Oral Science International, November 2010, p.72–75

A Case of Cat Cry Syndrome Associated with Cleft Lip

Koji Kashima, Kaori Igawa, Rie Yokota,
Izumi Yoshioka and Sumio Sakoda

Department of Oral and Maxillofacial Surgery, Faculty of Medicine, University of Miyazaki

Abstract: Cat cry syndrome (cri-du-chat syndrome) is an extremely rare condition characterized by a high shrill cry during infancy, resulting from either the deletion of the short arm of chromosome 5 or unbalanced translocation inherited from a parent. We report the case of a 1-year-old girl with cat cry syndrome associated with cleft lip. The patient showed a ventricular septal defect, cleft lip, growth and mental retardation, micrognathia, ptosis of the eyelids, hypertelorism, epicanthal folds, and a preauricular tag on the right side. A chromosomal study revealed the terminal deletion of chromosome 5 (46, XX, del(p14.2)ish del(5)). Repair of the cleft lip was carried out concurrently with resection of the preauricular tag, and the patient's postoperative course was uneventful.

Key words: cat cry syndrome, cri du chat syndrome, cleft lip, chromosome 5

Introduction

Cat cry syndrome (cri-du-chat syndrome) is an uncommon condition with the incidence ranging from 1 : 15000 to 1 : 50000 live-born infants[1]. The syndrome is characterized by a high shrill cry during infancy and growth and mental retardation, with a high incidence of congenital heart disease and chronic respiratory infection due to aspiration[2]. Although it appears that cleft lip/palate occurs in 8-15% of patients with this syndrome[3,4], reports in the literature are very scarce. The present article reports an additional case of cat cry syndrome associated with cleft lip.

Case report

The patient is the second child of a 38-year-old Japanese man and a 36-year-old Japanese woman, and was born in a private clinic on July 29, 2001, after a pregnancy that lasted 40 weeks and 4 days. During the pregnancy, a decrease in fetal movement was observed from week 31 to delivery. No member of the immediate family or other close relatives had similar congenital abnormalities. Delivery was spontaneous, and the baby had an Apgar score of 9 at 5 minutes. Her weight at birth was 2016 g, her height was 47.9 cm, and the circumference of her chest and head were 28.4 cm and 29.2 cm, respectively. The baby immediately developed cyanosis and was diagnosed with respiratory distress syndrome, and was transferred to the neonatal intensive care facility of a general hospital where she was placed on oxygen via mask and bag. Since she could not start to be breast-fed at first, enteral feeding was performed with a naso-gastric tube. Multiple congenital anomalies were found, including microcephaly, micrognathia, ptosis of the eyelids, hypertelorism and epicanthal folds. A systolic murmur was heard at age of 3 days, and echocardiography-doppler revealed ventricular septum defect (VSD). She was treated with diuretic agents from the 14th day, setting a tentative goal of 120 ml・kg/day water quantity. A follow-up echocardiographic examination showed

Received 11/21/08; revised 11/4/10; accepted 11/17/10.
Requests for reprints: Koji Kashima, Department of Oral and Maxillofacial Surgery, Faculty of Medicine, University of Miyazaki, 5200 Kihara, Kiyotake-cho Miyazaki 889-1692, Japan, Phone: +81-985-85-3786, Fax: +81-985-85-7190

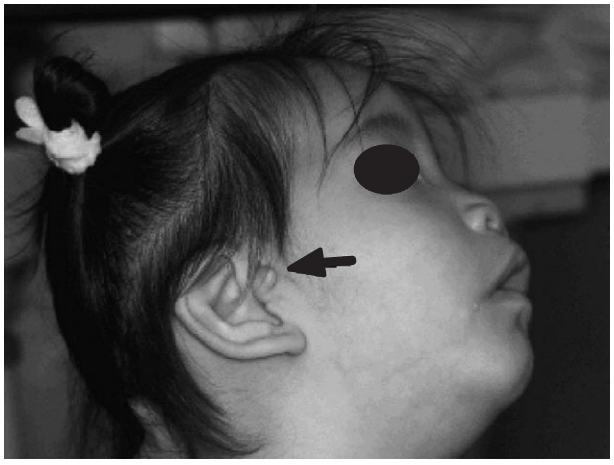

Fig. 1 Lateral view showing micrognathia and the preauricular tag on the right side at the age of 12 months.

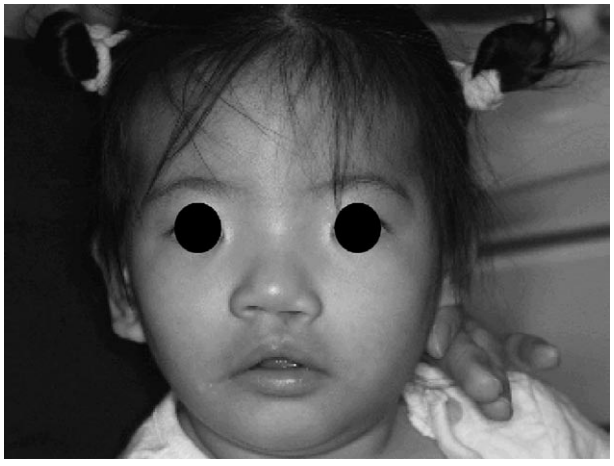

Fig. 2 Frontal view of the patient showing the cleft lip on the left side, ptosis of the eyelids and hypertelorism at the age of 12 months.

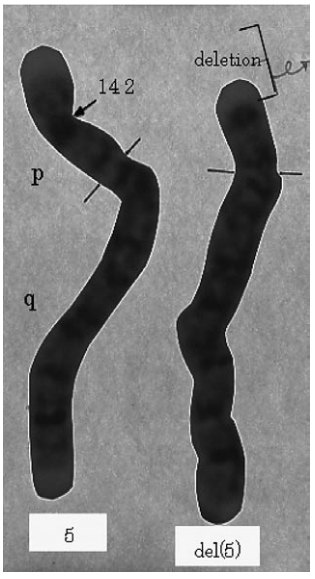

Fig. 3 Chromosomal findings showing the terminal deletion of chromosome 5 (46, XX, del(p14.2)ish del(5)).

improvement of heart function without any radical surgery after several weeks of custodial care. Magnetic resonance imaging (MRI) of the brain did not show any abnormalities. The patient remained hospitalized for 66 days and was referred after discharge to the Department of Pediatrics, University of Miyazaki Hospital, on October 10, 2001 for further examination. Physical evaluation showed growth retardation; the patient was 50.9 cm tall (mean: 58.3 cm), weighed 2.795 kg (mean: 5.440 kg), and had a head circumference of 33.2 cm (mean: 38.6 cm) and chest circumference of 31.1 cm (mean: 39.3 cm). Her cry was feeble and somewhat mew-like. Clinical examination also revealed an incomplete cleft lip on the left side and a preauricular tag on the right side, and micrognathia, ptosis of the eyelids, hypertelorism and epicanthal folds were confirmed (Fig. 1 and Fig. 2). A working diagnosis of cat cry syndrome was made, based on typical characteristics such as facial dysmorphisms in combination with the peculiar cat-like cry. Later, chromosome analysis with fluorescence in situ hybridization (FISH) analysis revealed the terminal deletion of chromosome 5 (46, XX, del(p14.2)ish del(5)(D5s23-)) (Fig. 3) and the final diagnosis of cat cry syndrome was made. After the patient's first visit, she suffered repeated upper airway inflammation, which was occasionally complicated with pneumonia. On July 4, 2002, she was referred to our department for treatment of the cleft lip to ameliorate the asymmetry of the lip. Repair of the cleft lip was carried out under general anesthesia on August 30, 2002 by the rotation-advancement method and concurrently with resection of the preauricular tag. Regarding intubation, a 4.5-mm spiral tube was inserted into the trachea without incident or difficulty, although the epiglottis was hypoplastic and hypotonic, and the larynx was narrow and hypoplastic. To prevent infective endocarditis, ampicillin was preoperatively given in doses of 500 mg, though the preoperative

echocardiogram revealed that the VSD spontaneously closed as the heart enlarged. The patient's postoperative course was favorable, and symmetry of the lip and nose and continuity of the muscle were achieved. She received speech therapy on an irregular basis at another institution from 3 to 6 years of age. When she was 6 years old, she started attending a special class, and when she was 7 years old she was transferred to us and has been receiving speech therapy and physiotherapy. Although her actual age is 8 years old at present, her receptive language abilities are at about a 21-month-old's level and expressive language abilities are less than those of a 12-month-old without any words. Also, self-care skills of toileting and feeding are at about 18 months, and motor skills of picking up and grasping objects are at about 18 and 21 months, respectively.

Discussion

Cat cry syndrome (cri-du-chat syndrome) is an uncommon condition first described by Lejeune in 1963. The incidence ranges from 1 : 15000 to 1 : 50000 in live-born infants[1]. The most frequent and characteristic craniofacial abnormalities include microcephaly, increased inner canthal distance, and a round face. Less frequent craniofacial abnormalities include downward slanting palpebral fissures, hypertelorism, epicanthal folds, posteriorly rotated pinnae, a broad nasal bridge with a prominent nasal root, and micrognathia[2]. Cleft lip/palate occurs in 8-15% of cases with this syndrome, and reports of this association in the literature are very scarce[3,4]. In the present case, the patient showed an incomplete cleft lip on the left side, micrognathia, ptosis of the eyelids, hypertelorism, epicanthal folds, and a preauricular tag on the right side.

It has been demonstrated that the partial deletion of the short arm of chromosome 5 is the cause of cat cry syndrome[5]. The introduction of molecular-cytogenic analysis has allowed the molecular and phenotype map of 5p to be defined, and has revealed large variability of the deletions. Mainardi *et al.* recently reported that in a total of 220 cases, there were 180 cases of 5p terminal deletions, 17 cases of familial translocations, 10 cases of *de novo* translocations, 7 cases of *de novo* interstitial deletions, 3 cases of mosaicism, one case of terminal deletions from a paternal inversion, one case of terminal deletions from a paternal mosaicism, and one case of ring chromosome[1]. The breakpoints range from p13 to p15.2, containing a large number of repetitive sequences that may account for its instability[6]. A genotype-phenotype correlation study confirmed the importance of deletion of the critical region for manifestation of clinical features in cat cry syndrome, and showed two critical regions, one for the typical cry in p15.3, and another for facial dysmorphisms in p15.2[7]. A more recent study showed a correlation between clinical severity and the size and type of deletion[6]. In the present case, terminal deletion of p14.2-pter was noted on chromosome number 5, and the conditions of this case appeared particularly severe.

It is generally accepted that there are two possible genetic explanations: mosaicism and translocation[5]. Support for the theory of translocation comes from the observation that an unbalanced translocation in one parent has been identified in approximately 15% of cases, while no specific support for the theory of mosaicism has yet been presented[5]. Chromosomal studies of the patient's parents were not carried out in the present case, since terminal deletion is attributed primarily to a non-inherited chromosomal abnormality and the patient's parents did not desire further examination.

Few studies have specifically examined speech, language, and communication skills in children with cat cry syndrome. Kristoffersen reported that progress in verbal development is particularly slow, and substitutions, omissions, and distortions are frequently seen in cat cry syndrome[8]. Moreover, a substantial number of individuals with cat cry syndrome do not develop spoken language at all[8]. Generally, typically developing children show signs of communicative behavior in the first few months after birth, and a prolonged period of babbling in the second half of the first year precedes the appearance of first words at around the first birthday. Also, they have acquired the basic skills necessary to communi-

cate efficiently with spoken language at around the age of 5[8]. In the present case, the receptive language abilities are at about a 21-month-old's level and expressive language abilities are less than those of a 12-month-old without any words, though her actual age is eight at present. A communication system has been recently developed that combines speech and sign called Sign Supported Communication as a part of educational support in patients with cat cry syndrome[9]. She is currently receiving speech therapy from our speech therapists.

A thorough understanding of the clinical problems of patients with cat cry syndrome is essential in order for oral surgeons to provide safe and effective treatment. Clinical issues to take into consideration in the case of cat cry syndrome are the following: 1) with a high incidence of congenital heart disease and chronic respiratory infection from aspiration, special care must be taken in treating patients with this syndrome, especially with reference to the extra risk which may be present when administering anesthetics and conducting surgery; 2) retrognathia and a high palate increase the complexity of intubation; 3) intubation may be further complicated due to abnormalities in the larynx and upper airway; and 4) the hypotonic muscle groups may show an accentuated response to muscle relaxants[10]. In the present case, attention to these issues allowed us to accomplish the repair of the lip safely under general anesthesia. First, a fiberoptic and nasal flexible laryngeal mask airway were prepared in the event of a difficult intubation. Actually, the intubation was uneventful without incident or difficulty in spite of the above-mentioned laryngeal abnormalities and micrognathia. Also, we gave her ampicillin to prevent infective endocarditis, not only postoperatively but also preoperatively.

Acknowledgements

The authors would like to express their appreciation to Dr. J. Takagi of the Department of Pediatrics, Ms. Y. Yamamoto of the Rehabilitation Unit in the University of Miyazaki Hospital, and Prof. S. Kasai at Kyushu University of Health and Welfare.

References

1) Mainardi P.C., Pastore G., Castronovo C., Godi M., Guala A., Tamiazzo S., Provera S., Pierluigi M., and Bricarelli F.D.: The natural history of Cri du Chat Syndrome. A report from the Italian Register. Eur J Med Genet 49: 363–383, 2006.
2) Gorlin R.J., Cohen M.M., Levins L.S.(eds).: Syndromes of the head and neck. 3rd ed. Oxford: Oxford University Press; 1990.
3) Niebuhr E.: The cri-du-chat syndrome. Hum Genet 42: 143–152, 1978.
4) Wilkins L.E., Brown J.A., Nance W.E., and Wolf B.: Linical heterogeneity in 80 home-reared children with cri-du-chat syndrome. J Pediatr 97: 528–533, 1980.
5) Ono K,. Ohashi Y., Nakano H., Togashi H., Kannari Y., and Isono S.: Partial monosomy 5p and partial trisomy 5q due to paternal pericentric inversion of chromosome 5. Jpn J Human Genet 38: 319–328, 1993.
6) Mainardi P.C., Perfumo C., Calì A., Coucourde G., Pastore G., Cavani S., Zara F., Overhauser J., Pierluigi M., and Bricarelli F.D.: Clinical and molecular characterisation of 80 patients with 5p deletion: genotype-phenotype correlation. J Med Genet 38: 151–158, 2001.
7) Gersh M., Goodart S.A., Pasztor L.M., Harris D.J., Weiss L., and Overhauser J.: Evidence for a distinct region causing a cat-like cry in patients with 5p deletions. Am J Hum Genet 56: 1404–1410, 1995.
8) Kristoffersen K.E.: Speech and language development in cri du chat syndrome: a critical review. Clin Linguist Phon 22: 443–457, 2008.
9) Erlenkamp S., and Kristoffersen K.E.: Sign communication in Cri du chat syndrome. J Commun Disord 43: 225–251, 2010.
10) Boraz R.A.: Cri-du-chat syndrome: dental considerations and report of a case. Spec Care Dentist 10: 13–15, 1990.