

Isolated Hematuria Associated with Varicella Infection: Report of Two Cases

SUÇİÇEĞİ İLE İLİŞKİLİ İZOLE HEMATÜRİ: İKİ OLGUNUN SUNUMU

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Abstract

Varicella is usually a self-limiting disease with relatively few and benign complications, although serious complications may occur. Urinary system involvement is a very rarely encountered complication of this disease, and may vary from hematuria to acute renal failure. Two cases of varicella-associated hematuria without a clinical picture of serious nephritis were presented in this paper due to unusual presentation. Varicella-associated urinary system involvement may present as an isolated hematuria with a benign course in which the clinical picture of serious nephritis does not develop.

Key Words: Varicella; complication; hematuria; children

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Özet

Suçiçeği, Varisella-zoster virüsün etken olduğu döküntülü enfeksiyöz bir hastalıktır. Genellikle selim seyirli olmakla birlikte farklı komplikasyonlara neden olabilir. Renal tutulum hastalığın seyri sırasında oldukça nadir karşılaşılan bir komplikasyondur ve hematüriden akut böbrek yetersizliğine kadar farklı derecelerde olabilmektedir. Suçiçeğine bağlı hematürisi bulunan, ancak ciddi nefrit tablosunun eşlik etmediği iki olgu ender görülmesi nedeniyle sunuldu. Suçiçeğine bağlı böbrek tutulumu ciddi nefrit tablosunun gelişmediği selim seyirli izole hematüri şeklinde de görülebilir.

Anahtar Kelimeler: Varisella; komplikasyon; hematüri; çocuklar

Varicella is a frequently encountered infectious disease with eruptions caused by the varicella-zoster virus.¹⁻⁴ The disease usually has a benign course and has self-limiting characteristics.³ However, it may cause various complications.¹⁻⁸ Urinary system involvement during the course of the disease is very rare.^{1,2,5-7} The aim of this case report is to stress that varicella-associated urinary system involvement may present as an isolated hematuria in which the clinical picture of serious nephritis does not develop.

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Case Reports

Case 1

A 3-year-old male patient was admitted with the complaints of skin eruptions and red urine. His medical history revealed that his complaints had begun 3 days prior to admission with fever and eruptions, and 1 day prior to admission blood was observed in his urine and his urine became red-dened in color. His personal and family histories were unremarkable. Physical examination revealed a body temperature of 37°C, pulse rate 88/min, respiratory rate 24/min, and arterial blood pressure 90/60 mmHg. Vesicular and occasionally crust-covered eruptions were found all over his body, including the scalp. In his laboratory tests, complete blood count and blood biochemistry analyses were found to be within normal limits. Total protein was 7.3 g/dl, albumin 4.2 g/dl, and total cholesterol 160 mg/dl. Erythrocyte sedimentation rate

(ESR) was 8 mm/h, prothrombin time (PT) 13 seconds, and active partial thromboplastin time (aPTT) 34 seconds. His urine was macroscopically reddish-brown and microscopic examination revealed abundant erythrocytes. Morphologically, most of these erythrocytes were spheric and some of them were fragmented, but they did not cause cylinder formation. Proteinuria did not accompany to hematuria. His antistreptolysin-O (ASO) titers, complement 3 (C3) and immunoglobulin A (IgA) levels were within normal range. No microorganism was identified in his throat and urine cultures. No abnormal finding was observed in renal ultrasonography (US). After supportive treatment, macroscopic hematuria and eruptions resolved on the 10th day of disease, whereas microscopic hematuria disappeared by the 15th day. During 6 months follow-up period recurrence of hematuria was not detected.

Case 2

A 6-year old male patient was admitted with the complaints of eruptions, pruritis and reddish-brown urine. Medical history revealed that the eruptions had begun 4 days prior to admission, while darkening of the urine color and appearance of blood in urine had begun 1 day prior to admission. His personal and family histories were unremarkable. Physical examination revealed that his body temperature was 36.5°C, pulse rate 80/min, respiratory rate 24/min and arterial blood pressure 100/60 mmHg; vesicular and occasionally crust-covered eruptions were found all over his body, including the scalp. Laboratory tests revealed normal complete blood count and blood chemistry. In serum analysis total protein was 7.5 g/dl, albumin 4.3 g/dl, and total cholesterol 180 mg/dl. ESR was 12 mm/h, PT 14 seconds, and aPTT 32 seconds. His urine was macroscopically in red colour and microscopic examination revealed abundance of erythrocytes. Most of these erythrocytes were in spheric morphology, and some of them in were fragmented morphology, but they did not cause cylinder formation. There was no proteinuria accompanying to hematuria. Immunologic and serologic tests revealed normal IgA, C3 and ASO levels. The patient's throat and urine cultures were normal, and renal US was also normal. Supportive

care was given the patient. Macroscopic hematuria resolved on the 4th day of disease, microscopic hematuria and eruptions disappeared on the 8th day of disease. During 4 months follow-up period hematuria didn't recur.

Discussion

Varicella infections have been being one of the common diseases of childhood with generally benign course.^{1,2} The primary infection results in varicella, which is characterized by mild fever and other systemic symptoms accompanied by typically pruritic diffuse polymorphic vesicular eruptions.^{5,9,10}

Other complications of varicella include bacterial superinfections of skin lesions, thrombocytopenia, arthritis, hepatitis, cerebellar ataxia, encephalitis, and meningitis.¹⁻¹⁰ If the bacterial superinfections are caused by group-A β -hemolytic streptococci, the bacteria may be localized in the skin, causing cellulites, bacteraemia, and rarely suppurative complications such as necrotizing fasciitis.² Transient bacteraemia may rarely cause pneumonia, pyogenic arthritis, and osteomyelitis. Rare but serious complications encountered in immunologically healthy individuals are Guillain-Barre syndrome, central facial paralysis, Reye syndrome, myocarditis, pericarditis, pancreatitis, orchitis, neutropenia, severe anemia, hematuria, and nephritis. Serious complications may lead to long-lasting sequelae in the patients.^{2,5}

Gucuyener et al.¹¹ have reported varicella-associated multi-organ failure in a 21-month-old male patient. Jaeggi et al.¹² have found in their study that the most commonly encountered varicella-associated complications are central nervous system involvement, skin infections, and pneumonia. Gomez et al.⁸ have observed that central nervous system involvement and respiratory complications secondary to varicella are frequently encountered, while gastrointestinal system, musculoskeletal system and hematological complications are much rare. Jackson et al.¹³ have reported non-suppurative complications such as central nervous system involvement in 15, dehydration in 8, and Reye syndrome in 6 of their 103 cases of varicella.

Varicella-associated urinary system involvement is a nonsuppurative complication frequently encountered in immune-deficient patients while it is extremely rare in immune-competent individuals.^{1,2,5,9,10} In cases with mild and nonfatal courses and in immune deficient individuals, varicella rarely may be associated with various renal involvement types ranging from mild nephritis to nephrotic syndrome and acute renal failure.¹⁴ Rapidly progressing nephritis has also been reported in occasional cases.⁷ Hematuria may be originated from the bladder.¹⁵ Both of our cases had the complaints of blood in the urine. Their physical examinations revealed no signs attributable to serious nephritis such as arterial hypertension, edema and reduction in the amount of urine excretion. Besides, other renal, hematological or systemic diseases that may cause hematuria were excluded with the aid of laboratory tests and radiological imaging. Depending on the clinical, laboratory and radiological findings, our patients were diagnosed as a mild form of urinary system involvement.

Histologically, there are endocapillary cell proliferation, epithelial and endothelial cell hyperplasia, and inflammatory cell infiltration in the kidneys. Tubular necrosis, endothelial cell hyperplasia and hemorrhagic congestion in glomeruli are observed in fatal cases.¹⁴ Electron microscopy reveals varicella antigen depositions in the glomeruli. IgG, IgM, IgA and C3 depositions are found in the glomeruli in immunohistochemical examinations. These findings support the presence of immune complex nephritis. High serum IgG and IgA levels and low C3 and C4 levels are the other findings supporting this theory.⁷ In our study, normal IgA and C3 levels indicate the absence of a severe renal involvement. Renal biopsies were not required because of absence of the signs of serious renal involvement and resolution of hematuria during the follow-up period.

Although varicella is a disease with benign course, it rarely may cause various complications. Urinary system involvement of varying degrees may develop during the course of the disease. Isolated hematuria may be encountered as a mild form

of varicella-associated urinary system involvement.

REFERENCES

1. Moros Pena M, Labay Matias M, de Miguel Pardo C, Valero Adan M, Puig Salvador S. Arterial hypertension, hematuria and renal involvement before varicella. *An Esp Pediatr* 2001; 55:73-5.
2. Ziebold C, von Kries R, Lang R, Weigl J, Schmitt HJ. Severe complication of varicella in previously healthy children in Germany: a 1-year survey. *Pediatrics* 2001; 108: E79.
3. Galil K, Brown C, Lin F, Seward J. Hospitalizations for varicella in the United States, 1988 to 1999. *Pediatr Infect Dis J* 2002; 21:931-5.
4. Coplan P, Black S, Rojas C et al. Incidence and hospitalization rates of varicella and herpes zoster before varicella vaccine introduction: a baseline assessment of the shifting epidemiology of varicella disease. *Pediatr Infect Dis J* 2001; 20:641-5.
5. Myers MG, Stanberry LR, Seward JF. Varicella-zoster virus. Behrman RE, Kliegman RM, Jenson HB, eds. *Nelson Textbook of Pediatrics*. 17th ed. Philadelphia: Saunders; 2004. p. 1057-62.
6. Miceli Sopo S, Valentini P, Ranno O. Childhood glomerulonephritis associated with varicella and streptococcal infection. *Minerva Pediatr* 2000; 52:375-9.
7. Pahara A, Walters S, Levin M. Infectious diseases and the kidney. In: Avner ED, Harmon WE, Niaudet P, eds. *Pediatric Nephrology*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2004. p. 955-86.
8. Riaza Gomez M, de la Torre Espi M, Mencia Bartolome S, Molina Cabanero JC, Tamariz-Martel Moreno A. Complications of varicella in children. *An Esp Pediatr* 1999; 50:259-62.
9. Pickering LK. *Red Book: Report of the Committee on Infectious Diseases*. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2000. p. 624-38.
10. Gershon AA, Larussa P. Varicella-zoster virus infections. In: Katz SL, Gershon AA, Hotez PJ, eds. *Krugman's Infectious Diseases of Children*. 10th ed. Missouri: Mosby-Year Book; 1998; p. 620-43.
11. Gucuyener K, Citak EC, Elli M, Serdaroglu A, Citak FE. Complications of varicella zoster. *Indian J Pediatr* 2002; 69:195-6.
12. Jaeggi A, Zurbrugg RP, Aebi C. Complications of varicella in a defined central European population. *Arch Dis Child* 1998; 79:472-7.
13. Jackson MA, Burry VF, Olson LC. Complications of varicella requiring hospitalization in previously healthy children. *Pediatr Infect Dis J* 1992; 11:441-5.
14. Lin CY, Hsu HC, Hung HY. Nephrotic syndrome associated with varicella infection. *Pediatrics* 1985; 75:1127-31.
15. Amar AD. Hematuria caused by varicella lesions in the bladder. *JAMA* 1966; 196:450.