Clinical Notes

CATCH 22 Syndrome

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CATCH 22 syndrome is characterized by cardiac defects, abnormal facial features, thymic hypoplasia, cleft palate, and hypocalcemia. It results from a deletion within chromosome 22q11. This syndrome is not a simple disease. It includes DiGeorge syndrome, conotruncal anomaly face syndrome, and velocardiofacial syndrome. The authors report two cases of CATCH 22 syndrome.

Key Words: CATCH 22 syndrome, DiGeorge syndrome, conotruncal anomaly face syndrome, velocardiofacial syndrome.

CATCH 22 syndrome is characterized by cardiac defects, abnormal facial features, thymic hypoplasia, cleft palate, and hypocalcemia. It results from a deletion within chromosome 22q11. This syndrome is not a simple disease. It includes DiGeorge syndrome, conotruncal anomaly face syndrome, and velocardiofacial syndrome.

In DiGeorge’s original report, he focused on thymic hypoplasia and hypocalcemia.1 The clinical spectrum was widened to include heart defects and dysmorphic facial appearance. In 1976, Japanese cardiologists reported a group of children with hypertelorism, narrow palpebral fissures, small mouth, nasal speech, and outflow defects of the heart, and suggested the term conotruncal anomaly face.2 In 1978, Shprintzen et al.3,4 reported a group of children with overt or submucous clefting of the palate, cardiac abnormalities, and developmental delay. The dysmorphic features of all of these conditions show considerable overlap and deletions within chromosome 22q11. Wilson et al.5 proposed that an encompassing term for referring to the group as a whole should be CATCH 22.

CATCH 22 syndrome is a recent conception, and in the field of plastic surgery, there are few reports about this syndrome. We describe two recently encountered cases of CATCH 22 syndrome.

CASE REPORT

Case 1

A 33-month-old girl was referred by pediatricians to the Department of Plastic Surgery, Saitama Medical School for repair of a cleft palate. She was the first-born child of a healthy 36-year-old mother and 44-year-old father. She was delivered by cesarean section because of threatened hysterorrhexis after 39 weeks’ gestation and weighed 2,632 g. There was no pertinent family history.

She was referred to the Department of Pediatric Cardiology, Saitama Medical School because of a cardiac murmur and cyanosis on crying. Cleft palate was recognized. Nutrition was provided by tube feeding. An echocardiographic examination revealed ventricular septal defect with pulmonary hypertension. Plain chest radiography showed thymic hypoplasia. Results of standard laboratory studies indicated hypocalcemia. Hypocalcemia was corrected with ingestion of calcium. Episodes of unconsciousness occurred at 9 months of age. An electroencephalographic examination indicated infantile epilepsy. DNA was analyzed by fluorescent in situ hybridization. A deletion within chromosome 22q11 was identified. The results led to the diagnosis of CATCH 22 syndrome.

At 26 months of age, the patient underwent cardiovascular surgery, and the ventricular septal defect was repaired with a patch graft. At 29 months of age, the cleft palate was repaired by means of a push-back method.

On facial examination, the eyelids were single and bloated. The palpebral fissures were short and narrow. Lateral displacement of the inner canthi and...
hypertelorism were recognized. The root of the nose was wide and flat, and the mouth was small (Fig 1). The auricles were also abnormal. On the right side, the helix was folded, and the auricular lobule was small. On the left side, the ear had a prominent shape, and the auricular lobule was hypoplastic.

At age 33 months, she could not speak well, and mental retardation was suspected. Her physical development was normal.

**Case 2**

A baby girl with cleft palate was the first-born child of a healthy 27-year-old mother and 27-year-old father. She was delivered by precipitate labor after 37 weeks’ gestation and weighed 2,160 g. Her mother had had ventricular septal defect. There were no pertinent findings in the family history. Multiple anomalies of the cardiovascular were obvious at birth, and she was transferred to the neonatal intensive care unit of Saitama Medical School.

![Fig 1](image1)

**Fig 1** Facial appearance of case 1 patient.

![Fig 2](image2)

**Fig 2** Facial appearance of case 2 patient.

Evaluation of cardiac function by catheterization and echocardiography showed transposition of the great arteries, pulmonary stenosis, total anomalous pulmonary venous connection of cardiac type, major aortopulmonary collateral arteries, and an aberrant origin of the right subclavian artery. Plain chest radiography showed thymic hypoplasia. The results of standard laboratory studies revealed hypocalcemia, which was corrected by ingestion of calcium.

DNA was analyzed by fluorescent in situ hybridization. A deletion within chromosome 22q11 was identified. The results led to a diagnosis of CATCH 22 syndrome.

On facial examination, the eyelids were single and bloated. The palpebral fissures were short and narrow. The root of the nose was wide and flat, and the mouth was small (Fig 2). The ears were rotated posteriorly. On the right side, the ear had a prominent shape, the helix was folded, and the auricular lobule was small (Fig 3). On the left side, poorly de-
veloped helices with folded and the auricular lobule was hypoplastic (Fig 4). She had a cleft palate, and mental and physical development was delayed.

At 2 months of age, a team of cardiovascular surgeons performed a unifocalization operation of the right pulmonary arteries. At 5 months of age, a unifocalization operation of the left pulmonary arteries was performed. After surgery, she still required respiratory assistance. The child remained under hospital care and died at 13 months of age.

DISCUSSION

CATCH 22 syndrome includes DiGeorge syndrome, velocardiofacial syndrome, and conotruncal anomaly face syndrome. These syndromes have pathologic similarities and are associated with deletions within chromosome 22q11.

DiGeorge syndrome is a developmental field defect of the third and fourth pharyngeal pouches. It comprises thymic hypoplasia or aplasia, hypoplastic or absent parathyroid glands, outflow tract defects of the heart, and facial abnormalities. A hypoplastic mandible, defective ears, and a short philtrum are also features of this disorder. Common cardiac defects include a right aortic arch, tetralogy of Fallot, transposition of the great arteries, transection of the aortic arch, and ventricular septal defect. Cytogenetic studies of patients with DiGeorge syndrome have demonstrated unbalanced translocations with monosomy 22pterq and visible interstitial deletions of 22q11.

Velocardiofacial syndrome is an autosomal dominant disorder with cleft palate, cardiovascular anomalies, learning disabilities, speech and language impairment, and typical facial features. Some patients also have neonatal hypocalcemia and decreased lymphoid tissue. Clefting occurs in the secondary palate and may present as an overt or submucous cleft. Patients have typical faces with a prominent nose, a broad nasal root, narrow palpe-
bral fissures, and retrognathia. Cardiac defects occur, the most common being ventricular septal defect with or without a right aortic arch. Many patients have some form of learning or behavioral disability, with mild mental retardation. Patients with velocardiofacial syndrome have molecular evidence of interstitial deletions within 22q11.

The conotruncal anomaly face syndrome is characterized by a typical face with hypertelorism, lateral displacement of the inner canthi, short palpebral fissures, bleated eyelids, a flat nasal bridge, minor ear lobe anomalies, nasal voice, mild mental retardation, and cardiac anomalies. The main cardiovascular defects seen in patients with conotruncal anomaly face syndrome are cardiac outflow tract defects or aortic arch anomalies, such as tetralogy of Fallot associated with pulmonary atresia, and major aortico-pulmonary collateral arteries. Neural crest cells also migrate to the cardiac neural crest. These problems may result in neural crest interaction. Some patients have tetany and thymus defects or hypoplasia. The conotruncal anomaly face syndrome is associated with a deletion within chromosome 22q11.

DiGeorge syndrome, velocardiofacial syndrome, and conotruncal anomaly face syndrome have pathologic similarities. These similarities support the hypothesis that DiGeorge syndrome, velocardiofacial syndrome, and conotruncal anomaly face syndrome are overlapping phenotypes due to the same deletions of 22q11. Common features of these three syndromes are partial monosomy, interstitial deletion, and hemizygosity caused by deletions of 22q11. Wilson et al. proposed that each phenotype should retain its established name, with CATCH 22 being used as an encompassing term referring to the group as a whole.

The conotruncus, thymus, and parathyroid glands have a common embryonic origin in the third and forth pharyngeal pouches at about 4 weeks of gestation. Abnormalities in the development of these structures resulting in CATCH 22 may suggest a defect in neural crest interaction. Cardiac outflow tract anomalies or aortic arch anomalies of CATCH 22 could reflect serious developmental problems in the cardiac neural crest. These problems may result from malformation of the premigratory or early migratory cardiac neural crest. Neural crest cells also give rise to the facial apparatus. Therefore, abnormalities related to CATCH 22 could arise secondarily to disruption of the contribution of the neural crest to development.

MacKenzie-Stepner et al. have described abnormal carotid arteries in patients with velocardiofacial syndrome. Internal carotid arteries of unusual size and tortuosity are found in patients with velocardiofacial syndrome. Similar abnormalities may occur in CATCH 22 syndrome. Malformations of the cardiovascular system are frequently seen in CATCH 22 syndrome, and abnormalities of the aortic arch are found in many patients. Abnormalities of the cerebrovascular system, such as tortuosity of the carotid arteries, appear to be rare. However, the possibility of abnormally located internal carotid arteries has important consequences for CATCH 22 syndrome patients who require pharyngeal flap surgery. The surgeon must always be alert to this possibility.

REFERENCES