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Editorial Board Member of *World Journal of Clinical Cases*, Arunchai Chang, MD, Assistant Professor, Lecturer, Staff Physician, Division of Gastroenterology, Department of Internal Medicine, Hatyai Hospital, Hatyai 90110, Songkhla, Thailand. busmdu58@gmail.com

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# Ipsilateral hemifacial microsomia with dextrocardia and pulmonary hypoplasia: A case report

Rui Guo, Shi-Hi Chang, Bing-Qing Wang, Qing-Guo Zhang

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**Rui Guo, Shi-Hi Chang, Bing-Qing Wang, Qing-Guo Zhang**, Department of Ear Reconstruction, Plastic Surgery Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100000, China

**Corresponding author:** Bing-Qing Wang, MD, Attending Doctor, Department of Ear Reconstruction, Plastic Surgery Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, No. 33 Badachu Road, Shijingshan District, Beijing, 100000, China. [plasticsurgern114@163.com](mailto:plasticsurgern114@163.com)

## Abstract

### BACKGROUND

Hemifacial microsomia (HFM) is a rare congenital malformation characterized by a combination of various anomalies, including the face, ears, eyes, and vertebrae. Prenatal diagnosis for HFM is possible, and quite accurate ultrasound can detect obvious defects. The etiology is still unknown, although some hypotheses have been proposed, including gene mutation, chromosome anomaly, and environmental risk factors. However, there are few reports of pulmonary hypoplasia and dextrocardia in HFM.

### CASE SUMMARY

A 2-year-old boy presented to the ear reconstruction department of our hospital complaining of deviation of the face to the right side and auricular anomaly. Physical examination revealed facial asymmetry, preauricular skin tags, and concha-type microtia with stricture of the external auditory canal on the right side. Head magnetic resonance imaging showed bilateral semicircular canal dysplasia and bilateral internal auditory canals stenosis. Audiometric examination showed bilateral severe sensorineural hearing loss. Chest radiography and computed tomography showed dextrocardia and right pulmonary hypoplasia.

### CONCLUSION

This case presented a rare finding and an unusual association of 3 malformations, ipsilateral HFM, pulmonary agenesis, and dextrocardia.

**Key Words:** Hemifacial microsomia; Oculoauriculovertebral spectrum; Dextrocardia; Pulmonary hypoplasia; Congenital anomaly; Case report

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**Core Tip:** Hemifacial microsomia (HFM) is a rare congenital malformation characterized by a combination of various anomalies including face, ears, eyes, and vertebrae. We present a rare case of ipsilateral HFM with dextrocardia and pulmonary hypoplasia. Those malformations may compose a laterality syndrome or just an extension of an expanded spectrum of HFM.

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## INTRODUCTION

Hemifacial microsomia (HFM) is a rare multi-system congenital malformation caused by hypoplasia of the first and second branchial arches[1]. The incidence reported ranges from 1/3500 to 1/5600 live births [2]. It is characterized by dysplasia of the mandible and auricle, resulting in facial asymmetry[3]. Other terms used for the description are craniofacial microsomia, oculoauriculovertebral spectrum, and goldenhar syndrome[1]. The anomalies associated with HFM include craniofacial and extracranial manifestations, such as microtia, facial asymmetry, cardiac malformations. No specific genes are associated with this syndrome, although chromosomal anomalies have been observed, such as del (22q), dup (22q) and trisomy 22[1]. Previous studies have also found that environmental factors are relevant, such as the use of retinoic acid during pregnancy, gestational diabetes mellitus, and multiple gestations [2]. In developmental biology, the branchial arches related to auricular development are evident in the 5<sup>th</sup> week of pregnancy, the respiratory system develops from the foregut at 4-7 wk of pregnancy, and the heart is the earliest organ formed during embryonic development[4,5]. Previous studies have proved that partial heart and auricle derived from neural crest cells (NCCs) and disturbance with their growth and migration can lead to microtia and cardiac anomalies[6]. Co-occurrence of malformations of the lungs, heart and auricle indicates a disturbance at the same stage of embryonic development.

Here, we describe a case of ipsilateral HFM with dextrocardia and pulmonary hypoplasia, and also conducted a literature review to have a comprehensive understanding of this syndrome. Pulmonary hypoplasia with dextrocardia in HFM has not been reported before in China. The present case adds to the variable clinical presentation of HFM and suggests a new association.

## CASE PRESENTATION

### **Chief complaints**

A 2-year-old Chinese boy, born to nonconsanguineous parents, presented to plastic surgery hospital with complaints of face deviation to the right side and abnormal appearance of the right ear.

### **History of present illness**

After birth, an abnormal appearance of the right ear and facial asymmetry was found in this child. The facial deviation gradually aggravated over time.

### **Personal and family history**

Because the patients lived in a rural area and lacked medical knowledge, they did not have a regular prenatal examination, such as ultrasound. The patient's birth history was uneventful, and there was no family history of congenital malformations or mental retardation. Developmental milestones were normal. The child also had a bilateral hearing impairment and speech retardation.

### **Physical examination**

Physical examination revealed facial asymmetry (face and mouth deviated to the right side), preauricular skin tags, and concha-type microtia with stricture of the external auditory canal on the right side (Figure 1). During chest auscultation, no breath sounds could be heard on the right hemithorax, but normal heart sounds could be heard. The other examinations were unremarkable.

### **Imaging examinations**

Head magnetic resonance imaging showed bilateral semicircular canal dysplasia and bilateral internal auditory canals stenosis. Chest radiography showed dextrocardia and single left lung (Figure 2), and chest computed tomography confirmed that the thoracic aorta was located on the right front side of the thoracic vertebrae, right pulmonary hypoplasia, and the left pulmonary artery arose directly from the



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**Figure 1 Physical examination revealed facial asymmetry.** A: Right-sided concha-type microtia with preauricular skin tags and facial asymmetry; B: The contour of the left-sided auricle is basically normal.



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**Figure 2 X-ray chest showing a homogenous opacity occupying most of the right hemithorax.**

right ventricle (Figure 3). Echocardiography also showed situs solitus, dextrocardia, ectopic origin of the left pulmonary artery, and moderate regurgitation of mitral, tricuspid, and aortic valves. Audiometric examination showed bilateral severe sensorineural hearing loss.

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## FINAL DIAGNOSIS

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Ipsilateral HFM with dextrocardia and pulmonary hypoplasia.

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## TREATMENT

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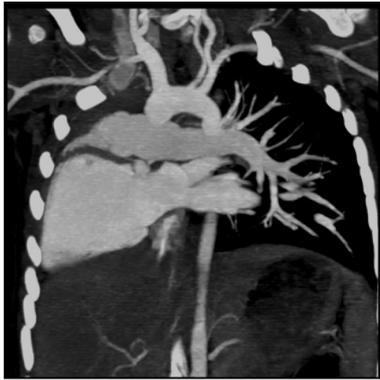
The patient was too young to receive surgical treatment for auricular malformation, so we only provided diagnosis and consultation in the outpatient department. We suggested the parents feed the child scientifically, provide diversified and nutritious foods (cereals, fish, meat, vegetables and fruits, *etc.*), and cultivate the child's habit of regular diet. Moreover, the child could go to the otolaryngology department to improve hearing, such as wearing hearing aids. When the child is 6-year-old with 120 cm in height, he can come to the hospital again for a comprehensive evaluation to decide whether to perform the auricle reconstruction. In addition, no genetic testing was conducted on this patient, which was unavailable in our center, and his parents could not afford it.

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## OUTCOME AND FOLLOW-UP

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Periodic follow-ups were conducted every 6 mo to monitor progress of the deformity. The patient's condition was stable during the 10 months' follow-up.



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**Figure 3** Chest computed tomography showing the thoracic aorta located on the right front side of the thoracic vertebrae, right pulmonary hypoplasia, and the left pulmonary artery arising directly from the right ventricle.

## DISCUSSION

HFM is a heterogeneous, multifactorial congenital disease. Its diagnosis is mainly clinical, while radiographic examinations help to support the clinical diagnosis. Prenatal diagnosis is possible, and accurate ultrasound can detect obvious defects. From a developmental perspective, the involved mandible and ear that embryologically originated from the first and second branchial arches suggest that this condition may be due to the maldevelopment of these branchial arches during the 1<sup>th</sup> week of gestation. The vascular disruption theory and the NCCs disturbance theory are pathogenetic hypotheses that might explain the malformations correlated with HFM[7]. Primitive lungs generally form in the 4<sup>th</sup> week of pregnancy. At this time, pulmonary hypoplasia may occur, accompanied by other ipsilateral congenital anomalies, such as cardiovascular system, gastrointestinal system, central nervous system, and musculoskeletal system[8]. As a rare congenital anomaly, right pulmonary hypoplasia can lead to secondary dextrocardia in situs solitus in scimitar syndrome[9]. The heart is the earliest organ formed during embryonic development. Cardiac malformations with pulmonary hypoplasia include Ebstein's anomaly, tetralogy of Fallot, pulmonary stenosis, and right heart dysplasia[10,11]. Previous studies have found that pulmonary hypoplasia and cardiovascular anomalies are most commonly associated with minor auricle deformity, while this patient suffered from concha-type microtia[12,13].

A comprehensive search of PubMed and Embase was performed to identify studies using MeSH terms and keywords "HFM" or "oculo-auriculo-vertebral syndrome" or "Goldenhar Syndrome" or "microtia". Only three cases[14-16] of HFM combined with pulmonary hypoplasia and dextrocardia were retrieved and reviewed (Table 1). Two patients were male with an ipsilateral malformation (right-side involvement), and one case was female with left HFM. Our patient was also male and had a right-side involvement. Male and right-side predominance has been observed in HFM. One hypothesis is the establishment of left-right asymmetry before organogenesis, resulting in subtle differences in the morphology of the left and right sides of the embryo. In rat embryos, the right-side predominance may be related to the observation of delayed maturation of the right mitochondria, resulting in decreased energy reserves and increased tissue damage during hypoxia[14]. In addition, male sex hormones might reduce the mitochondrial respiration rate and increase the sensitivity to chemical hypoxia[17]. Previous studies have confirmed that some genes are expressed differently on both sides of developing vertebrate embryos, leading to differential susceptibility of specific bilateral structures to teratogens during organogenesis. Furthermore, some human genes related to laterality are located on sex chromosomes, indicating a high correlation between male sex and laterality patterns[17].

## CONCLUSION

The contribution of the present case report lies in discovering a rare finding and an unusual association of 3 malformations: (1) Ipsilateral HFM; (2) pulmonary agenesis; and (3) dextrocardia. Those malformations may compose a laterality syndrome or an extension of an expanded spectrum of HFM. The etiology and epidemiology of pulmonary and cardiovascular anomalies in HFM are still unclear and demand a further investigation to explore relevant pathogenic mechanisms.

**Table 1 Clinical features of hemifacial microsomia patients with pulmonary hypoplasia and dextrocardia reported in this study and literature**

Clinical features	This study	Maymon <i>et al</i> [14] (2001)	Fan <i>et al</i> [15] (2015)	Chaudhary <i>et al</i> [16] (2017)
Sex	M	M	M	F
Age of examination	2 yr	20 wk gestation	3 yr	7 yr
Microtia				
Side	R	R	R	L
Type	Concha-type	Lobule-type	Concha-type	Concha-type
EAM stenotic/atresia	+	NA	+	-
Facial asymmetry	+	NA	+	+
Preauricular tags	+	+	-	+
Macromastia	-	NA	-	+
Hearing impairment	+	NA	+	-
Epibulbar dermoid	-	NA	-	+
Pulmonary hypoplasia				
Side	R	R	R	R
Cardiovascular anomalies				
Atrial septal defect	-	-	+	-
Dextrocardia	+	+	+	+
Heart valve disease	+	-	-	+
Others	Ectopic origin of left pulmonary artery	Main pulmonary artery dilated	Hepatic vein drainage directly into right atrium	Pulmonary stenosis
Inguinal hernia	-	NA	+	-
Treatment	NA	Termination of the pregnancy	Indirect inguinal hernia repair + Repair of atrial septal defect	NA

“-”: Not reported; “+”: Reported; F: Female; M: Male; NA: Not available; L: Left; R: Right; EAM: External auditory meatus.

## FOOTNOTES

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**Country/Territory of origin:** China

**ORCID number:** Rui Guo 0000-0002-6878-2788; Shi-Hi Chang 0000-0001-9658-305X; Bing-Qing Wang 0000-0002-8836-3759; Qing-Guo Zhang 0000-0002-9044-5526.

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