise in approximately one-half of patients, and riding in a car can be uncomfortable
- Pain typically is severe, leading physicians to consider or prescribe narcotic therapy
- Some loin pain hematuria syndrome patients describe upper abdominal pain, but costovertebral angle punch tenderness also is present
- The onset of pain often is associated with nausea and vomiting, and the patient may be unable to manage the pain with oral opioids[2,13]

Glomerular Hematuria and Basement Membrane Abnormalities

The underlying causes of loin pain and hematuria in loin pain hematuria syndrome are not known, but glomerular hematuria, often associated with abnormal glomerular basement membranes (GBMs), may contribute to both symptoms. A 2006 study by Spetie et al[13] describing kidney biopsy findings in 34 patients with idiopathic loin pain hematuria syndrome reported that those with loin pain hematuria syndrome were