Genitourinary Tract Involvement in a Child with Epidermolysis Bullosa

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ABSTRACT

Epidermolysis bullosa (EB) is a rare, inherited, bullous disorder of the skin that occasionally involves the urinary tract. We report a 3-month-old, premature infant with EB, who presented with gross hematuria. Urine analysis revealed macrohematuria and proteinuria. The urine culture was negative. On ultrasonic evaluation, there was bilateral hydronephrosis and the distal ureters had echogenic shadows, suggestive of clotted blood. This case is consistent with the rare involvement of the urinary tract with hydronephrosis and bullous lesions.

Key words: Epidermolysis bullosa, genitourinary, hematuria, hydronephrosis

INTRODUCTION

Epidermolysis bullosa (EB) was first reported in the late 19th Century. It is a heterogeneous group of rare inherited disorders, caused by mutations in various structural proteins within the skin that lead to marked mechanical fragility of the epithelial tissues. Usually, patients develop noninflammatory blistering at areas subjected to trauma.[1,2] Four major types have been described; EB simplex, junctional EB (JEB), dystrophic EB (DEB), and Kindler syndrome. These are divided into more than 30 subtypes based on the level of skin cleavage, mode of inheritance, phenotype, immunofluorescence antigen mapping, and mutation.[1]

EB is recognized to be a rare disorder, with an incidence of 20/million live births.[3] The prevalence of EB in Saudi Arabia is unknown. In the Eastern Province of Saudi Arabia, Abahussein and Al-Zayer found 16 cases over a 7-year period (1984–1990), which confirms the rarity of EB.[4] Studies conducted on EB patients in the Western Province of Saudi Arabia showed that the most common type is JEB.[5]

CASE REPORT

A 3-month-old infant, born prematurely at 35 weeks, presented with gross hematuria, which was bright red in color and had been associated with blood clots for the previous 2 weeks. There were no similar conditions, inherited disorders, or kidney diseases in her family. The parents of the infant are not consanguineous.

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On physical examination, the infant looked pale, had frontal alopecia and multiple hyper- and hypo-pigmented areas mainly over the face, neck, and the lower extremities. On examination, it was found that although there were no active blisters, there were areas of ulcers, both active and healed [Figures 1 and 2]. In addition, the infant had dystrophic nails [Figure 3]. There were no dysmorphic features. The growth parameters revealed that the weight, height, and the head circumferences were all below the fifth percentile for her age. Genital examination showed multiple areas of ulceration and crusted lesions. All remaining systemic examination was normal.

The patient was born by spontaneous vaginal delivery to a 28-year-old healthy mother, who is gravida 3, para 3, with no history of abortion. The infant’s birth weight was 1.2 kg. The fetal ultrasound did not show oligohydramnios or polyhydramnios. Physical examination at delivery was significant for blisters, mainly over the neck and lower extremities. In the early neonatal period, she was admitted to neonatal intensive care unit for 1 month due to prematurity and difficulty in feeding because of oral ulceration, which required a nasogastric tube.

Laboratory investigations were as follows: Urinalysis showed turbid urine; red blood cells 50–100/high power field; protein ≥300 mg/dl (moderate); leukocytes were trace; nitrates and urine culture were negative; blood urea nitrogen 3.5 mmol/L (1.4–4.3); creatinine 23 µmol/L (30–53); serum sodium 136 mmol/L (134–142); serum potassium 4.4 mmol/L (3.5–5.8); white blood cells 15 × 10^9/L (6–18); hemoglobin 109 g/L (95–135); platelets 640 × 10^9/L (140–450); C3 complement 1.2 g/L (0.9–1.8); antistreptolysin titer <13.8; and IgA level 1240 mg/L (700–4000). Urine calcium to creatinine ratio was 0.26, which is below the 95th percentile for her age.

Ultrasound examination revealed bilateral mild hydronephrosis with multiple echogenic shadows at the pelvicalyceal area and distal ureters suggestive of clotted blood [Figure 4a and b].
The diagnosis of EB was made at birth based on clinical findings. In addition, she was diagnosed with hiatus hernia, severe gastroesophageal reflux disease, and esophageal strictures, based on upper gastrointestinal (GI) gastrografin study. These findings were suggestive of DEB.

**DISCUSSION**

EB consists of a group of inherited diseases that involve the skin and mucous membranes of various body systems. Therefore, its clinical presentation ranges widely, from localized blistering of the hands and feet to generalized blistering of the skin with extracutaneous involvement. Different organs may be severely affected with possible complications, including the nails, hair, eyes, musculoskeletal system, heart, bone marrow, oral cavity, ears, nose, throat, upper airway, and GI and genitourinary tracts. Another significant sequel of severe EB is failure to thrive and delayed puberty. Wounds, systemic infections, and squamous cell carcinomas may be fatal.

The classification of EB can be based on the phenotypic characteristics such as the distribution severity of the disease along with extracutaneous features. In 1973, Kretkowski reported the first case of genitourinary tract involvement in EB in a 3-year-old boy with recessive DEB, who presented with straining at micturition secondary to urethral meatal stenosis.

Fine et al. demonstrated that the genitourinary tract may be involved in any EB type but usually arises with the most severe subtypes. The reported frequency of urological complications ranged from 16.6% to 31.1%, depending on the severity of EB, with higher frequency in JEB subtypes.

Possible urologic complications of EB include scarring of the glans penis, fusion of the labia, urethral stricture, bladder hypertrophy, cystitis, ureteral stenosis, obstruction of ureter vesicular junction, hydronephrosis, pyelonephritis, and renal insufficiency. Minor pressure to the urothelium during storage and urination may result in repetitive urothelial blistering and strictures leading to obstruction of the urinary tract and the development of areas of dilatation namely hydrourereter and hydronephrosis.

Patients with EB should be evaluated for the possibility of genitourinary involvement starting with ultrasonography. If an obstruction or vesicoureteric reflux is suspected, then voiding cystourethrography (VCUG) and diuretic renography may be indicated. Cystoscopy helps to identify urethral and bladder lesions. Instrumentation of the urinary tract should be limited to avoid trauma and subsequent strictures and if required, should be performed using small sized instruments.

The renal parenchyma may be affected in EB. The involvement may take several forms, including postinfectious glomerulonephritis after skin streptococcal infection, IgA nephropathy, and secondary renal amyloidosis. All those forms of renal parenchymal disease may progress to chronic renal insufficiency.

Effective treatment for EB has not been established. However, patient management requires a multidisciplinary approach. Basic care of EB patients includes preventing exposure to trauma, heat, and secondary infection. Wound care, nutritional support, and medical or surgical interventions are further needed to correct possible extracutaneous complications.

Our patient was diagnosed with DEB based on the early and extensive involvement of her skin, dystrophic nails, esophageal stenosis, and growth retardation. She developed hematuria, which was probably secondary to the bladder and ureteral blistering. Cystoscopy was not indicated at presentation due to her age and to avoid further injury to the genitourinary tract. Glazier and Zaontz reported that gross hematuria was the most common presentation of urological disease in EB (nine of 17 cases). We ruled out renal parenchymal disease by the normal C3 and IgA levels and the resolution of the proteinuria on follow-up. Hypercalciuria, as a cause of hematuria, was excluded by normal urine calcium to creatinine ratio. The bilateral hydronephrosis in our patient can be explained by ureteral strictures. Fine et al. reported that ureteral strictures cause hydronephrosis in 0.24% of DEB patients, due to ureteral obstruction.

The patient was observed for a week in the hospital with daily monitoring of the urinalysis. She was discharged with mild microhematuria. However, during her follow-up at our nephrology clinic, she continued to have intermittent gross hematuria without any symptoms that were suggestive of a urinary tract infection.

**CONCLUSION**

Despite the rarity of genitourinary tract complications in EB, annual follow-up, and routine urinalysis may provide earlier clues for genitourinary disease. Ultrasonography is a good diagnostic procedure to screen for possible...
genitourinary involvement. If any abnormalities are detected, appropriate imaging should be performed such as VCUG or diuretic renography, and a specialist opinion from a nephrologist and urologist should be sought.

**Declaration of patient consent**
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**
There are no conflicts of interest.

**REFERENCES**

1. Intong LR, Murrell DF. Inherited epidermolysis bullosa: New diagnostic criteria and classification. Clin Dermatol 2012;30:70-7.
2. Burgu B, Duffy PG, Wilcox DT. Single-centre experience of genitourinary complications of epidermolysis bullosa. J Pediatr Urol 2006;2:583-9.
3. Glazier DB, Zaontz MR. Epidermolysis bullosa: A review of the associated urological complications. J Urol 1998;159:2122-5.
4. Abuhussein AA, al-Zayir AA, Mostafa WZ, Okoro AN. Epidermolysis bullosa in the eastern province of Saudi Arabia. Int J Dermatol 1993;32:579-81.
5. Jalalah SM, Sawan AS, Zimmo SK. Epidermolysis bullosa: Experience from the western Province of Saudi Arabia. JKAM Med Sci 2006;13:49-58.
6. Fine JD, Mellerio JE. Extracutaneous manifestations and complications of inherited epidermolysis bullosa: Part II. Other organs. J Am Acad Dermatol 2009;61:387-402.
7. Fine JD, Bruckner-Tuderman L, Eady RA, Bauer EA, Bauer JW, Has C, et al. Inherited epidermolysis bullosa: Updated recommendations on diagnosis and classification. J Am Acad Dermatol 2014;70:1103-26.
8. Kretkowsk RC. Urinary tract involvement in epidermolysis bullosa. Pediatrics 1973;51:938-41.
9. Fine JD, Johnson LB, Weiner M, Stein A, Cash S, DeLeoz J, et al. Genitourinary complications of inherited epidermolysis bullosa: Experience of the national epidermolysis bullosa registry and review of the literature. J Urol 2004;172 (5 Pt 1):2040-4.
10. Arifi M, Arifi S, Demni K, Bouhafs MA, Belgacem R, Barahiou M. Genitourinary complications as initial presentation of inherited epidermolysis bullosa. Afr J Paediatr Surg 2011;8:72-4.
11. Kajbafzadeh AM, Elmi A, Mazahiery P, Talah SS, Ian D. Genitourinary involvement in epidermolysis bullosa: Clinical presentations and therapeutic challenges. BJU Int 2010;106:1765-6.
12. Almaani N, Mellerio JE. Genitourinary tract involvement in epidermolysis bullosa. Dermatol Clin 2010;28:343-6.