

The Ochoa urofacial syndrome: recognize the peculiar smile and avoid severe urological and renal complications

Síndrome urofacial de Ochoa: reconheça o sorriso peculiar e evite complicações urológicas e renais graves

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ABSTRACT

Ochoa syndrome is rare and its major clinical problems frequently unrecognized. We describe facial characteristics of six patients to help health professional recognize the inverted smile that these patients present and refer them to proper treatment. Patients' medical records were reviewed and patients' urological status clinically reassessed. At last evaluation patients' mean age was 15.5 years, and age ranged from 12 to 32 years. Mean follow-up was 35 months (12 to 60). Initial symptoms were urinary tract infections in four patients (67%) associated with enuresis and incontinence in three of them (50%). One patient had only urinary tract infection and two lower urinary tract symptoms without infections. Initial treatment consisted of clean intermittent catheterization with anticholinergics for all patients. Four patients (67%) were submitted to bladder augmentation. Two patients had end-stage renal disease during follow-up, one received kidney transplantation and one patient remained on the waiting list for a renal transplantation. Familial consanguinity was present in only one case. This significant condition is rare, but it must be recognized by pediatricians, nephrologists and urologists in order to institute early aggressive urological treatment.

Keywords: Urologic diseases/gentics; Enuresis; Urinary incontinence; Lower urinary tract symptoms; Urinary bladder, neurogenic; Case reports

RESUMO

A síndrome de Ochoa é rara, e seus principais problemas clínicos são frequentemente não reconhecidos. Descrevem-se aqui características faciais de seis pacientes para auxiliar profissionais de saúde a reconhecer o sorriso invertido que eles apresentam e encaminhá-los para o tratamento adequado. Os prontuários médicos foram revisados

e a condição urológica dos pacientes foi reavaliada clinicamente. A média de idade na última avaliação foi de 15,5 anos, variando de 12 a 32 anos. O seguimento médio foi de 35 meses (12 a 60). Os sintomas iniciais foram infecções do trato urinário em quatro pacientes (67%) associadas com enurese e incontinência urinária em três deles (50%). Um paciente apresentou infecções do trato urinário isoladamente e dois apresentaram sintomas do trato urinário inferior, porém sem infecções. O tratamento inicial consistiu em cateterismo intermitente limpo, com anticolinérgicos em todos os pacientes. Reconstrução urinária foi realizada em quatro pacientes (67%) por meio de ampliação vesical. Dois pacientes apresentaram doença renal em estágio terminal no seguimento, um recebeu transplante renal e outro manteve-se em lista de espera para transplante renal. Consanguinidade familiar esteve presente em apenas um caso. Essa condição significativa é rara, porém deve ser reconhecida por pediatras, nefrologistas e urologistas, a fim de instituir tratamento urológico agressivo precoce.

Descritores: Doenças urológicas/genética; Enurese; Incontinência urinária; Sintomas do trato urinário inferior; Bexiga urinária neurogênica; Relatos de Casos

INTRODUCTION

The Ochoa syndrome⁽¹⁾ is a rare condition characterized by functional obstructive uropathy and unusual facial abnormalities with a recessive autosomal inheritance pattern. This syndrome ultimately results in upper urinary tract deterioration and eventual renal failure if not diagnosed early.^(2,3) The Ochoa syndrome is also known as urofacial syndrome that affects both genders and occurs more likely when parents are closely related.⁽⁴⁾

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We retrospectively report on our experience with six patients referred to our institution. Physical examination revealed peculiar facial expression in all patients (Figures 1 and 2) and facial grimace when attempting to smile at the time when symptoms started.



Figure 1. Facial pictures of patients 1, 2 and 3, showing the unusual facial expression of grimace when attempting to smile. Note that in the top pictures, patients are in a neutral facial expression while in the bottom line they were asked to smile



Figure 2. Facial pictures of patients 4, 5 and 6, showing the peculiar expression. Top pictures show patients in a neutral facial expression while in the bottom line they were asked to smile

CASE REPORT

Patient 1 was a 15-year-old girl who had recurrent urinary tract infections (UTIs) since she was 12 years old (Figure 1). She had no history of other urinary tract symptoms and no signs of occult spinal dysraphism. Radiography

of lumbosacral region was normal; ultrasound scan revealed bilateral hydronephrosis; urodynamics test showed elevated post-void residual (PVR) urine volume and imercaptosuccinic acid (DMSA); renal scan showed severe bilateral renal scars. Initial management consisted of clean intermittent catheterization (CIC) and use of anticholinergics. Although she lacked other UTI after treatment, a worsening in renal function was noted in the follow-up and currently she is being prepared for renal transplantation.

Table 1 summarizes the clinical information of all patients.

Patient 2 was a 32-year-old man with history of recurrent UTIs in childhood (Figure 1). Urinary tract investigation, while he was followed at another care center, showed dysfunctional voiding and the initial diagnosis was non-neurogenic bladder. Despite the initial management he underwent bilateral ureterostomies at age 4 years old, which successfully keep him free of infection. At the age 9 years old, the ureterostomies were closed and CIC was started but bladder augmentation using a transverse colon was necessary.

Patient 2 family history was negative for Ochoa syndrome and his parents were not consanguineous. He was 32 years old at the moment we carried out this study and continued on anticholinergics therapy and CIC every 4 hours, remaining without infection. His upper urinary tract was scar free despite the history of UTIs.

Patients 3 and 4 were siblings aged 16 and 13 years old, respectively. Their parents were not consanguineous and did not have history of urofacial syndrome on the family before. Patient 3 was a 16-year-old boy who was referred to our clinic for recurrent UTIs, dysfunctional voiding, daytime urinary incontinence, enuresis and urgency (Figure 1). Results of ultrasound scan revealed left hydronephrosis, trabeculated bladder and diverticula, and urodynamics test showed a poorly compliant bladder, elevated PVR volume and detrusor-sphincter dyssynergia. The patient had a trabeculated bladder of small capacity and left high-grade vesico-ureteral reflux (VUR) in voiding cystourethrography (VCUG). Initial management consisted of CIC and oxybutynin. Because of anticholinergic side effects, the tolterodine was introduced with partial success. Continence interval was only 1 hour and 30 minutes. Subsequently, he had undergone bladder augmentation with ileum and continued on CIC every 5 hours without any leakage.

Patient 4 was a 13-year-old girl (Figure 2) who presented urgency and enuresis but without any episodes of UTI. Results of ultrasound scan demonstrated a normal urinary tract, VCUG showed no reflux, normal

Table 1. Characteristics of six patients

Patient	Follow-up (months)	Age at initial management (years)	Present age at the moment of the study (years)	Gender	Parents consanguinity	Initial symptoms	Renal impairment	UTI	Surgery
1	12	14	15	F	Cousins	UTI	Yes	Yes	Waiting for renal transplantation
2	24	4	32	M	No	UTI	No	Yes	Bilateral ureterostomies Bladder augmentation
3	60	11	16	M	No	UTI Incontinence Enuresis Urgency	No	Yes	Bladder augmentation
4	60	8	13	F	No	Urgency	No	No	
5	32	9	12	M	No	UTI Incontinence	Left kidney Kidney	Yes	Left nephrectomy + bladder augmentation
6	24	7	16	M	No	Incontinence Enuresis	Yes	No	Mitrofanoff Bladder augmentation Renal transplant

F: female; UTI: urinary tract infections; M: male.

bladder with large capacity and PVR of 80mL. In addition, urodynamics test showed a poorly compliant bladder, detrusor overactivity and dysfunctional voiding with sphincter dyssynergia.

To patient 4 an early management was proposed to avoid deterioration of upper urinary tract. She successfully underwent CIC and anticholinergics therapy. Currently, she remained well adapted to CIC, continence interval of 6 hours and with upper urinary tract preserved.

Patient 5 was a 12-year-old boy with daytime incontinence, recurrent UTIs, lumbar pain and an episode of urinary retention (Figure 2). At physical examination no signs of occult spinal dysraphism were found. Ultrasound scan revealed left ureterohydronephrosis and thick-walled bladder. In addition, he had a trabeculated bladder with diverticula and left high-grade VUR found in VCUG. Urodynamics test showed a poorly compliant bladder, detrusor-sphincter dyssynergia and elevated PVR volume. DMSA demonstrated severe scarring on left kidney.

Initial management consisted of CIC and anticholinergics but due to discomfort during urethral CIC, the treatment compliance was compromised. The patient had febrile UTIs and worsening of left renal function. He underwent left nephrectomy and a bladder augmentation with ileum and continued with CIC every 4 hours, no leakage was observed. Patient's right kidney was preserved.

Patient 6 was a 16 year-old boy (Figure 2) whose 7 siblings were normal. A history of recurrent UTIs and dysfunctional voiding was noted with elevated PVR volumes. Urodynamics test showed a poorly compliant bladder, elevated PVR volume and detrusor-sphincter

dyssynergia. He was followed at another center and had undergone an appendicovesicostomy when he was 7 years old. CIC and anticholinergics therapy were administered that decreased episodes of UTIs.

After 6 years, he had hypertension and was referred to the nephrology clinic for evaluation. He also had moderate renal impairment with an inadequate response to antihypertensive drugs. Results of ultrasound scan revealed bilateral ureterohydronephrosis, thick-walled bladder and a small left kidney. VCUG showed bilateral VUR and a small trabeculated bladder. DMSA demonstrated bilateral renal scarring with severe right kidney impairment. The patient underwent a bladder augmentation with ileum and was kept under CIC. After a 3-year follow-up he had a severe renal impairment and received a cadaver donor renal transplantation.

DISCUSSION

Bernardo Ochoa described a group of children with symptoms of neurogenic bladder (enuresis, incontinence, UTI, constipation, trabeculated bladder and vesicoureteral reflux), but with neither apparent neurological condition nor mechanical obstructive abnormalities that could justify the urological findings.⁽¹⁾

These cases would be classified as non-neurogenic neurogenic bladder as previously described by Hinman⁽⁵⁾ if a peculiar finding on their facial expression was not present. Ochoa noticed that children who participated in the study showed a pathognomonic inversion of the facial expression such as facial grimace or cry when they

attempted to smile. For this reason, he proposed the name “urofacial syndrome”.

Recent studies have localized the defective gene for urofacial syndrome in a region on chromosome 10q23-q24, with evidence of mutations on Heparanase 2 (HPSE2) gene that would be responsible for this syndrome.⁽⁶⁻⁹⁾ Although the exactly biological function has not yet been established, complete loss of HPSE2 function in patients with urofacial syndrome suggests it may be implicated on the genesis of the syndrome.⁽⁶⁾ The gene seems to be transmitted in a recessive autosomal inheritance pattern.

In the upper pons of the midbrain are located the crying and laughing centers, very close to the micturition center, and this proximity could explain how a neurologic lesion may affect both regions simultaneously,⁽⁴⁾ but this theory has not been proved yet. Many of these patients are not diagnosed and the lack of appropriate treatment results in upper urinary tract injury and ultimately renal failure.⁽³⁾

Early diagnosis is then essential to achieve a better prognosis. An aggressive urological management is necessary to improve bladder emptying and avoid infections. The suspicious must be raised when observed the combination of urological problems and inverted facial expression upon attempts to smile.⁽¹⁰⁾

This experience justifies the need to communicate and educate health professions about this syndrome,

the picture of patients’ smile is self-explanatory. Pediatricians, nephrologists and urologists should be aware of the relationship between voiding symptoms and this peculiar facial sign.

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