The Urofacial (Ochoa) Syndrome – First Case in the Central European Population

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Abstract: The urofacial (Ochoa) syndrome (UFS) is a very rare autosomal recessive disorder characterized by abnormal facial expression and urinary abnormalities. Patients with this syndrome have urinary tract infection, hydronephrosis, hydroureter and voiding dysfunctions resulting from neurogenic bladder, together with a peculiar inverted facial expression, mainly when smiling or crying. This syndrome has been so far observed in Colombia, USA, France and Spain. We report the first case of Ochoa syndrome in the central European population.

Introduction

The urofacial (Ochoa) syndrome (UFS) is a very rare autosomal recessive disorder characterized by abnormal facial expression and urinary abnormalities. Patients with this syndrome have urinary tract infection, hydronephrosis, hydroureter and voiding dysfunctions resulting from neurogenic bladder, together with a peculiar inverted facial expression, mainly when smiling or crying [1–4].

Case report

Our patient was a girl of young unrelated parents of Czech origin. Father has been treated for Crohn's disease, while mother and patient's brother, who was 5 years of age at that time, were healthy. Prenatal ultrasound was normal in the 20th week of pregnancy, however, later, in the 35th week, hypotrophy and megavesica with bilateral hydronephrosis were apparent. Therefore, the child was delivered on the 36th week of pregnancy by a Caesarean section. In the course of the delivery, rupture of the urinary bladder occurred, which was consequently treated by the bladder suture. There were no signs of abdominal wall abnormalities. The girl's birth weight was 1760 grams. The postnatal period was complicated by recurrent sepsis and hypertension, both of which were successfully treated. Abdominal ultrasonography revealed dilated calices and a large neurogenic bladder. There were no signs of vesicoureteral reflux on voiding cystourethrography. Infravesical obstruction was not present. Due to the urinary retention, Blocksom's vesicostomy was performed at three months of age. Bizarre facial expression was observed when the child was crying and this was even more apparent after the 3rd month of age when the girl attempted to smile (Figure 1). Furthermore, recurrent septic states occurred within the first 3 months of age, this being attributed to a transient hypogammaglobulinaemia. The girl was dismissed at the age of 5 months and was continuously followed-up, receiving prophylactic regimen with co-trimoxazole or furantoin, and repeatedly hospitalised for recurrent pyelonephritis which was treated with cefuroxime, amoxicilline/clavulonate, gentamicine and cefixime, respectively. Due to hypogammaglobulinaemia, intravenous immunoglobuline was periodically administered until 18 months of age. The urinary tract dilation gradually progressed and the facial inversion became even more apparent. At the age of

25 months the child was admitted to our department because of several hours lasting history of fever and vomiting. Urosepsis was diagnosed and this rapidly progressed to septic shock, and in spite of antibiotic therapy and re-animation the child died within 24 hours after the admission.

Discussion

The UFS has been described by Prof. Bernardo Ochoa in a Colombian population [1–4]. As mentioned above, the typical signs of UFS are urinary tract infection, hydronephrosis, hydroureter and voiding dysfunctions resulting from neurogenic bladder, together with a peculiar inverted facial expression, mainly when smiling or crying. About two thirds of the patients also have moderate to severe constipation due to bowel dysfunction [2, 3]. The simultaneous involvement of bladder and facial muscles stems from the fact, that normal micturition is a brain stem reflex centred in the reticular formation where it has a close anatomical relationship to the origin of facial nerves. As the center for micturition (the pontine micturition center) and closely related pontine urine storage center are located at the reticular formation [5], these share the same topographic location with the so-called laughing and crying center located above the facial and respiratory nuclei, most probably in the upper pons or midbrain [6]. Lesions in this area could conceivably produce dyssynergia manifested in a variety of organ systems [3, 4].

Understanding the three complementary but different components of the UFS is essential for the correct diagnosis and management of these children. The three components are the genetic background, the dysfunction of the facial expression, and the dysfunctional emptying of urine and faeces [4]. This most unusual disorder

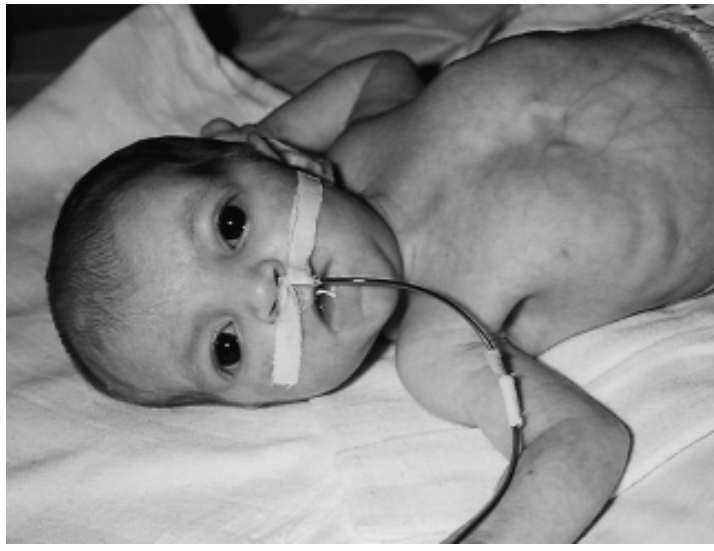

Figure 1 – Peculiar facial expression. Patient's attempt to smile.

was initially considered a local observation, as majority of patients with UFS came from Colombia [1–4]. However, children with UFS have been also later reported from various countries, in particular in Americans of Irish descent [7], and in two Arabic children [8, 9]. The first reported European cases of Ochoa syndrome are from France [10] and Spain [11, 12]. In a recent report from Canada, 3 patients of Caucasian origin were diagnosed with UFS [13]. The haplotype analyses in the French family [9] were compatible with those described in Colombian and American-Irish families [7, 14, 15]. The UFS gene has been mapped to chromosome 10q23–q24 [7, 9, 14, 15, 16] and was reported as responsible for all UFS patients from various ethnic groups [16]. The occurrence of the disorder in multiple siblings with normal parents and increased consaguinity, as well as equal distribution according to sex, support autosomal recessive inheritance [2, 3, 4]

The inversion of the facial expression that characterizes the UFS is not a structural facial defect, but a dysfunctional expression [4]. The facial identity in patients with UFS is similar to normal individuals, but not the facial expression when they laugh. When the patients with UFS are at rest or when they are sad or suffer pain or when they cry the facial expression is same as in normal persons. However, when they laugh, they grimace as if expressing sadness, discomfort or pain [4].

Bladder dysfunction syndrome, voiding dysfunction syndrome, elimination dysfunction syndrome, non-neurogenic neurogenic bladder and urofacial syndrome all have the characteristic spectrum of symptoms and signs of the neurogenic or obstructive bladder, without apparent neurological or obstructive disease [4]. Dysfunctional elimination and dysfunctional voiding is an aggressive disease, as the patients proceed to serious renal deterioration. The management of these patients essentially does not differ from that used in the treatment of other voiding disorders of neurological origin [1–4]. The principal goal is to prevent irreversible renal failure.

The presence of urinary tract abnormalities and bizarre facial expression in our patient suggest the diagnosis of Ochoa syndrome. The recurrent urinary tract infections should be attributed to the urinary tract malformation, however, transient hypogammaglobulinaemia might have influenced this as well. The combination of urinary tract abnormalities and hypogammaglobulinaemia might have contributed to the unfavourable outcome of our patient. To our knowledge, this is the first reported case of UFS in a Central European population. The occurrence of UFS can be expected in various unrelated populations.

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