

HEMATURIA; ITS CLINICAL SIGNIFICANCE

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Hematuria, although one of the more common symptoms of urinary disease, is frequently underestimated in its importance by the patient and often, unfortunately, by his physician. It should be emphasized that the presence of blood in the urine is not a clinical entity or disease per se, but rather a sign of an existing pathologic lesion requiring immediate and exhaustive investigation to determine the underlying etiologic factors.

Usually, the presence of gross blood in the urine is sufficiently alarming to cause the patient to seek medical advice. However, when the hematuria is intermittent, the cessation of the bleeding lulls the patient into a false sense of security; he may presume he is well. To the physician, however, this subsidence of hematuria is no indication that its significance is to be minimized. A complete urologic investigation should not be delayed.

Frequently, hematuria is the outstanding symptom. Often it is the only complaint, and at other times the blood may be only found upon microscopic examination. Fortunately, the bleeding in many instances is associated with concomitant symptoms. The presence of other symptoms often causes the individual to seek investigation and medical advice earlier than does the recognition of blood in the urine, although from the urologic point of view, the latter may be more serious. First among the symptoms is pain. Other complaints accompanying the hematuria may be burning and frequency of urination, chills and fever, sweats, the presence of a mass, loss of weight, history of trauma, etc.

MacKenzie¹ reported an excellent study of hematuria from the Royal Victoria Hospital in 1932. He stated that 20.24 per cent of urologic admissions passed urine containing blood, and in 75 per cent of the cases, the blood was caused either by tumor, infection, calculus, or nephritis. In 96 per cent of the cases with hematuria, a causative lesion was found within the urinary tract, and over 40 per cent of these lesions were neoplastic. Reports by Kretschmer,² Cahill,³ the senior author,⁴ and others have shown convincingly that blood in the urine is a serious symptom, and that its source and cause should be ascertained even though at times it may involve extensive examinations and lab-

oratory procedures. The type of bleeding may be of some aid in explaining its source; e.g., when it originates from the anterior urethra, the blood is usually initial and bright; terminal hematuria may arise from the posterior urethra or from the bladder; total hematuria is more often from the bladder, ureter, or kidney. However, these evidences are insufficient to ascertain the location of the pathologic lesion without complete urologic survey.

The following tabulation and grouping has been found very useful in classifying hematuria and emphasizes the most important causes of hematuria as seen at the Cleveland Clinic.

I. Hematuria in general disease

- A. Acute fevers: Tonsillitis, scarlet fever, rheumatic fever, etc.
- B. Chronic infections: Endocarditis (renal infarction), malaria
- C. Blood dyscrasias: Purpura, leukemia, hemophilia, polycythemia vera
- D. Deficiency and dietary disease: Scurvy and liver deficiency
- E. Diseases of unknown etiology: Hodgkin's disease, hypertension or arteriosclerosis with renal involvement, periarteritis nodosa
- F. Following medication: Sulfonamides, methanamine, salicylates, barbiturates, mandelic acid, etc.

II. Hematuria due to intrinsic diseases of the urinary tract

- A. Renal
 - 1. Calculi or crystals
 - 2. Nephritis
 - 3. Tumor—capsular, parenchymal, pelvic
 - 4. Infection—acute or chronic including tuberculosis
 - 5. Anomalies—polycystic disease, horseshoe kidney, nephroptosis, etc.
 - 6. Trauma
- B. Ureteral
 - 1. Calculi
 - 2. Infection
 - 3. Stricture
 - 4. Tumor
- C. Vesical
 - 1. Tumor
 - 2. Infection
 - 3. Calculi or foreign bodies
 - 4. Ulcer
 - 5. Trauma
- D. Bladder neck
 - 1. Prostate including seminal vesicles

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- E. Urethral
 - 1. Infection
 - 2. Stricture
 - 3. Tumor
 - 4. Following instrumentation

III. Hematuria associated with extraurinary pathology

- A. Acute appendicitis
- B. Diverticulitis of the colon
- C. Neoplasm of the colon, rectum, or pelvic structures
- D. Acute or chronic salpingitis

This classification is by no means exhaustive; practically every disease of the urinary tract at some time or other may be accompanied by hematuria. It does indicate, however, the extensive investigation which may be necessary to uncover the etiologic factor producing blood in the urine. Complete study of the urinary tract is essential: this includes cystoscopy, estimation of individual kidney function, examination of specimens of urine from each kidney, pyelography, and intravenous urography. With these procedures in addition to the routine physical examination and routine laboratory examination, an accurate diagnosis can be established in the vast majority of cases, and appropriate therapy instituted early in the course of the disease.

The following case reports illustrate a number of conditions associated with hematuria, and the investigation which may be necessary to disclose the cause of bleeding.

CASE REPORTS

Case 1. Hematuria due to blood dyscrasia. This patient was registered at the Clinic in 1933 at which time a diagnosis of rheumatoid arthritis was made. She returned in 1942 at the age of 23 with the chief complaint of marked weakness.

General physical examination was essentially negative except for pronounced pallor. The spleen was not palpable, nor was there lymphadenopathy.

Blood study showed a hemoglobin of 35 per cent; the red blood count was 1,780,000. Urinalysis showed many red blood corpuscles.

Further blood studies were undertaken. Fragility tests showed increased hemolysis. The smear revealed spherocytosis and autoagglutination of the red cells; the white blood count and differential study were normal; red cell volume was 40 per cent of normal; reticulocytes were 25.8 per cent; icterus index was 38; sternal puncture showed a hyperplastic marrow.

The final diagnosis was acquired hemolytic anemia. A splenectomy was done.

This patient showed microscopic hematuria, and urologic investigation was necessary to eliminate the possibility of a coexisting lesion in the urinary tract, although the laboratory tests readily disclosed the cause of the urinary tract hemorrhage.

Case 2. Hemorrhagic Bright's disease. A 22 year old woman first registered at the Clinic in 1940 at which time general examination revealed no abnormalities. Two years later, following an episode of sore throat which had been treated with sulfanilamide, she returned with the primary complaint of marked hematuria. Bloody urine had been present on every voiding for several weeks, but no blood clots had been passed. No other urinary symptoms were present.

Physical examination was essentially negative. Blood pressure was 106/80.

Blood count revealed a mild hypochromic anemia. The urine was grossly bloody. Urinalysis showed a specific gravity of 1.017, and a trace of albumin. Microscopic examination revealed many red blood cells, many casts, and an occasional white blood cell.

The blood urea was 39 mg. per cent; urea clearance was 73 per cent of normal the first hour and 74 per cent the second hour.

Although this appeared to be a "medical" renal disease, an excretory urogram and cystoscopy were done to eliminate a coexisting surgical disease of the urinary tract inasmuch as the bleeding had been profuse; both revealed normal findings.

The final diagnosis was mild hemorrhagic Bright's disease.

Case 3. Hematuria due to drug administration. A 44 year old man admitted to the Clinic Hospital with a chronic osteomyelitis of the right tibia was given a course of sulfathiazole therapy. He had received 27 Gm. of this drug and 7 Gm. of sulfadiazine when he suddenly developed pain in the right flank. The examination of the urine, which is made routinely during sulfonamide administration, revealed microscopic hematuria on repeated specimens. Because of this finding, urologic consultation was requested.

Cystoscopy showed a collection of acetylated sulfonamide crystals obstructing the right ureteral meatus. Ureteral catheterization and pelvic lavage were done. The sulfonamides were discontinued, and the patient was free both of renal colic and hematuria.

Diagnosis: Hematuria associated with the administration of sulfathiazole and sulfadiazine.

Case 4. Hematuria from a renal neoplasm. A 41 year old accountant registered at the Clinic with the complaint of passage of bright red blood and clots in the urine. There had also been a slight ache in the loin and loss of weight. The bloody urine had been present on every voiding for 3 days preceding examination, and several large clots had been passed.

Cystoscopy showed no bladder lesion. Retrograde pyelography disclosed a marked hydronephrosis of the right kidney. At operation, several neoplastic areas were present in the cortex of the kidney. Pathologic diagnosis revealed these to be sarcomatous nodules. Final diagnosis: Stromal sarcoma of the right kidney. The passage of blood clot would have led to the superficial diagnosis of bladder tumor, but complete investigation was necessary to disclose the true lesion.

Case 5. Hematuria resulting from the presence of a calculus. A 56 year old man came to the Clinic with the complaint of blood in the urine associated with pain in the left flank. The gross hematuria had been of intermittent character over an entire year, the pain becoming progressively more severe. The general physical examination revealed no abnormal findings. Urologic investigation disclosed the presence of a calculus in the left kidney. A left pelviolithotomy was performed, and the patient was relieved of

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his symptoms. Final diagnosis: Calculus, left kidney. Here the hematuria had been minimized, and the patient had been brought under medical care only because of the pain.

Case 6. Hematuria due to coexisting pathologic lesions of the urinary tract. For the past 6 years a 32 year old man had been having episodes of recurring hematuria, particularly severe in the two months preceding the patient's registration at the Clinic. Grossly bloody urine had been present on many occasions during this period and had disappeared spontaneously. No clots had been passed. No other urinary symptoms had been present. An attack of left renal colic, which had occurred later and returned at intervals, finally caused him to seek medical aid.

The roentgenogram revealed a calculus in the left lower ureter. Manipulation of the calculus was decided upon, and at the time of cystoscopy a papilloma of the bladder was noted and fulgurized. This latter lesion apparently had produced the long-standing hematuria. Ordinarily, one might expect the passage of blood clots in the presence of a bladder tumor, but it can readily be seen that there is no characteristic pattern for hematuria with urologic lesions.

Final diagnosis: Left ureteral calculus and papilloma of the bladder.

Intermittent hematuria of several years' duration failed to bring this patient for medical advice. When pain appeared and the patient finally sought relief, complete urologic investigation revealed the presence of two coexisting pathologic conditions.

Case 7. Extensive bladder tumor as cause of hematuria. A 56 year old man registered at the Clinic in November 1942 with a complaint of recurring bloody urine since 1935. The hematuria would disappear spontaneously, only to return. Numerous blood clots had been passed. Since he had been troubled with no other symptoms, such as pain, he had disregarded the bloody urine until he had developed severe frequency and dysuria 7 years after the onset of the bleeding.

Except for pallor, the general physical examination was essentially negative. Blood count revealed a marked anemia. The urine was frankly bloody. Cystoscopy disclosed an extensive malignancy of the bladder. Bilateral hydronephrosis was demonstrated on intravenous urography.

Because of the extensive involvement of the bladder by the neoplasm, complete surgical resection could not be accomplished. X-ray therapy was administered. Diagnosis: Carcinoma of the bladder. The patient had ignored the recurrent bleeding from the bladder for 7 years until other symptoms prompted him to seek relief. A history of intermittent painless hematuria with passage of clots is characteristic of bladder tumor.

Case 8. Polycystic kidneys as a cause of hematuria. A 50 year old farmer reported that his urine had been bloody for 10 days prior to his visit to the Clinic in December 1941. The urine had ranged in color from "pink to red" on different voidings; no clots had been passed. No other urinary symptoms were present.

Physical examination revealed a large mass in the left upper quadrant, and a neoplasm of the left kidney was suspected. However, bilateral pyelograms disclosed the presence of typical congenital polycystic kidneys. Conservative treatment was advised.

Final diagnosis: Polycystic kidneys. Bleeding in these cases is not unusual, and accurate diagnosis must be made in order to avoid unnecessary exploratory surgery.

Case 9. Renal tuberculosis as cause of hematuria. A 28 year old man complained of pain in the left flank and associated gross hematuria with the passage of blood clots. The bleeding had been of only a week's duration and was present on each voiding, although clots were passed less frequently. No other urinary symptoms were present.

The patient was apparently in good health. No abnormalities were present on physical examination. By intravenous urography the right kidney was observed to be normal; the left kidney was insufficiently filled for diagnosis. Cystoscopy was then performed, and a pyelogram of the left kidney revealed a destructive lesion in the upper calyx suggestive of tuberculous infection. Later guinea pig inoculation was positive for tuberculosis.

Final diagnosis: Tuberculosis, left kidney. It is to be noted that although bleeding had been of but one week's duration, the kidney lesion was already well advanced. A nephrectomy was performed.

Case 10. Hematuria from prostatic varices and recurrent prostatic hypertrophy. A 73 year old man had a transurethral resection for hypertrophy of the prostate in 1935. He was symptom free for 7 years. He returned in 1942 with the history of bloody urine of 2 weeks' duration. Bleeding was present on each voiding, and numerous clots had been passed. There was no pain, nor other urinary symptoms. Bleeding had been rather profuse, and attempted cystoscopic visualization of the bladder was unsuccessful because of severe hemorrhage.

After the bleeding had been controlled by bladder irrigation, cystoscopy disclosed recurrent hypertrophy of the prostate with numerous dilated veins on the surface of the prostate. Rupture of these vessels accounted for the bleeding. A transurethral resection of the obstructing prostatic tissue was performed, and bleeding subsided.

Final diagnosis: Prostatic varices and recurrent prostatic hypertrophy.

From the previously reported cases, it is evident that from the history elicited from the patient and by a general examination the causative lesion responsible for the hematuria cannot be ascertained. Only by a comprehensive urologic survey aided by laboratory procedures can an accurate diagnosis be established and the proper therapeutic program instituted.

The clinical significance of hematuria cannot be minimized. Delay in establishing an accurate diagnosis frequently deprives the patient of the opportunity for a cure either by medical or surgical treatment, the therapy to be instituted depending upon the lesion present.

CONCLUSIONS

1. Hematuria is not a disease nor a clinical entity; it is merely a symptom which demands complete investigation and early diagnosis.
2. Although specific intrinsic diseases of the urinary tract usually account for hematuria, systemic disease may also be the cause of blood in the urine.

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3. Complete medical and urologic study may be required to establish an accurate diagnosis. Early determination of the causative pathologic lesion is essential for a good prognosis.

REFERENCES

1. MacKenzie, D. W.: Hematuria, a study of 2240 cases. *Canad. M.A.J.* 27:405-406 (Oct.) 1932.
2. Kretschmer, Herman L.: Hematuria: A clinical study based on 935 consecutive cases. *Surg. Gynec. & Obst.* 40:683-686 (May) 1925.
3. Cahill, George F.: Hematuria: its clinical significance. *J. Urol.* 47:224-234 (March) 1942.
4. Higgins, C. C.: Clinical significance of hematuria. *C.C.Q.* 5:4-12 (Jan.) 1938.