Clinical Case Report

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# Congenital asymmetric crying facies syndrome
## A case report

Xiaoqiu Liang, MD*, Birong He, MD

**Abstract**

**Introduction:** Congenital asymmetric crying facies (ACF) in newborns is a rare condition usually caused by unilateral agenesis or hypoplasia of the depressor anguli oris muscle on one side of the mouth (symmetric face at rest and asymmetric face while crying), which is often accompanied with other malformations.

**Case report:** We present a case of a female newborn with nonconsanguineous ethnic Han Chinese parents who presented with 37 minutes of breathlessness and asymmetrical face when crying. A thorough physical examination had been conducted. The patient was diagnosed with aspiration pneumonia and congenital ACF syndrome, accompanied with congenital bilateral anophthalmia, left homolateral auricle dysplasia, malformation in the left-hand thumb, patent ductus arteriosus (PDA), and patent foramen ovale (PFO) and tracheoesophageal fistula. The patient's mother underwent routine fetal sonogram at 25 weeks gestation, which showed major anatomical anomalies in the eyes of the fetus. The mother chose to pregnancy until vaginal delivery. This case is unique because congenital bilateral anophthalmia has not been reported in such patients before.

**Conclusion:** Careful physical examination of newborns and genetic testing are important for early diagnosis of neonatal asymmetric crying facies (NACF), especially if ACF is present. Early determination of the etiology and future screenings are very important for the management of this condition. The lower lip on the affected side looks thinner because of the lack of the muscle agenesis, so the use of ultrasound to observe facial muscles and electrodiagnostic testing could be helpful for the differential diagnosis of NACF from congenital facial nerve dysplasia.

**Abbreviations:** ACF = asymmetric crying facies, DAOM = depressor angularis oris muscle, HBcAb = hepatitis B core antibody, HBeAb = hepatitis B e antibody, MRI = magnetic resonance imaging, NACF = neonatal asymmetric crying facies, PDA = patent ductus arteriosus, PFO = patent foramen ovale, VACTERL = vertebral anomalies, anal atresia, cardiac defect, tracheoesophageal fistula and/or esophageal atresia, renal and radial anomalies, limb defects.

**Keywords:** asymmetric crying facies, congenital, ultrasound

## 1. Introduction

Asymmetric crying facies (ACF) in newborns is a rare condition, which is estimated to occur in 0.2% to 0.6% of infants,[1] and left-sided predominance was determined in 80% of neonatal ACF (NACF) cases.[2,3] This can be an isolated clinical finding or be coupled with other congenital malformations; ACF is associated with other birth defects in approximately 45% to 70% of cases.[4] When associated with other anomalies, it is known as ACF syndrome.

We report, herein, a case of a female newborn who had an asymmetrical face when crying, with congenital bilateral anophthalmia, left homolateral auricle dysplasia, left-hand thumb malformation, patent ductus arteriosus (PDA), and patent foramen ovale (PFO), and tracheoesophageal fistula to facilitate a better clinical understanding of this condition.

## 2. Case report

We report a case of a female newborn who presented with 37 minutes of breathlessness and asymmetrical face when crying. Written informed consent for the publication of this report was obtained from the patient's parents. She was born at 41–4/7 weeks after an uncomplicated pregnancy and an uncomplicated vaginal delivery. She had a birth weight of 2900 g, birth length of 49 cm, head circumference of 33 cm, and Apgar scores of 9, 10, and 10 at 1, 5, and 10 minutes, respectively. The infant was the second-born child of nonconsanguineous ethnic Han Chinese parents, whose first-born was normal. Her father was 36 years old with good health, and her mother was a 34-year-old hepatitis b virus carrier. The mother underwent routine fetal sonogram at 25 weeks gestation, which showed major anatomical anomalies in the eyes of the fetus. No remarkable obstetric perinatal factors were observed, and the family history did not show any congenital defects.

The infant's examination after delivery showed a normally configured head, symmetrical lip corners at rest (Fig. 1), and an asymmetric face while crying, with the right lip corner and right

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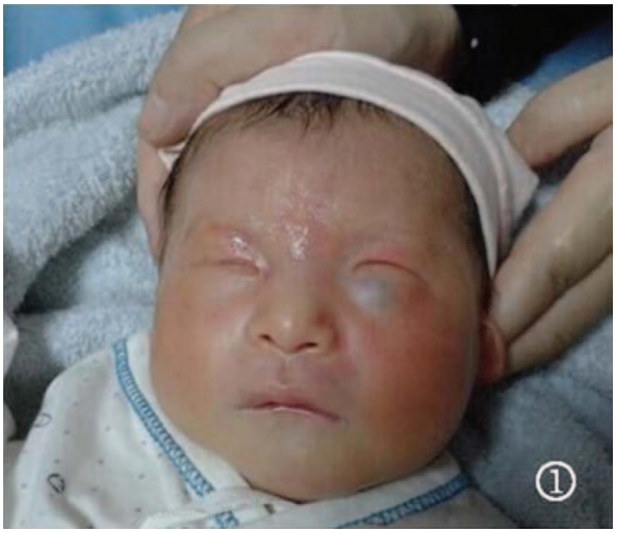

**Figure 1.** Facial symmetry observed at rest at postnatal day 1: the upper and lower eyelids could not be separated, and congenital bilateral anophthalmia was observed.

half of the lower lip falling, while the left corner did not move (Fig. 2). The lower lip was thin, and the bilateral wrinkles on the forehead and depth of the nasolabial folds were symmetrical. She also showed a congenital dysplasia of the left auricle (Fig. 3). Both eyes appeared malformed, the upper eyelid could not be separated from the lower lid (Fig. 1), and an ophthalmologist's examination revealed that the eyeballs were not observed in the orbits. In addition, hypoplasia of the left-hand thumb was observed (Fig. 4). The hearing test result was normal and a few moist rales were audible over the bilateral lungs. Cardiac auscultation revealed a grade 2/6 continuous murmur in the left second intercostal space.

Furthermore, a chest X-ray image showed a normally configured heart silhouette, and the vascular structures of the lungs were increased, with regular pulmonary perfusion and normal transparency. Electrodiagnostic testing of the facial muscles was normal. Echocardiography indicated PDA and PFO.

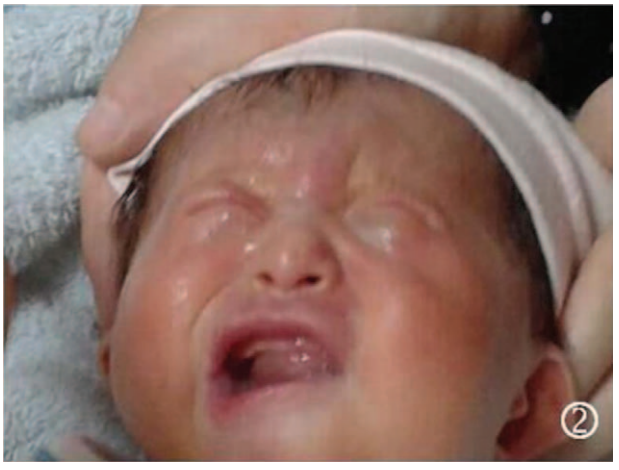

**Figure 2.** Facial asymmetry observed while crying at postnatal day 1: drooping of the right corner of the mouth and right half of the lower lip; the lower lip appears to be pulled toward the intact right side.

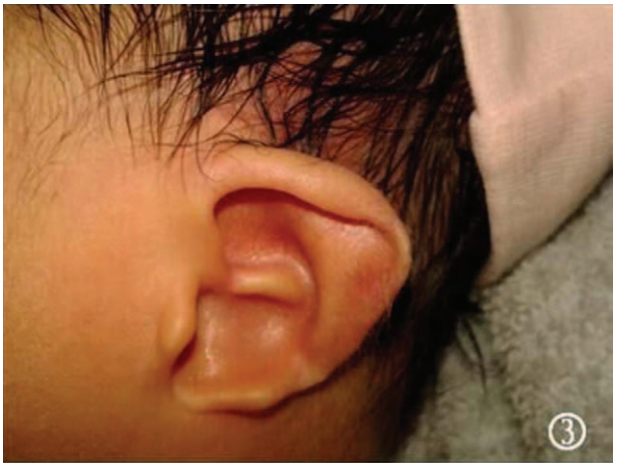

**Figure 3.** Malformation of the left auricle: the earlobe is absent.

Abdominal ultrasound and magnetic resonance imaging (MRI) of the brain were normal. The postnatal ultrasound (Figs. 5 and 6) showed that the fetus' eyes were consistent with those observed in the prenatal ultrasound (Fig. 7), the shape of both eyes was abnormal, and crystalline lenses were not observed in the orbits. However, the prenatal ultrasound did not detect the anomalies of the left hand and left auricle. Electrocardiography revealed a heart rate of 132 beats/min. Other laboratory findings included white blood cell count of $13.23 \times 10^9$/L, neutrophil level of 51.1%, lymphocyte of 37.3%, hemoglobin of 158 g/L, and platelet count of $307 \times 10^9$/L, and the hepatitis B e antibody (HBeAb) and hepatitis B core antibody (HBcAb) were increased. Moreover, the hepatic and renal functions were normal, as well as the serum electrolytes and calcium.

During hospitalization, the infant was always choked when feeding and did not eat anything. The pediatrician suspected that she had a tracheoesophageal fistula and suggested an endoscopy, which was refused by the parents. The parents also refused genetic testing. The baby was discharged from the hospital within 6 days and was kept under follow-up. Because there was nothing treatment for the patient, the infant died on the ninth postnatal day.

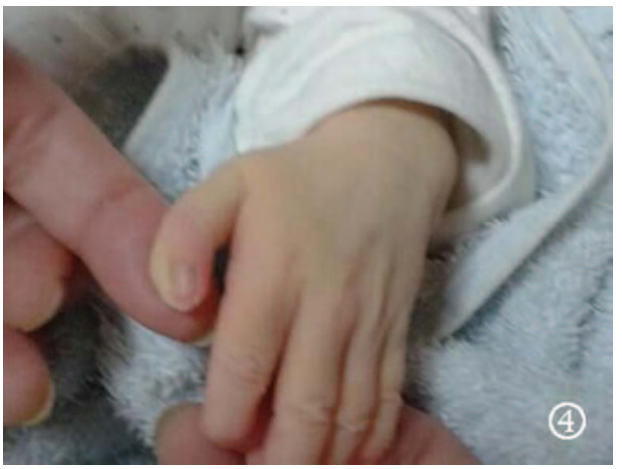

**Figure 4.** Malformation of the thumb of the left hand: the thumb is warped inward.

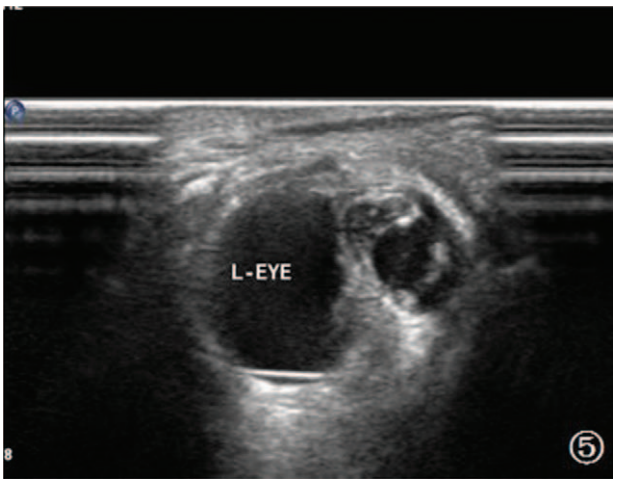


**Figure 5.** Postnatal 2-dimensional ultrasound image of the left eye: the shape of right eye is abnormal. The structures appear disordered and a crystalline lens cannot be observed in the orbit.

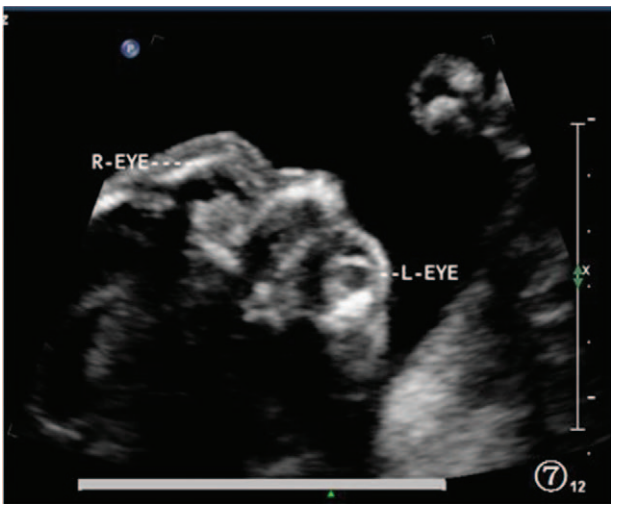


**Figure 7.** Prenatal 2-dimensional ultrasound image of both eyes: the structures of both eyes appears abnormal, and crystalline lenses cannot be observed in the orbits.

The patient was diagnosed with aspiration pneumonia and congenital ACF syndrome, accompanied with congenital bilateral anophthalmia, left homolateral auricle dysplasia, malformation in the left-hand thumb, and tracheoesophageal fistula.

## 3. Discussion

NACF is characterized by facial asymmetry only when a newborn is crying, wherein one angle of the mouth deviates to one side, which is the unaffected side, and downwards, while the other side does not move; however, the face is symmetric at rest. The major symptom of NACF is the absence or weakness in the outer and lower movements of the commissure while crying and primarily on the affected side.[5] The etiology of NACF is multifactorial and can be due to faulty muscle or nerve development.[6] Intrauterine viral infections, chromosomal aberrations, hereditary factors, or a defect located at the brainstem level can cause a defect in the depressor anguli oris muscle (DAOM) development,[2] one of the muscles that control the movements of the lower lip, on one side of the mouth.[4,7] Familial occurrence has been reported, and the mode of inheritance has been suggested as autosomal dominant inheritance with variable expressivity.[8,9] Some studies revealed that it is associated with chromosomal anomalies, such as 22q11.2 deletion.[10,11] Therefore, genetic deletion testing should be suggested when ACF is suspected in a newborn. In this case, the pediatrists hypothesized that ACF was possibly due to the increase of HBeAb and HBcAb levels.

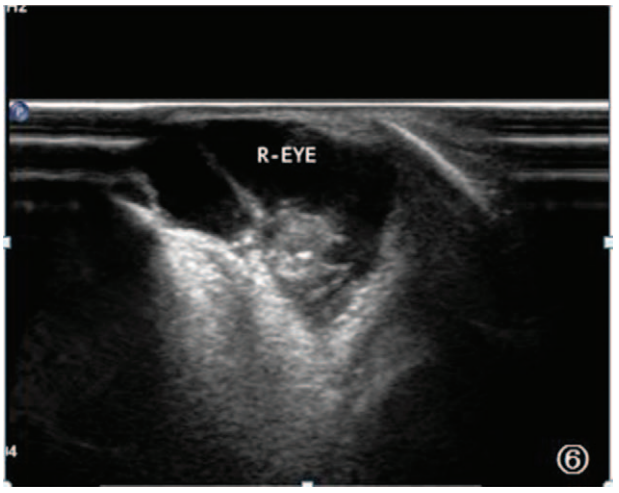


**Figure 6.** Postnatal 2-dimensional ultrasound image of the right eye: the shape of the right eye is abnormal, and a crystalline lens cannot be observed in the orbit.

NACF has been suggested to be an indicator of coexisting anomalies, which can involve nearly all systems, such as the cardiac system, central nervous system, cervicofacial region, gastrointestinal and genitourinary system, respiratory system, musculoskeletal system, skin, and soft tissues,[2,9] the cervicofacial region and cardiovascular system being the most commonly involved.[4] Major cervicofacial malformations frequently occur on the same side as the DAOM hypoplasia.[9] In our case, the ear and left hand malformations were observed on the same side as the dysplasia of the DAOM. ACF may be present in isolation or as part of some other syndrome, such as Digeorge syndrome and VACTERL syndrome (vertebral anomalies, anal atresia, cardiac defects, tracheoesophageal fistula and/or esophageal atresia, renal and radial anomalies, and limb defects).[8] In this case, the prenatal ultrasound only detected the eye anomalies, the anomalies of the fetus' left-ear and left-hand were misdiagnosed; thus, careful attention should be paid when observing the fetus' ears and hands. Prenatal ultrasound cannot detect isolated anomalies, and some defects might not be evident in a newborn. Emotion and spirit of movement disorders may appear with age. In such situations, a thorough physical examination and future screening should be conducted.

No treatment may be required in isolated anomalies if the cosmetic problems are minor. Some studies reported that patients underwent bidirectional fascia grafting in horizontal and vertical directions to restore the aesthetic appearance of the asymmetrical lower lip.[12]

NACF is often confused with facial nerve compression of the fetus in the uterus, facial nerve palsy secondary to trauma, or

developmental etiologies accompanied with this facial anomaly. A thinner lower lip on the affected side, retention of normal bilateral wrinkling of the forehead, closure of the eyelids, and deep nasolabial folds can be observed in NACF.[9] Congenital facial nerve palsy is manifested with facial asymmetry both at rest and while crying, without other malformations, and electrodiagnostic testing could help confirm the condition. Gupta and Prasad[13] found that the use of ultrasound to observe facial muscles could be helpful for differential diagnosis. Ultrasonography could show palpable thinning or absence of the lateral portion of the lower lip, which is usually present on the affected side in a fetus with NACF.[2,5,9,14]

In conclusion, careful physical examination of newborns and genetic testing are important for the early diagnosis of NACF, especially if ACF is present. Ultrasonography and electrodiagnostic testing could be helpful for the differential diagnosis of NACF from congenital facial nerve dysplasia. In addition, an accurate diagnosis is essential to provide parents with information regarding the prognosis, recurrence risk, and future prenatal diagnostic options of NACF.

## Author contributions

**Conceptualization:** Xiaoqiu Liang.
**Data curation:** Xiaoqiu Liang, Birong He.
**Formal analysis:** Xiaoqiu Liang, Birong He.
**Writing – original draft:** Xiaoqiu Liang.
**Writing – review & editing:** Xiaoqiu Liang.

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