Toriello-Carey syndrome – a report of two new cases with additional findings

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Abstract

Toriello-Carey syndrome is a rare multiple midline malformation. This report presents two patients with a new combination besides additional findings of clinical presentation and surgical management.

Key words: Toriello-Carey syndrome, clitoris agenesis, Pierre Robin sequence, omphalocele.

Introduction

Toriello-Carey syndrome was reported in fewer than 16 infants worldwide before September 2002 [1]. Toriello et al. reviewed approximately 20 published cases of this syndrome and 25 unpublished cases in 2003 [2]. It was characterized for the first time in 1988 by Toriello and Carey [3] by midline field defects such as agenesis of the corpus callosum, facial anomalies, cardiac defect and abdominal wall defect.

Here, we present two consecutive sibling cases with new clinical findings and call attention to an unbalanced sex ratio.

Case report

Case I

The first affected patient was a male, born at term to first cousin parents. The mother was a 37-year old G3P2 and the father was 45 years old. He manifested ambiguous genitalia including ovaries, uterus, normal but small penis and lack of testes or vagina (genotype is 46XY); other findings were cleft lip and palate, depressed nasal bridge, anteverted nares, hypertelorism, exophthalmia and gastroschisis. His IQ was normal. He managed successfully in the neonatal period and infancy. He had encephalitis and brain abscess at 8 and unfortunately died.

His parents were cousins and had a history of postnatal death of one offspring with multiple anomalies and second fetal death at 12 weeks. His genotype was normal 46XY and he had multiple malformations in phenotype such as low-set ear and severe deformities of all extremities.

Case II

The second patient was the first child born to non-consanguineous parents. She was the cousin of the first case. She was born at term by

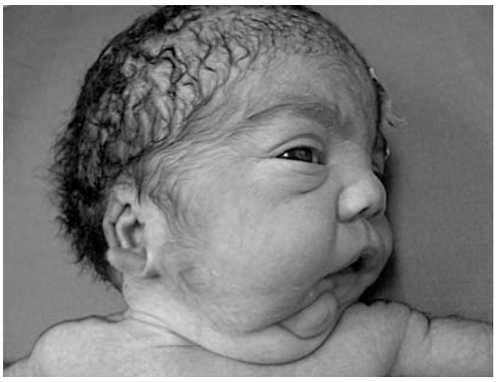

Figure 1. Pierre Robin sequence and excess nuchal skin

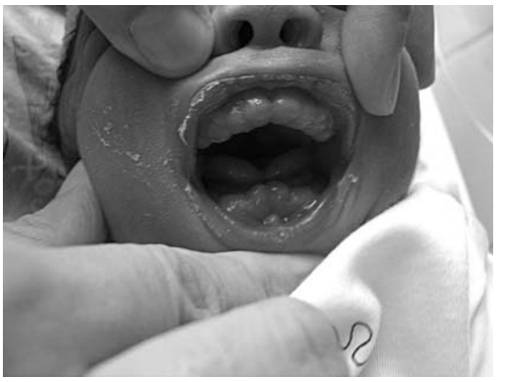

Figure 2. Hypertrophied gum

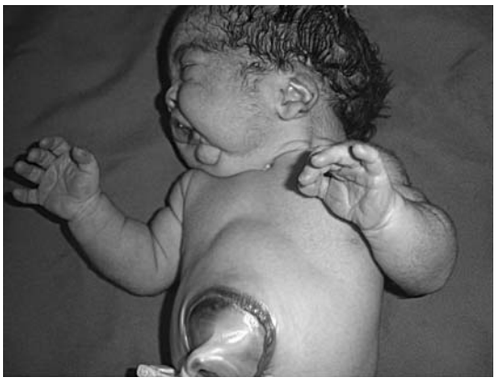

Figure 3. Omphalocele

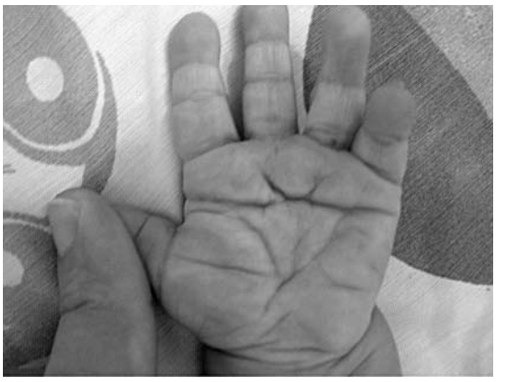

Figure 4. Triangular creases (similar to simian crease)

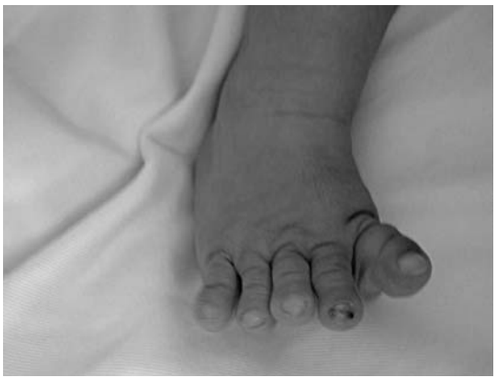

Figure 5. Gap between large and second toes

Caesarean section due to breech position. Her weight and height were normal. Her karyotype was 46XX – apparently normal female. The anomalies on her head and neck were brachycephaly, large fontanelles, low-set ear, cleft palate, hypertrophied gum, short tongue, micrognathia (Pierre Robin sequence), absence of uvula, anteverted nares, depressed nasal bridge and excess nuchal skin. In her eyes she had hypertelorism and telecanthus. On examination of the extremities she had some anomalies such as clinodactyly of fifth finger, brachydactyly, hypoplastic toenails, rocky and course feet and creases in palms similar to simian lines. There was an excessive gap between the large and second toes. Her skin was thick; pathological study showed increased collagen bundles. The nipples distance was abnormally long. In her genital system, there was no clitoris and labia minor were small. Gastrointestinal tract manifested a large omphalocele and anteriorly placed anus. Heart auscultation showed a 4/6 holosystolic murmur on the left sternal border and the following anomalies were documented by echocardiography: large VSD, Small ASD, large PDA and mild aortic overriding. Imaging studies of the urinary tract revealed bilateral G-4 vesicoureteral reflux.

Because any surgical management was dangerous, the conservative treatment for omphalocele was started initially by silver sulfadiazine ointment. Her parents rejected continuous management after a week and took her home without any drugs. After 6 months she came back to hospital for cosmetic operation of a large abdominal eventration. This operation was performed successfully and eventually the cleft palate was repaired with an excellent result at month 18. She is two years old now and her IQ is normal (Figures 1-5).

Discussion

These manifestations are highly suggestive of the Toriello-Carey syndrome. Affected patients show several important signs of midline field disruption such as craniofacial deformity, heart and abdominal wall defects [4].

Other congenital syndromes were considered in the differential diagnosis, but the findings did not appear consistent. Also, the main manifestation is agenesis or hypoplasia of the corpus callosum [5]; in our cases and in some reports the patients had evidence of the major findings of the syndrome except for this sign. Therefore, agenesis of the corpus callosum is not a requisite in Toriello-Carey syndrome [6].

We found some additional signs such as skin thickening with pathological study showing increased collagen bundles. Furthermore, her gum was hypertrophied, and there was agenesis of uvula and clitoris and another midline anomaly such as abdominal wall defect (gastroschisis). Ambiguous genitalia were not previously reported. We are not sure yet if these are new syndromes or some additional findings of Toriello-Carey syndrome.

The predominance of affected males and the milder phenotype in female patients suggests an X-linked gene or sex-influenced gene [7]. It was also reported by Czarnecki [8], but another report concerning two sisters with a severe phenotype and possible parental consanguinity suggested autosomal recessive inheritance of Toriello-Carey syndrome [9]. As shown by Toriello et al. [2] and Jespers et al., we believe these anomalies must have arisen during blastogenesis [10] and presence of healthy consanguineous parents suggests autosomal recessive inheritance for which a recurrence risk of 25% should be discussed with families. As a result, prenatal diagnosis may be advised.

References

1. Kataoka TR, Ito A, Nakabori T, et al. Toriello-Carey syndrome associated with respiratory failure and non-mechanical ileus. Am J Med Genet A 2003; 120A: 537-41.
2. Toriello HV, Carey JC, Addor MC, et al. Toriello-Carey syndrome: delineation and review. Am J Med Genet A 2003; 123A: 84-90.
3. Toriello HV, Graff RG, Florentine MF, Lacina S, Moore WD. Scalp and limb defects with cutis marmorata telangiectatica congenita: Adams-Oliver syndrome? Am J Med Genet 1988; 29: 269-76.
4. Barisic I, Peter B, Mikecin L. Further delineation of the Toriello-Carey syndrome: a report of two siblings. Am J Med Genet 2003; 116A: 188-91.
5. Lacombe D, Creusot G, Battin J. New case of Toriello-Carey syndrome. Am J Med Genet 1992; 42: 374-6.
6. Camera G, Righi E, Romagnoli G. Toriello-Carey syndrome: report of a new case. Clin Dysmorphol 1993; 2: 260-3.
7. Czarnecki P, Lacombe D, Weiss L. Toriello-Carey syndrome: evidence for X-linked inheritance. Am J Med Genet 1996; 65: 291-4.
8. Aftimos S, McGaughran J. Toriello-Carey syndrome: case report with additional findings. Am J Med Genet 2001; 98: 273-6.
9. Chinen Y, Tohma T, Izumikawa Y, et al. Brief clinical report: two sisters with Toriello-Carey syndrome. Am J Med Genet 1999; 87: 262-4.
10. Jespers A, Buntinx I, Melis K, Vaerenberg M, Janssens G. Two siblings with midline field defects and Hirschsprung disease: variable expression of Toriello-Carey or new syndrome? Am J Med Genet 1993; 47: 299-302.