Pediatrics

Urofacial syndrome: Uncommon and unforeseen cause of lower urinary tract dysfunction in children

Saad Alqasem a,*, Basim Albaqawi b, Abdelazim Abasher b, Omaya Banihani b

a College of Medicine, Prince Sattam Bin Abdulaziz University, AlKharj, Saudi Arabia
b Urology Department, King Saud Medical City, Riyadh, Saudi Arabia

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ABSTRACT
Dr. Ochoa proposed a condition known as Urofacial syndrome (UFS) which is characterized by the abnormal facial expression while smiling along with dysfunctional lower urinary tract in 1987. This study investigated 7 years old boy who presented with recurrent urine retention, dysuria, and inversion facial expression. Radiological and genetic work-up diagnosed him with UFS.

Introduction
In 1987, Ochoa and Gorlin described a syndrome in a group of children with congenital obstructive uropathy. It is a rare autosomal recessive disease. It includes complications like urinary tract infection (UTI), urgency, enuresis, constipation, bladder trabeculation, and vesicoureteral reflux (VUR). Additionally, inversion of facial expression while smiling or laughing is also characteristic of the syndrome.1,2 Although its rarity, this condition has to be well thought-out in the differential diagnosis of kids with enuresis and recurrent UTI.

We are reporting this case due to its rarity, increase the awareness about the special facial characteristic to facilitate the diagnosis and to share our experience with the management and outcome in such cases.

Case presentation
A 7-year-old boy was referred to the outpatient department of our hospital as a case of recurrent urine retention, incontinence, dysuria, and constipation. On physical examination, a characteristic of inversion facial expression was noticed (Fig. 1), palpable bladder, and abdominopelvic ultrasound showed severe bilateral hydronephrosis with thinning of the parenchyma and distended bladder with irregular outline (Fig. 2). Upon admission, the creatinine level was 1.65 mg/dL and for that Foley catheter was inserted. Later, voiding cystourethrogram (VCUG) showed thickened trabeculated bladder with irregular outline (pine cone bladder), good capacity with increased sphincter tone and left grade 4 VUR (Fig. 3). Mercaptoacetyltriglycine (MAG3) scan was conducted with Foley catheter showed severe renal impairment with bilateral renal poor function. After two weeks of management with the nephrology team, creatinine came down to 1.23 mg/dL and hydronephrosis slightly improved. Cystoscopy was done and showed normal anterior urethra, wide posterior urethra, normal external sphincter, no posterior urethral valve, severely trabeculated bladder with multiple saccules, and diverticula. Genetic testing showed, a homozygous pathogenic variant that was identified in the HPSE2 gene, this confirmed the diagnosis of USF.

The patient has a positive family history with one similarly affected sibling, consanguineous parents (second cousins). The parents were counseled about clean intermittent catheterization and discharged home. During follow up with a regular bedside US, the hydronephrosis is slightly improved also the creatinine level back to a normal level. The patient planned for urodynamic study and appendicovesicostomy in the future.

Discussion
UFS is characterized by detrusor – sphincter discoordination, severe bladder dysfunction with a distorted facial expression while smiling. Although UFS is rare, it is crucial to distinguish this problem in patients with repetitive UTI, constipation, and incontinence.3

The relationship between distorted facial expression and voiding dysfunction remains unclear. It denotes a discrete article. The Center of weeping and snickering are situated at the upper pone midbrain

* Corresponding author.
E-mail addresses: saad.r.alqasem@gmail.com (S. Alqasem), itti871@gmail.com (B. Albaqawi), a.abasher@ksmc.med.sa (A. Abasher), obanihani@ksmc.med.sa (O. Banihani).

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proximally to the ordinary micturition center. So, it hypothesized that neurologic lesion in this area would probably affect both regions, which is resulted in this rare syndrome.

It is worthy of note, that an abnormal facial expression is related to a defect in the coordination between the facial muscle. Interestingly, brain magnetic resonance images (MRI) of UFS patients were unremarkable without lesions in the brain or normal spine revealed non-neurological pathogenesis of disease course.

Genetically, UFS is autosomal recessive disorder, which is a heterogeneous condition resulting from both alleles of a gene pathogenic variants in either HPSE2 (inactive heparanase-2) or LRIG2 (Leucine-rich repeats and immunoglobulin-like domains protein 2).

Mapping of the causative gene located in the HPSE2 gene at chromosome 10q23-q24, and the LRIG2 gene located at chromosome 1p13.2.

The molecular pathogenesis currently is unknown. Previously, it had been thought that UFS feature could result from abnormality in the central nervous system. However, recently it is considered more likely that UFS syndrome related to an abnormality in the peripheral neuro-development or function because both genes (HPSE2 and LRIG2) are localize in the peripheral nervous system.

**Fig. 1.** Inversion of facial expression with smiling.

**Fig. 2.** Kidney – Bladder ultrasound showed bilateral severe hydronephrosis and irregular outline of urinary bladder.

**Fig. 3.** VCUG showed irregular outline with thickened trabeculated bladder wall as a pine cone (Christmas tree) bladder, left grade 4 VUR, the finding representing severe neurogenic bladder.
Todate, no conventional diagnostic criteria has been published yet, but the diagnosis can be determined by the presence of the clinical feature involving the urinary bladder and facial feature in addition to identification of the pathogenic variants in either HPSE2 or LRIG2. The severity of the disease is a wide spectrum range from mild (represent facial finding with mild or no voiding dysfunction symptoms) to severe obstructive feature, including urine retention, high post-void residual, hydronephrosis, VUR, and renal insufficiency. Which is demonstrated in our patient.

Early recognition of UFS is crucial to prevent deterioration of the urinary tract through simple physical examination of the facial features and to consider this syndrome in the differential diagnosis. The mainstay of treatment is to prevent urinary tract deterioration by control bladder emptying. As we did in our patient by using clean intermittent catheterization. The administration of drugs can be added based on urodynamic study findings. Surgical intervention such as bladder augmentation or urinary diversion is an alternative to prevent further damage to the kidneys. Which is a long-term treatment planned for our patient.

Conclusion

USF is autosomal recessive disease, non-neurogenic bladder dysfunction, can be suspected simply from distorted facial expressions. Early recognition of this syndrome and treatment will prevent further deterioration in renal function.

References

1. Newman WG, Woolf AS. Urofacial syndrome. In: Adam MP, Ardinger HH, Pagon RA, et al., eds. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 2013:1993–2021. PMID: 23967498.
2. Ochoa B. Can a congenital dysfunctional bladder be diagnosed from a smile? The Ochoa syndrome updated. Pediatr Nephrol. 2004;19(1):6–12. https://doi.org/10.1007/s00467-003-1291-1.
3. Stamatiou K, Karakos C. Urofacial syndrome: a subset of neurogenic bladder dysfunction syndromes? Indian J Urol. 2010;26(4):582. https://doi.org/10.4103/0970-1591.74460.
4. Al-Qahtani FN. Ochoa syndrome: new features. Saudi J Kidney Dis Transpl. 2003;14(1):61.
5. Tu Y, Yang P, Yang J, et al. Clinical and genetic characteristics for the urofacial syndrome (UFS). Int J Clin Exp Pathol. 2014;7:1842-1848.