

# Discordance of Oral-Facial-Digital Syndrome Type 1 in Monozygotic Twin Girls

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The oral-facial-digital syndrome type 1 (OFD1) includes limb, facial, intraoral malformations and the gene for the disorder was recently mapped to Xp22.3-p22.2. We report on monozygotic twin girls discordant for OFD1. Monozygosity is supported by placental pathology (monochorionic diamniotic) and molecular studies with probability of dizygosity  $< 1 \times 10^{-6}$ . The affected twin has oral cavity abnormalities including median cleft lip, cleft palate, lobulated hamartomatous tongue, aberrant hyperplastic oral frenula, alveolar notches, and absent lateral incisors. Facial manifestations include telecanthus, hypoplastic alae nasi, and transient neonatal facial milia. The patient also has short and deviated fingers with partial cutaneous syndactyly. At 10 years, she has not had central nervous system or kidney problems. X-inactivation study revealed similar X-inactivation patterns in the lymphoblasts of both twins. We conclude that skewed X-inactivation is an unlikely cause for the discordance, which is more likely due to a postzygotic mutation in the affected twin. *Am. J. Med. Genet.* 86:269-273, 1999.

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**KEY WORDS:** oral-facial-digital syndrome type 1 (OFD1); discordant MZ twins; postzygotic mutation; X-inactivation

## INTRODUCTION

The oral-facial-digital syndrome type 1 (OFD1: OMIM 311200) is thought to be a single gene malformation syndrome inherited in an X-linked dominant pattern. The gene for the disorder was mapped to Xp22.3-p22.2 [Feather et al., 1997] and the critical region was recently narrowed to 12 Mb [Gedeon et al., 1999]. Here we report on monozygotic twin girls discordant for OFD1 most likely caused by a postzygotic mutation.

## CLINICAL REPORT

Twin girls were born to a 23-year-old, G2P1 Caucasian mother and a 34-year-old, nonconsanguineous Caucasian father. The pregnancy was complicated by maternal hyperemesis gravidarum treated with intravenous hydration and promethazine hydrochloride. There was no history of fever, spotting, tobacco, alcohol, or illicit drug use or X-ray exposure. Prenatal tests including maternal serum alpha-fetoprotein and four ultrasound studies were reportedly normal (The existence of twinning was noted.) Due to the risk of fetal erythroblastosis, their mother received Rh (D) immunoglobulin during the pregnancy. Maternal weight gain was 14 kg with normal fetal activity. The labor lasted 6 hr and was followed by Caesarean section at 36 weeks of gestation because of previous Caesarean section. APGAR scores of both twins were 8 and 9 at 1 and 5 min, respectively. The twins birth weights were 2350 g and 2490 g (both normal), and birth lengths 45.7 cm and 47.0 cm (both normal), for Twins A and B, respectively. The placenta was diamniotic and monochorionic.

Twin A had no physical anomalies. However, Twin B was noted to have dysmorphic features of the face, oral cavity, and limbs. Both twins went home with an apnea monitor, however, Twin B was readmitted at the age of 6 weeks due to apnea. A sepsis evaluation was negative. She was discharged after 2 days on theophylline without further episodes of apnea. Twin B had multiple ear infections, requiring the insertion of four sets of

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tympanostomy tubes. The median cleft lip and the cleft palate were repaired at the ages of 4 months and 11 months, respectively. She also had an esotropia requiring eye patching. Besides these operations, frequent otitis media, and the esotropia, she has been in good health. Twin A was healthy with the exception of exercise-induced asthma.

At the age of 10 years twin B weighed 56.5 kg (>95th centile for age), and was 141.2 cm tall (50th–75th centile). Her hair was sparse anteriorly with normal texture and hairline. The forehead was normal and the palpebral fissures were neutral. She had telecanthus (inner canthal distance of 3.6 cm (>+2 SD), but no hypertelorism (interpupillary distance of 5.6 cm (between

75th and 97th centile)) (Fig. 1A,B). The ears were normal in position, configuration, and size. Her alae nasi were hypoplastic with a prominent columella. There was a well-healed surgical scar from a median cleft lip repair. The mouth was downturned and there was thinning of the lateral vermilion border. The palate was repaired. There were alveolar notches on both sides of upper and lower alveolar ridges. There were several frenula joining the alveolar ridges and the buccal mucosa (Fig. 2A). The lateral incisors were missing and the tongue had a longitudinal groove on the left side. There was a hamartoma on the left posterior part of the tongue (Fig. 2B). The neck was mildly shortened. No chest deformities were noted. Cardiac and abdomi-

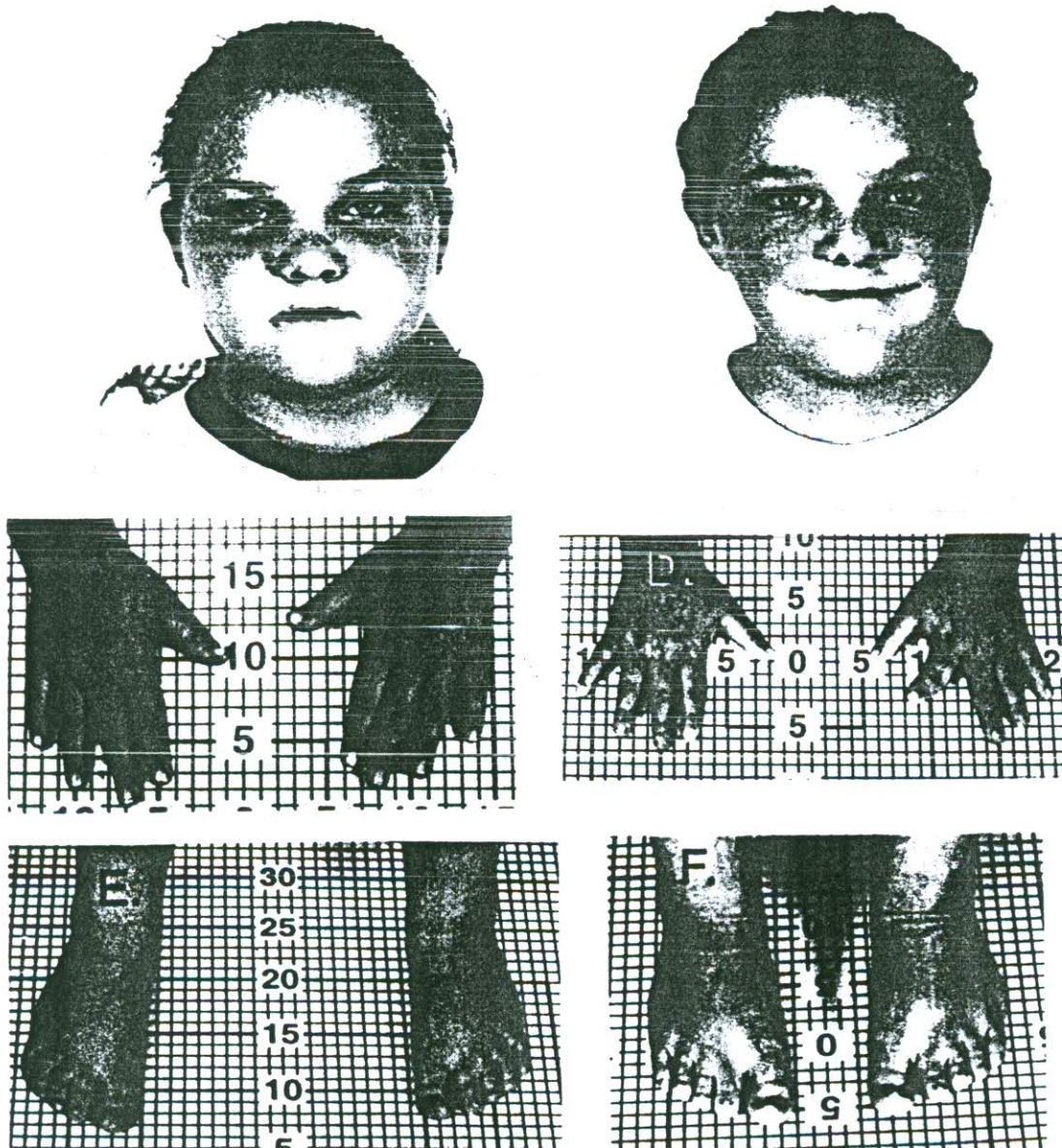


Fig. 1. Faces (A, B), hands (C, D), and feet (E, F) of Twin A (A, C, E) and Twin B (B, D, F) at 10 years of age. Note telecanthus, hypoplastic alae nasi, repaired median cleft lip, and thinning of the lateral border of vermilion border (B); brachydactyly, clinodactyly, and partial cutaneous syndactyly of third and fourth fingers of the left hand (D); partial cutaneous syndactyly of the second and third toes bilaterally, mildly hypoplastic toenails, and everted first toenails (F) present in Twin B but not in Twin A.

