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Case report

Crossed idiopathic hemihypertrophy diagnosed incidentally in an adolescent with voice disorders: A case report

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ABSTRACT

Background: Hemihypertrophy (HH) is a rare congenital malformation usually recognized at birth. It is often diagnosed due to impaired aesthetics and mobility caused by asymmetry of the face, body, or limbs. Some patients are diagnosed due to the presence of tumors and mental abnormalities.

Case presentation: A 14-year-old boy with hoarseness since infancy and progressively increasing with age. Laryngoscopy and CT of the larynx suggested bilateral asymmetry of the laryngeal structures, and voice analysis suggested severe voice disorders. The boy had no history of trauma or other medical conditions, but had physical asymmetry since birth, which coincided with the laryngeal asymmetry. After a detailed examination and evaluation, we considered that his voice disorders were unexpectedly caused by crossed idiopathic HH. Since the boy in his growth spurts is not a candidate for surgery, we implemented individualized voice correction therapy. After practicing, the boy's voice disorders were significantly relieved.

Conclusion: Congenital HH can cause asymmetrical development of the larynx, which leads to voice disorders. Voice correction therapy is an effective treatment for patients unsuitable for surgery.

1. Introduction

Voice disorders are common clinical conditions in otorhinolaryngology. They are usually caused by inflammation of the vocal folds, vocal nodules or polyps, laryngeal tumors, or vocal motor disorders such as vocal fold paralysis and cricoid dislocation. A 14-year-old boy with hoarseness since childhood, but his voice disorders were not due to any of the above reasons. During the clinic visit, we inadvertently found that the patient was born with bilateral facial and limb asymmetry, which seemed to reasonably explain the presence of voice disorders. After a detailed examination and evaluation, we considered that the patient's voice disorders were unexpectedly caused by Idiopathic Hemihypertrophy (IH), an extremely rare congenital disorder.

Hemihypertrophy (HH) is a rare congenital abnormality characterized by asymmetric growth of the body [1]. Approximately 50 % of HH patients have skin abnormalities [2], which may be also associated with mental retardation, genitourinary abnormalities, and carcinogenic potential [3]. In this case, congenital HH results in abnormal laryngeal development, which affects his voice quality. The boy exhibited atypical manifestations that diverged from the common symptoms of HH, expanding our understanding of the disease.

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To our knowledge, this is the first described case of voice disorders caused by HH.

2. Case presentation

A 14-year-old boy presented hoarseness beginning in infancy and progressively increasing with age, especially after puberty. With a decreased pitch, hoarseness increases significantly and pronunciation fatigue occurs during the past 6 months. Since his childhood, the boy had visited several hospitals for voice disorders. He was diagnosed with vocal cord inflammation and vocal cord closure insufficiency and was treated with oral anti-inflammatory medication and nebulized inhalation, but the results were unsatisfactory.

He reported no history of medical or trauma but was found to be physically asymmetrical from birth, which did not affect his growth, development, movement, or intelligence, it was not much of a concern. On examination, we found a soft protuberance on the right nasal flank (Fig. 1A), thicker hair on the right sideburn (Fig. 1B), the left hand is 1 cm longer than the right, and a bony protuberance at the greater pisiform, shortened thumb and nails on the right hand (Fig. 1C), thicker hair on the right foot, and deformed second and third toes (Fig. 1D). Measurements showed that the left upper limb was thicker and longer, and the right lower limb was thicker and longer (Table 1).

Stroboscopic laryngoscopy shows that the mucosal surfaces of the vocal cords bilaterally are smooth but asymmetrical in length. The right vocal cord is significantly shorter, more relaxed, and has less tension. From a vertical perspective, the vocal cords are asymmetrical, with the right side noticeably higher. The aryepiglottic folds were bilaterally asymmetrical, with the right aryepiglottic fold being hypertrophic, invaginated, and fixed. The left aryepiglottic fold was mobile and showed a gap when the vocal folds were closed. The vibration exhibits an asymmetric and non-periodic state when the vocal cords close, with reduced mucosal waves and amplitude of the vocal folds, and no supraglottic activity. A contact ulcer-like change on the mucosa behind the left vocal cord (Fig. 2A and B, Supplementary video). Laryngeal CT showed an abnormal morphology of the right arytenoid and cricoid cartilages and the absence of the left arytenoid cartilage (Fig. 2C and D). Both subjective and objective assessments of the voice showed a high degree of voice disorder. The grade, roughness, breathiness, asthenia, strain (GRBAS) scale score was G3R3B3A2S1, voice handicap index (VHI) score was 73; maximum vocal time (MPT) was 7.9 s; fundamental frequency (F0) was 72.3Hz; fundamental frequency perturbation (jitter) was 9.43 %; and dysphonia severity index (DSI) was −8.91 %.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.heliyon.2024.e33915

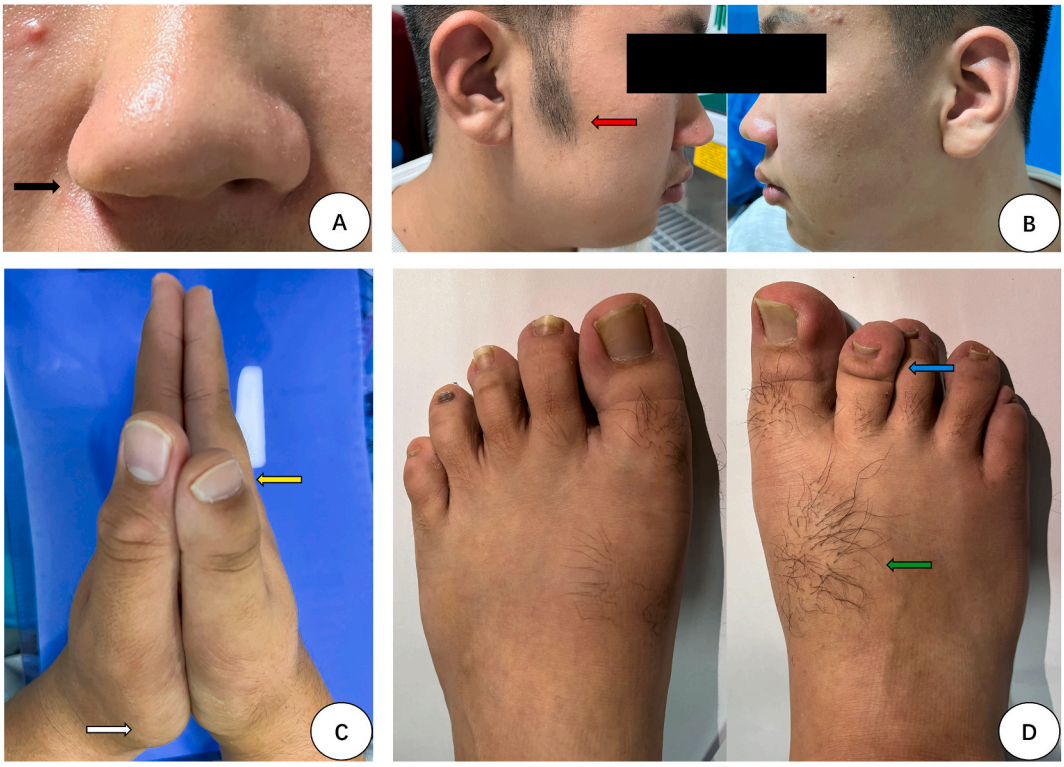

Fig. 1. Bilateral comparison of the face and extremities.
A. Comparison of the bilateral nasal flanks (the black arrow indicates the protuberance of the right nasal flank). B. Comparison of the bilateral face (the red arrows indicate the thick hair on the right sideburns). C. Comparison of both hands (the yellow arrows indicate the shorter thumb and shortened nail on the right; the white arrows indicate the bony protuberance of the left hand at the greater pisiform). D. Comparison of both feet (the blue arrow indicates the deformed toe; the green arrow indicates dense hair on the dorsum of the right foot). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Measurement data of the bilateral limbs.

Position		Right (cm)	Left (cm)
Upper limbs	Circumference of the upper arm (10 cm above elbow)	28.1	29.5
	Circumference of the elbow	26.2	28.0
	Circumference of the forearm (10 cm below elbow)	26.3	27.5
	Circumference of the wrist	17.5	18.0
	Circumference of the palm	21.5	22.5
	Length of the upper arm (from shoulder to elbow)	33.0	34.0
	Length of the forearm (from elbow to wrist)	23.1	24.0
	Length of the palm	18.1	19.0
Lower limbs	Circumference of the thigh (10 cm above knee)	54.0	50.3
	Circumference of the knee	44.0	41.2
	Circumference of the calf (10 cm below knee)	44.1	40.0
	Circumference of the ankle	25.0	23.2
	Circumference of the foot	25.0	24.0
	Length of the thigh (from waist to popliteal fossa)	50.2	50.0
	Length of the lower leg (from popliteal fossa to heel)	43.5	44.0
	Length of the foot	26.0	24.5

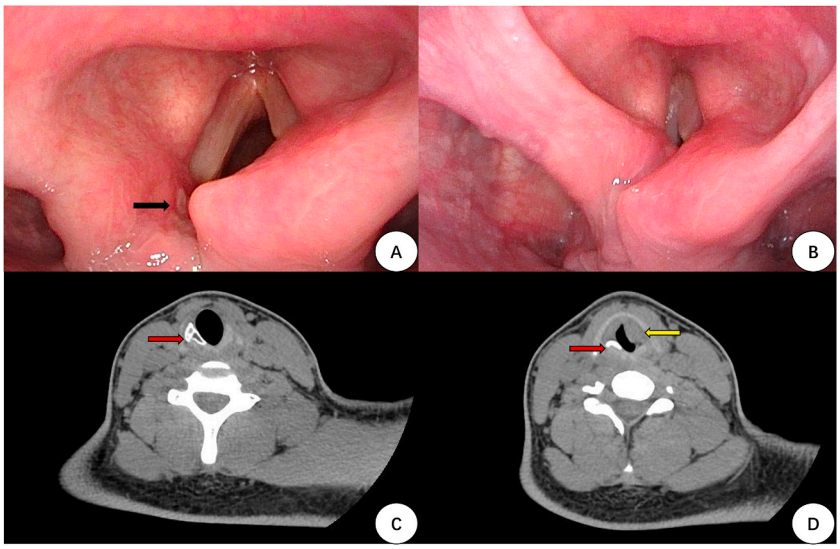

Fig. 2. Laryngoscopy and CT of the larynx.
A, B. Laryngoscopy (A: open phase of the vocal folds, B: closed phase of the vocal folds; the black arrow indicates the contact ulcer). C, D. CT of the larynx (the red arrow indicates abnormal development of the right arytenoid cartilage; the yellow arrow indicates the collapsed left vocal cord). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

The asymmetry of the body coincided with the asymmetry of the laryngeal structures, and after reviewing a large body of literature, we considered that the boy was consistent with HH. Patients with HH may sometimes have comorbid tumors and neurological disorders and therefore undergo relevant investigations. Ultrasound of the urinary tract showed a 0.8 cm separation of the left renal sinus. CT of the abdomen was unremarkable. Neurological examination showed symmetrical findings for limb power and muscle strength, bilaterally symmetrical nerve reflexes, and negative results for Babinski's and Kernig's signs.

A comprehensive analysis of symptoms, signs, and ancillary findings indicated crossed IH. The voice disorders were attributed to

Table 2
Comparison data of voice assessment before and after treatment.

Voice Assessment	Parameters	Before treatment	After treatment
Subjective assessment	GRBAS score	G3R3B3A2S1	G2R2B2A1S1
	VHI	73	33
Objective assessment	MPT (s)	7.9	11.6
	F0 (Hz)	72.3	106.8
	jitter (%)	9.43	6.01
	DSI (%)	−8.91	−6.33

congenital HH, which caused asymmetrical laryngeal development resulting in asymmetrical vocal fold movements and uncoordinated laryngeal muscle movements during vocalization and eventual hoarseness and vocal fatigue. This boy is in his growth spurt and is not a good candidate for surgical intervention. Therefore, we adopted a four-step voice correction treatment program for voice treatment, which included relaxation training, breathing training, articulation training, and resonance training. Under the guidance of the professional voice therapist, the patient mastered the technique and practiced it. After 2 months of training, his vocal fatigue had improved significantly and the hoarseness had reduced slightly. GRBAS score: G2R2B2A1S1; VHI: 33; MPT: 11.6 s; F0: 106.8 Hz; jitter: 6.01 %; DSI: −6.33 %. Both subjective and objective assessments of voice suggested improvement in symptoms (Table 2). During more than one year of follow-up, the boy's voice condition was stable with slight hoarseness and no vocal fatigue.

Statement: Informed consent was obtained from the patient and his parents for the publication of his case and images.

3. Discussion

The boy presents with voice disorders that cannot be explained by common diseases and were refractory to conventional treatment. The history and findings of the laryngoscopy did not adequately explain the reasons for the appearance of the voice problem. The asymmetry of the laryngeal structure and the contact ulcer of the laryngeal mucosa were not explained until the inadvertent discovery of the asymmetry of his face and extremities. Hemihypertrophy (HH) was eventually diagnosed as the real cause of the voice disorders.

HH is a rare congenital anomaly characterized by asymmetric growth of the limbs, trunk, face, or half of the entire body with or without visceral hypertrophy, which includes both soft tissue and bone [1] and an extremely low incidence of approximately 1/13,000–1/86,000 [4]. HH can exist independently as IH or as a part of certain congenital anomaly syndromes, including Beckwith-Wiedemann Syndrome, Klippel–Trenaunay–Weber syndrome, and Proteus syndrome [5]. The exact etiology of HH remains unknown; it can be categorized as primary, which shows an asymmetry between the right and left sides of systemic organs, probably due to the fertilized egg dividing into two cells of different sizes, or secondary, which may show hemangiomas or local changes in the circulation or lymphatic system on the same side [6]. The pathological mechanism underlying HH involves an increased rate of proliferation of mast tissue cells rather than increased cell volume [4]. The pathogenesis of HH may be related to genetic defects such as paternal uniparental disomy 11p15 defects, KGNQ1OT1 demethylation, LIT1, and H19 hypermethylation [7].

In patients with HH, birth weight is normal for gestational age and hypertrophy may occur on either side, although it occurs more commonly on the right side [8]. Hypertrophy may be global or segmental, unilateral or crossed [5], with a variable degree of asymmetry so that mild cases may be overlooked and the asymmetry may become more or less pronounced with age [9]. Approximately 50 % of patients present with associated skin abnormalities, which may be located on the hypertrophic side or the contralateral side, including edema, ichthyosis, coarse hair, hirsutism, nevi, hemangiomas, capillary dilation, venous tortuosity, celiac spots, dystrophic nails, and slight changes in skin pattern [2]. HH has also been associated with mild mental retardation, genitourinary abnormalities, and carcinogenic potential [3]. The incidence of abdominal tumors in children with HH is higher than the baseline incidence in the general population [10], particularly in patients with HH-related syndromes, who are susceptible to embryonal tumors such as nephroblastoma, hepatoblastoma, neuroblastoma, and nephroblastoma in childhood and adolescence [7]. Therefore, initial investigations following a diagnosis of HH should include a search for associated tumors. Recommendations for tumor surveillance include alpha-fetoprotein tests every 6–12 weeks until 4 years of age and abdominal and renal ultrasound every 6 months until 8 years of age to detect the most common tumors, namely Wilms' tumor and hepatoblastoma [11]. HH is primarily diagnosed based on clinical manifestations. Skeletal limb radiography, abdominal ultrasound, and cranial CT can characterize the development and involvement of bones and organs. Patients without tumors or mental abnormalities do not usually require treatment. Surgical correction is only indicated when the deformity seriously affects the quality of life, but surgery is not appropriate during the growth spurt [12].

In this case report, the boy conceived naturally, rather than through other methods such as in vitro fertilization or a surrogate mother. He was born naturally at full term and weighed 3400 g at birth. After birth, he was found to have a protruding right nasal wing, asymmetrical hair growth on the face, and bilateral limbs that were not equally thick, which did not affect respiratory function and limb movement, and therefore did not receive treatment. The boy presented with a hoarse voice in infancy and a right toe deformity in childhood, and the bilateral limb asymmetry became more pronounced with age. Still, his mental and physical development showed a normal trajectory. In adolescence, the patient presented to the ENT department with a marked aggravation in voice symptoms. He was 14 years old at the time of presentation, which is beyond the age at which embryonic tumors occur most commonly. Abdominal tumors that often occur in HH-related syndromes were not detected on examination and asymmetries presented crossness, so the findings were more consistent with crossed IH. No other family members of the boy have suffered from similar diseases, and there is no history of other genetic diseases. However, unfortunately, due to the concerns of the patient's parents, no genetic test results were obtained.

Embryologically, the larynx originates from the endoderm and mesoderm. At embryonic day 32, the arytenoid cartilage forms an arytenoid protrusion on each side between the sixth pharyngeal arch. At embryonic day 57, most muscles of the larynx are largely formed. About embryonic weeks 9–12, the vocal cords begin to develop. By the end of the embryonic week 12, the arytenoid cartilage is completely chondrogenic [13]. Asymmetrical development of the arytenoid cartilage may cause asymmetrical development of the laryngeal muscles and vocal folds as well. During vocalization, the movements of the bilateral arytenoid folds and the bilateral vocal folds are asymmetrical and the vocal folds are not fully closed; therefore, the vocal folds do not produce normal mucosal waves when they vibrate. Stroboscopic laryngoscopy, the examination of choice for evaluating voice disorders, shows details of the laryngeal structures as well as the state of the mucosal wave vibration during vocal fold movement. These manifestations in the boy were precisely described in detail in the stroboscopic laryngoscopy findings.

The boy is currently undergoing a period of vocal change in which the larynx, particularly the vocal folds and laryngeal muscles,

change considerably with changes in hormone levels. During this process, the thyroid cartilage enlarges rapidly and the vocal folds become wider, thicker, and longer, changing the amplitude from small to large, and frequency from fast to slow, and reducing the pitch. This process may cause coarseness of the voice, hoarseness, or an involuntary, recurrent, and sudden change in pitch [14]. These symptoms may be attributed to inadequate control of the laryngeal muscles, uncoordinated movements of the laryngeal muscles, or abnormal movements of the laryngeal joint, which significantly increase hoarseness than before puberty. From the results of the patient's voice analysis, the MPT was significantly shortened, which to some extent reflected the poor degree of vocal fold closure; the obvious abnormalities of F0 and Jitter showed a high degree of hoarseness; and the DSI was only −8.91 %, indicating a very severe voice disorder, and these parameters of acoustic analysis were consistent with the patient's current symptoms and signs.

In the present case, we have tried a four-step training method for voice correction treatment [15]. The treatment aimed to increase the strength of the vocal folds while improving the balance of the laryngeal muscles. To this end, an individualized treatment program incorporating laryngeal massage, laryngeal muscle relaxation training, abdominal breathing training, "dog panting" training, /hou/sound training, yawning and sighing pronunciation, semi-swallowing "boom" sounds, bubble sounds, interrupted breathing training, breathing and articulation coordination, coughing and grunting training, and articulatory strength training was developed [15]. With the guidance of the voice therapist and the diligent practice of the boy, his articulation fatigue was reduced significantly and hoarseness improved. In comparison with the before voice correction treatment, the MPT was 3.7 s longer, the F0 was significantly higher, the jitter value was lower, and the DSI was improved. Furthermore, the GRBAS and VHI scores indicated subjective improvements in the voice disorders, highlighting the therapeutic effects of the voice correction treatment.

4. Conclusion

The present case highlights the importance of not ignoring the systemic condition of the patient and considering the possibility of some rare diseases in cases of voice disorders that cannot be explained by conventional etiology. Congenital HH can cause asymmetrical development of the bone, cartilage, muscle, and other structures of the larynx, which leads to asymmetrical vocal movements and ultimately to voice disorders. Voice correction therapy is an effective treatment for patients unsuitable for surgery.

Data availability statement

All relevant data that support the findings of this study are available from the corresponding author upon request.

Care statement

The complete CARE checklist has been attached, of which 10d and 12 are not applicable and no patient perspectives have been retained.

Ethics statement

All authors have no example conflicts of interest to disclose.

CRediT authorship contribution statement

Lei Dong: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Shasha Kang:** Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation. **Xiumei Chen:** Writing – review & editing, Project administration, Formal analysis. **Xicheng Song:** Writing – review & editing, Supervision, Project administration, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e33915.

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