

Hearing, Voice and Speech Disorders in 10-Year-Old-Boy with Facio-Scapulo-Humeral Dystrophy (FSHD) – Case Study

Emilia Duchnowska¹ , Bożena Koszyła-Hojna¹, Maciej Zdrojkowski¹, Sarah Burton-Jones² , Wojciech Kułak³

¹Department of Clinical Phonoaudiology and Speech Therapy, Medical University of Białystok, Białystok, Poland; ²South West Genomic Laboratory Hub, Bristol, England, UK; ³Department of Paediatric Rehabilitation, Medical University of Białystok, Białystok, Poland

Correspondence: Emilia Duchnowska, Department of Clinical Phonoaudiology and Speech Therapy, Medical University of Białystok, ul. Szpitalna 37, Białystok, 15-270, Poland, Tel +48 603 330 294, Email emilia.duchnowska@umb.edu.pl

Purpose: The aim of the study was to evaluate hearing, voice, and speech in 10-year-old boy with facio-scapulo-humeral dystrophy (FSHD).

Patients and Methods: Hearing, voice, and speech were assessed in a 10-year-old boy with FSHD due to scarcity of detailed audiophonological assessment in this disorder. Evaluation of muscle tension in upper and lower limb posture, gait, muscle enzyme activity, ECG, USG, bone densitometry, lower limb muscles MRI, handgrip strength were conducted. Hearing was examined using pure-tone, impedance, speech audiometry, and DPOAE. Voice assessment included GRBAS and endoscopic laryngeal examinations. Speech evaluation was conducted using Child Speech Assessment Cards (Karty Oceny Logopedycznej Dziecka, KOLD).

Results: Diagnosis of FSHD was genetically confirmed by haplotype testing. Muscle hypotonia and atrophy were observed in limbs and face, along with gait disturbances. The 6-minute walk test (6MWT) result was 570 m, and the upper limb muscle strength was 9.3 kg (right limb) and 11.0 kg (left limb), both limbs: 15.7 kg. Audiological evaluation revealed severe bilateral sensorineural hearing (mean 73 dB HL). Bilateral type As tympanogram was recorded (right ear: 0.27 mL; left ear: 0.18 mL). Stapedial reflex was absent at high frequencies. DPOAE testing revealed sporadic bilateral cochlear responses. Speech audiometry showed reduced speech comprehension. Endoscopic examinations revealed edema of both vocal folds mucosa, preserved mobility. GRBAS scale showed G2R1B3A3S0. Acoustic analysis demonstrated slight reduction in fundamental frequency (F0) and elevated shimmer (10.566%). MPT was slightly shortened to 20 s. Speech evaluation revealed mouth breathing, shortened expiratory phase during phonation, bradylalia, articulation disorders with prolonged pauses between words, high-arched soft palate, shortened lingual frenulum, open bite, reduced tone of facial, lip, and tongue muscles.

Conclusion: Genetic testing confirmed the presence of facio-scapulo-humeral muscular dystrophy (FSHD). Bilateral severe sensorineural hearing loss was documented. Speech disorders in FSHD were associated with reduced tension of articulatory muscles.

Keywords: genetic diagnostics, FSHD, muscular dystrophy, sensorineural hearing loss, vocal folds edema, articulation disorders

Introduction

Facio-scapulo-humeral dystrophy (FSHD) is one of the most common muscular dystrophies diagnosed in 1/8000 cases in world.¹⁻³ The genetic analysis of FSHD is based on the determination of the size and haplotype of the D4Z4 repeat arrays on chromosomes 4 and 10. For FSHD1, analysis is focused on D4Z4 repeat arrays between 1 and 10 units (Southern blotting after linear gel electrophoresis; SB-LGE), which requires standard liquid DNA of high quality (>100 kb). In the majority of cases the disease is of autosomal dominant inheritance with approximately 10% of de novo mutations and high frequency of somatic mosaicism.⁴ Recent studies show that the reduction of D4Z4 repeats causes chromatin relaxation and transcriptive derepression of DUX4 – the gene that is normally expressed only in germline.^{5,6}

The disease is connected with progressive, asymmetric muscle atrophy, which usually includes facial skeletal muscles, muscles of the upper limbs and arms and afterwards muscles of lower limbs.⁷ The onset of symptoms is usually observed between second and third decade of life – the onset in the first decade of life is more frequently connected with high severity of the disease and higher risk of significant disability, which in 20% of cases is connected with the necessity to use a wheelchair.^{3,8,9}

The clinical image of FSHD is characteristic. Usually, the first symptoms of the disease are facial muscles weakness (problem with puffing out the cheeks, limited lip movement, failure to close eyelids – also while asleep) and shoulder girdle muscles. Also impaired shoulder abduction and characteristic scapular winging syndrome – alleged protrusion of the shoulder blades above the girdle of the upper limb, are observed.¹⁰ Neurological evaluation usually reveals periscapular muscles weakness, especially lower trapezius muscle, which causes wing movement and upward movement of the shoulder blade with rounding of shoulders and collarbones. Deltoid muscle in the initial stage of the disease is not affected but biceps, triceps and pectorial muscles are weakened which causes horizontal axillary folds. Asymmetric muscle weakness is observed more frequently than in case of other muscular dystrophies but it becomes less visible in advanced stages of the disease.⁸

Extramuscular symptoms as part of the clinical image of FSHD include hearing and vision impairments, which are observed in as many as 60% of patients. More severe hearing and vision impairments are usually connected with early onset FSHD (before 10 years) which may lead to speech delays especially with simultaneous weakness of facial muscles.³

What is more, in several percent of patients with FSHD, breathing disorders are observed which are not dominant but according to high risk of breathing insufficiency should be the subject of regular pulmonologic control. The group of high risk are patients with thoracic and spine malformations that occurred due to the weakness of postural muscles as well as patients with comorbidities such as COPD.³ One of the less frequent symptoms observed in patients with FSHD are swallowing disorders present in isolated cases.¹⁰ Intellectual disability or epilepsy are the less commonly observed comorbidities. Extremely rare cases of central nervous system (CNS) damages are observed in the most severe forms of FSHD and their connection with underlying disease has not been proved.³ The scarcity of complex hearing-voice-speech evaluation in patients with early onset of FSHD was the reason to undertake the study on this topic.

Objective

The objective of the study was the evaluation of hearing, voice and speech of 10-year-old boy with facio-scapulo-humeral dystrophy (FSHD).

Materials and Methods

A 10-year-old boy was admitted to the Department of Paediatric Rehabilitation, for application of steroid therapy and rehabilitation course. Genetic testing confirmed FSHD type 1.

Genomic DNA isolated from peripheral blood was digested with EcoRI restriction enzyme, and also with a combination of EcoRI and BlnI enzymes. Size separation of the digested DNA was performed by linear gel electrophoresis (LGE). DNA fragments were transferred to a positively charged Nylon membrane by Southern blotting and visualized by chemiluminescent detection following hybridization with labelled p13E-11 probe. The p13E-11 probe recognized the region immediately proximal to the D4Z4 macrosatellite repeat array on chromosomes 4q35 and 10q26. Restriction enzyme EcoRI cut proximal and distal to the D4Z4 array. BlnI specifically digested 10q-type D4Z4 repeats. For a 4q35 D4Z4 array, the expected size difference between the EcoRI single digest fragment and the corresponding EcoRI/BlnI double digest fragment were 3.2 kilobases (approximated to 3 kb).

Muscle tension of upper and lower limbs was assessed using the Lovett scale. In addition the boy's posture, walking pattern, and eyelid insufficiency were evaluated. Number of tests have been conducted including, muscle enzymes levels, electrocardiogram (ECG), abdominal ultrasound (USG), bone densitometry, magnetic resonance (MRI) of lower limbs, 6 min walk test (6MWT) as well as dynamometric strength of the upper limb muscles.

Assessment of hearing, voice and speech disorders was conducted at the Department of Clinical Phonoaudiology and Speech Therapy, Medical University of Białystok, Poland.

Audiologic evaluation included pure tone audiometry with the determination of air and bone conduction hearing threshold using the audiometer by MADSEN Astera2 by Otometrics. Impedance audiometry was conducted in order to register tympanometry curve and stapedial reflex in right and left ear using Sentiero device by Path Medical. Distortion Product Otoacoustic Emissions (DPOAE) for right and left ear was conducted using MADSEN Capella2 by Otometrics. The speech comprehension was evaluated in speech audiometry using MADSEN Astera2 by Otometrics.

The severity of voice disorders was assessed using perceptive scale GRBAS where G is the grade of hoarseness, R = voice roughness, B = voice breathiness, A = asthenicity of voice and S = its strain. Each parameter was evaluated in 4° scale where 0 means physiological voice, 1 = slight disorders, 2 = moderate disorders and 3 = severe voice disorders.¹¹

The morphological examination of larynx was conducted using EndoSTROB EL by Xion. Respiratory and phonatory mobility of vocal folds were assessed as well as symmetry of vibrations, glottal closure geometry and mucosal wave (MW).

Acoustic examination of voice was also performed, assessing vowel “a” pronounced in isolation as well as continuous linguistic text in Polish, phonematically balanced starting with the words “Dziś jest ładna pogoda”. (“Today, the weather is nice”). Parameters F0, Jitter, Shimmer, Noise-to-Harmonics Ratio (NHR) were evaluated as well as maximum phonation time (MPT). The presence of harmonic and nonharmonic components was registered in narrowband spectrography. The examination was performed using Praat 6.4.43.

Logopedic diagnosis was conducted using the test “Logopedic Assessment Cards for Children” (Karty Oceny Logopedycznej Dziecka – KOLD) by Joanna Gruba. The test consists of six subtests: (A) speech understanding, (B) speech production, (C) auditory reactions, (D) speech organs, (E) articulation and articulatory efficiency, and (F) pragmatic and social skills. In each subtest the patient may obtain the maximum of six points. Following results indicate disorders in examined area: in part (A) 4–0 points., (B) 3–0, (C) 3–0, (D) 5–0, (E) 5–0, and (F) 5–0 points.

Results

The first symptoms of the disease were observed by his parents when the boy was 5 years old. The boy had difficulties running, walking on his toes or climbing the stairs. In 2018 moderate bilateral sensorineural hearing loss was diagnosed and the patient was equipped in hearing aids on both sides. Family history was without cases of FSHD.

In genetic testing single EcoRI digest showed a fragment measuring approximately 14 kb. This fragment was estimated to contain 2 D4Z4 repeat units (uncertainty of measurement for the LGE Southern blot assay is $\pm 1U$). Double EcoRI/BlnI digest showed a fragment measuring approximately 11 kb. Resistance to BlnI digest, with fragment size reduced by approximately 3 kb, indicates that the 2U D4Z4 array is a likely to be a typical chromosome 4q35 type repeat. A 2U D4Z4 repeat array on 4q35 is consistent with a diagnosis of (early onset) Facio-scapulo-humeral muscular dystrophy type 1. Further tests using the 4qA and 4qB probes reveal that this 14kb/2U fragment is associated with the 4qA haplotype in this patient.

During admission to the Department of Paediatric Rehabilitation, in physical examination, good general condition, slim body structure, and no general ailments were observed. Reduced muscle tension and muscle strength in upper and lower limbs were registered (3° on Lovett’s scale for different muscle groups of upper and lower limbs), generalised muscle atrophy, poor face mimics, Achilles tendons contractures, deep lordosis, walking on toes for approximately 15 m were registered. In case history, parents reported eyelid insufficiency during sleep and necessity of using wheelchair for longer distances and at school. The activity of muscle enzymes was 60 U/L (normal values 55–370 U/L), no pathologies were observed in EKG and abdominal USG. Densitometry and magnetic resonance were normal. In the 6MWT the result of 570 was obtained (in a wheelchair). In dynamometric test muscle strength were assessed for 9.3 kg for right upper limb and 11 kg for left upper limb, both limbs: 5.7kg (Figure 1).

Audiologic evaluation revealed severe bilateral sensorineural hearing loss (the bone curve coincided with the air curve, no cochlear reserve, severe hearing loss: right ear (RE) = 73.75 dB; left ear (LE) = 72.5 dB) according to WHO/ASHA criteria (Figure 2).

Tympanometric examination revealed bilateral As curve (for RE = 0.27 mL, for LE = 0.18 mL). Assessment of stapedial reflex revealed its presence at 0.5, 1, and 2 kHz for RE and 0.5 and 1 kHz for LE. At other frequencies the reflex was absent (Figure 3).



Figure 1 Phenotype.

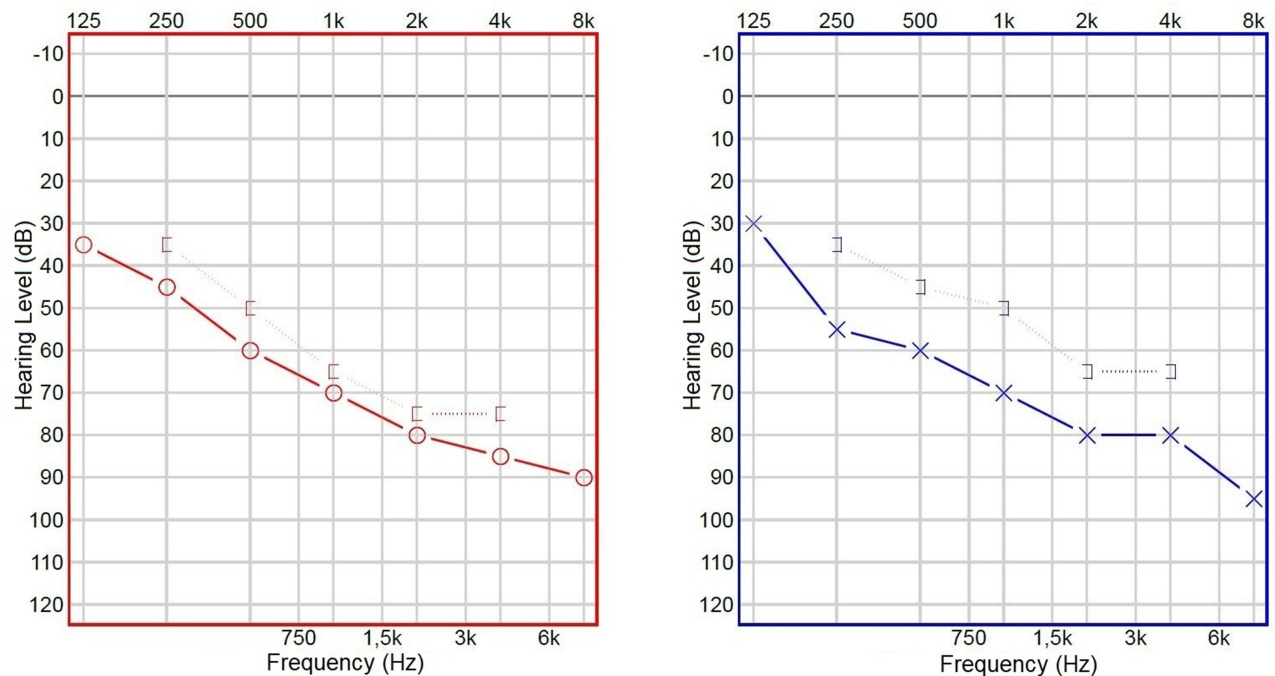


Figure 2 Pure-tone audiogram for RE and LE.

In DPOAE the majority of cochlear responses for acoustic stimuli for both ears was absent (Figure 4).

Audiometry speech comprehension was severely reduced (Figure 5).

Endoscopic and stroboscopic examination of the larynx revealed normal respiratory and phonatory mobility of vocal folds. Vibrations were synchronic, regular, symmetrical. Glottal closure was almost physiological. Vocal folds mass was increased, vibration amplitude was elevated and MW was limited. Morphological changes observed in larynx indicated edematous laryngitis of slight degree (Figure 6).

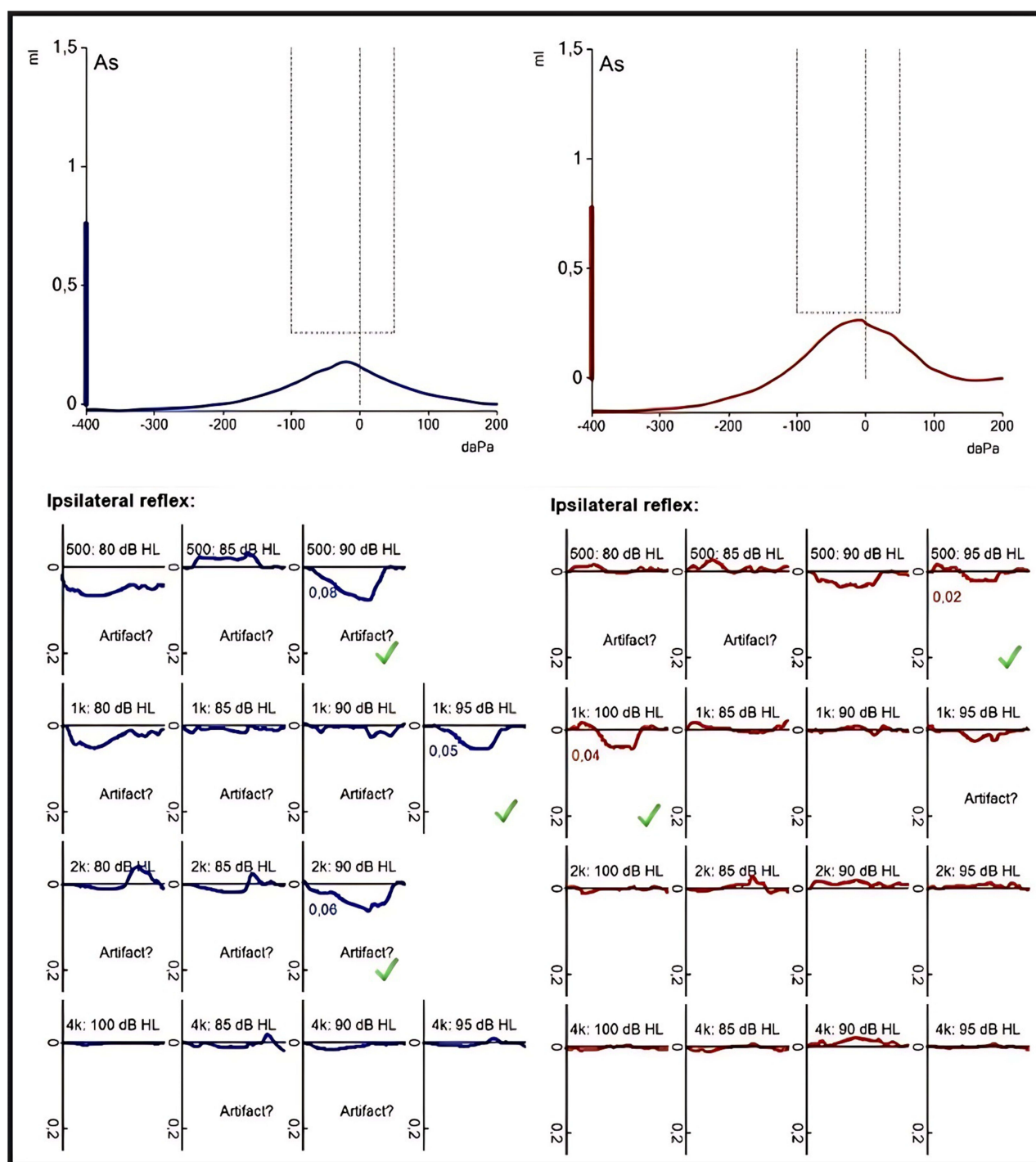


Figure 3 Impedance audiometry results for RE (red lines) and LE (blue lines) (green marker = acoustic otoemissions presence).

Voice assessment with GRBAS scale revealed moderate hoarseness: G2, slight voice roughness: R1, severe breathiness: B3, asthenic voice: A3, and the lack of voice strain: S0 (G2R1B3A3S0).

Acoustic analysis of vowel “a” in isolation revealed F0 value of 241 Hz and increase of Shimmer parameter: 10.566%, values of Jitter and NHR were normal (Jitter: 0.57%; NHR: 0.08) (Box 1).

Spectrographic analysis of during double phonation vowel “a” revealed the presence of nonharmonic components within high frequencies (Figure 7).

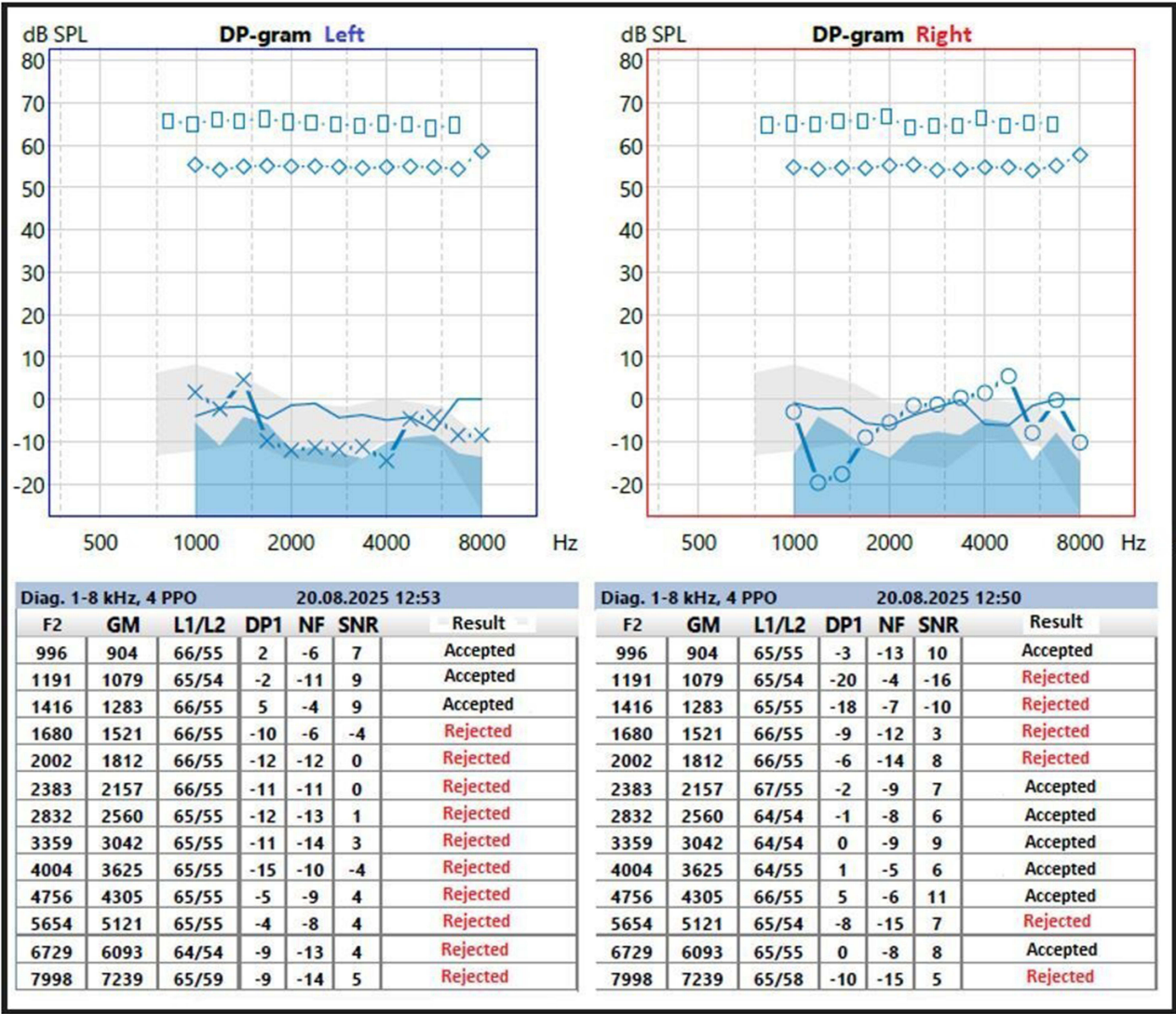


Figure 4 Result of the DPOAE test.

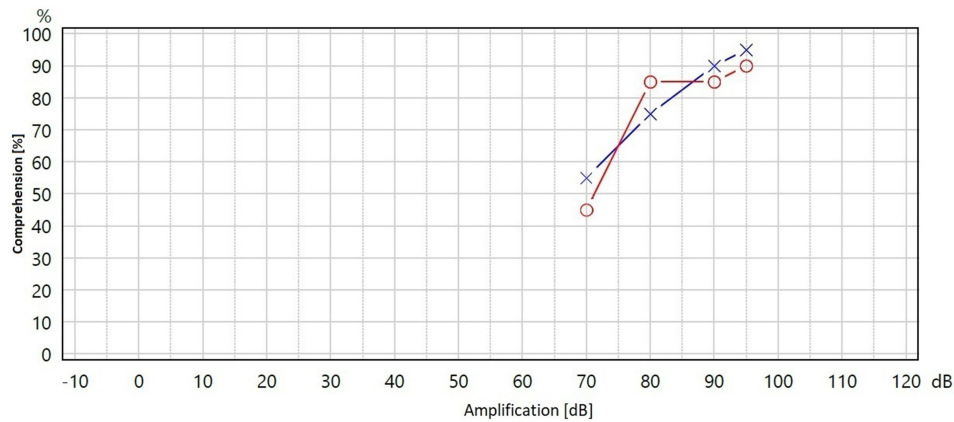


Figure 5 Speech audiogram.

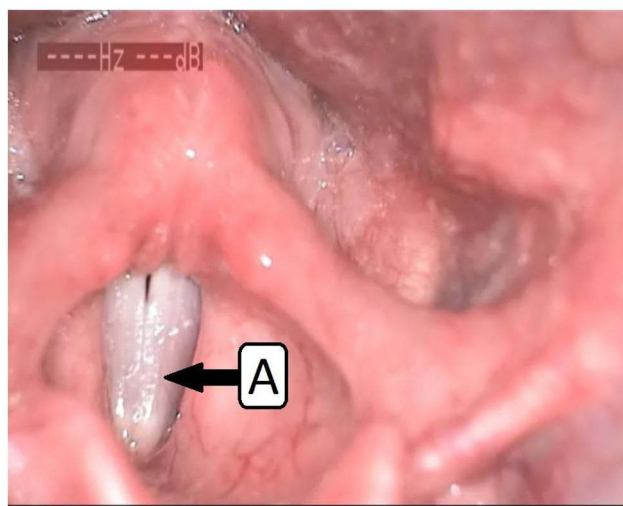


Figure 6 Morphological image of vocal folds mucosa during phonation (A) edematous changes.

MPT average value for three attempts was 20 s.

In logopedic diagnosis, mouth breathing, regular resting breathing, reduced expiratory phase during speaking, decreased speaking pace, blurred speech, extended pauses between words were observed. In the structure of articulatory organs, high-arched palate, ankyloglossia, open bite were observed. Facial muscle tension was significantly decreased. What is more, infantile swallowing was registered.

In the assessment of speech comprehension, speech production, auditory reactions, speech organs structure, articulation and sociopragmatic competence with KOLD the boy obtained 5 points., 5, 2, 1, 3, and 5 points, respectively. The most significant disorders were observed within auditory reactions, speech organs structure and articulation. Examination of auditory reactions indicated auditory memory deficit and inability to recognize rhymes. In the subtest regarding speech organs structure, mouth breathing during the day and while sleeping, irregular breathing, reduced expiratory phase, bradylalia, and slight rhinolalia were observed. What is more, the boy developed abnormal chewing and swallowing functions. No parafunctions such as lip and tongue biting, tumb sucking, nail biting, bruxism were observed. Articulation assessment revealed incorrect realization of sounds f, w, p, b, é (palatal [tʃ]), z, cz ([tʃ]), sz ([ʃ]).

Discussion

Facio-scapulo-humeral dystrophy is the third (after Duchenne dystrophy and myotonic dystrophy type 1) most frequent type of muscular dystrophy.^{12,13} Usually the disease has its onset in the second decade of life affecting, in the initial stage, facial muscles, periscapular muscles and shoulder muscles excluding deltoid muscle.¹⁴ The disease, usually is progressing slowly but differently in particular cases and in approximately 20% of cases it is connected with the necessity to use a wheelchair after 50 years old.^{4,5,12} In this case, the 10-year-old patient, who was diagnosed at 5 years old used a wheelchair since he was 7 years old. According to Medical Research Council as many as 57% of patients with early onset of the disease are wheelchair-dependent.²

In diagnosed case, in genetic testing of P13E11 EcoRI BlnI enzyme the decrease of 2 (kb) fragment length was revealed to 11 kb. Research conducted by Tawil et al² indicates that hearing loss is connected with large deletion (≤ 20 kb) which is consistent with the results obtained in our patient.

According to Goselink et al,¹⁵ patients with FSHD type 1 require regular audiological, ophthalmological and pulmonological control due to statistically significantly higher risk of anomalies in these areas. Similar results in patients with FSHD type 1 observed Brouwer et al,¹⁶ Dorobek et al¹⁷ and Trevisan et al.¹⁸ In our case study, audiological disorders were recognized in the second day of the patient's life. Control examination was recommended after 2 weeks and after 3 months which revealed no changes. At the age of 2 years and 6 months audiologic examination revealed bilateral sensorineural hearing loss. The child was equipped in hearing aids bilaterally at the age of 3 years and 5 months.

Box I Comprehensive Analysis of Acoustic Voice Parameters

Pitch Median pitch: 241.193 Hz Mean pitch: 240.405 Hz Standard deviation: 3.135 Hz Minimum pitch: 229.711 Hz Maximum pitch: 244.563 Hz
Pulses Number of pulses: 297 Number of periods: 296 Mean period: 4.164439E-3 seconds Standard deviation of period: 0.094243E-3 seconds
Voicing Fraction of locally unvoiced frames: 0 (0/124) Number of voice breaks: 0 Degree of voice breaks: 0 (0 seconds/ 1.240466 seconds)
Jitter Jitter (local): 0.571% Jitter (local, absolute): 23.761E-6 seconds Jitter (rap): 0.330% Jitter (ppq5): 0.408% Jitter (ddp): 0.989%
Shimmer Shimmer (local): 10.566% Shimmer (local, dB): 0.942 dB Shimmer (apq3): 4.102% Shimmer (apq5): 6.314% Shimmer (apq11): 10.930% Shimmer (dda): 12.307%
Harmonicity of the voiced parts only Mean autocorrelation: 0.933383 Mean noise-to-harmonics ratio: 0.080436 Mean harmonics-to-noise ratio: 14.209 dB
H1-minus-H2 Mean of the points: -10.079 dB Mean of the curve: -10.048 dB

In diagnosed boy, bilateral sensorineural hearing loss was recognized which is consistent with the research conducted by Lutz et al¹⁹ who observed bilateral, progressive high frequency sensorineural hearing loss in 11 patients. DPOAE and impedance audiometry confirmed the results obtained by Frezza et al,²⁰ who reported occurrence of tympanometric curves type A for both ears as well as decreases in DPOAE examination.

Wohlgemuth et al²¹ while examining respiratory insufficiency in patients with FSHD, only in 1% of cases observed insufficiency which needed mechanical ventilation (MV). Also Klimer et al²² in their 10 year prospective study observed severe respiratory insufficiency only in 13% of patients with FSHD. Santos et al²³ suggest that in the group of risk for respiratory insufficiency are patients with smaller D4Z4 repeats, more severe disability and with higher BMI. In our case, respiratory insufficiency was not stated despite abnormal breathing pattern and slightly reduced phonation time.

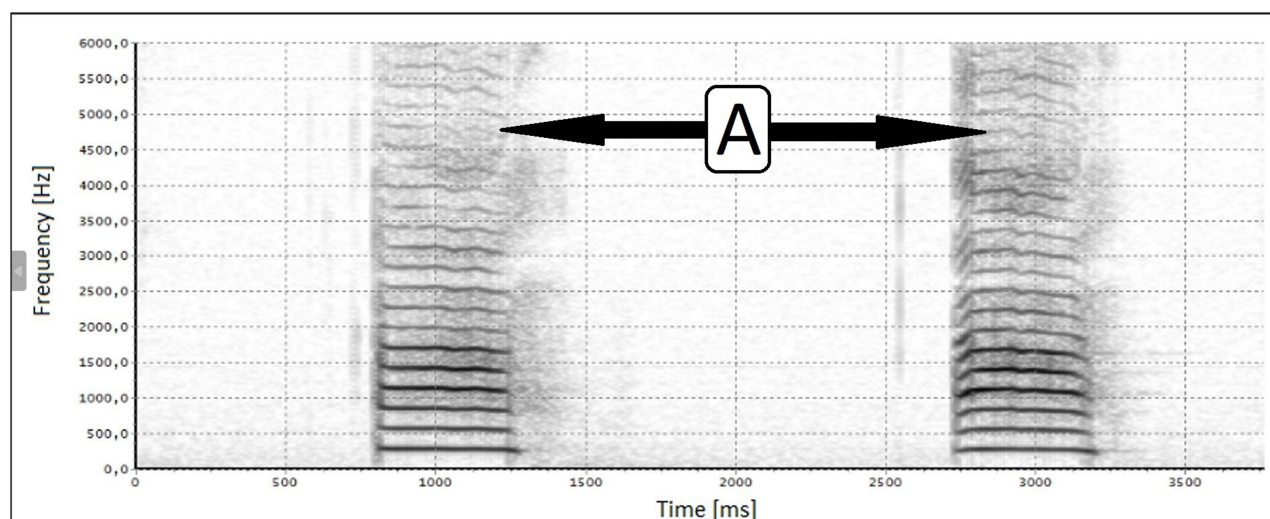


Figure 7 Narrowband spectrogram (A) nonharmonic components.

Aforementioned disorders were a result of reduced breathing muscle tension and mild edematous changes in larynx without significant dysfunction of internal larynx muscles. Respiratory and phonatory mobility of vocal folds was normal.

The evaluation of internal larynx muscles influencing the mobility of vocal folds and voice production did not reveal mobility disorders. Glottal closure was full – medial position. During breathing, vocal folds were in intermedial position. Slight increase in vibrations amplitude was observed which confirmed edematous changes within vocal folds mucosa of mild character.

Acoustic analysis of voice samples in the examined boy proved the existence of changes regarding many parameters. Similarly to Brzoskowski dos Santos et al²⁴ we registered the increase of Shimmer and slight reduction of MPT. The value of F0 was lowered for this age group which was also confirmed in our study. Authors also registered increased values of Jitter in three patients with FSHD, which was not observed in our case.

Acoustic voice analysis with perceptive GRBAS scale (G2R1B3A3S0) revealed voice disorders (dysphonia). The relationship between hearing loss and laryngeal findings warrants further investigation. Obtained results indicate the necessity of early audiological diagnostics and hearing monitoring in children with recognized dystrophy in order to apply hearing aids as early as possible.

In the assessment of speech and articulation, the most significant difficulties were observed in realization of labial or labiodental (which regarded closure of upper and lower lip or lips and teeth) sounds which resulted from severely lowered tension of orbicularis oris muscle and zygomaticus major muscle. Similar difficulties were observed in patients with FSHD by Brzoskowski dos Santos et al,²⁴ connected with lower lip protrusion indicating the fact that those muscles are most severely affected in patients with FSHD. The occurrence of articulation disorders and decrease in muscle tension influences negatively speech development, communication and social functioning and regards early diagnostics and speech therapy implementation.

Limitations

A limitation of this study is undoubtedly the comprehensive yet single-time assessment of the voice, hearing, and speech organs in the examined boy. A comprehensive evaluation of voice, hearing, and speech disorders was not performed immediately after the introduction of hearing aids, which took place at the age of 3 years and 5 months, but only later, at the current age of 10 years. Retrospective assessment based on clinical documentation is currently not possible, as such a comprehensive analysis was not conducted over the years.

Conclusions

Genetic determination of haplotype allowed unambiguous determination of clinical form of muscle dystrophy. In the 10-year-old boy with FSHD occurrence of severe bilateral sensorineural hearing loss was confirmed in impedance audiometry, pure tone audiometry, and otoacoustic emissions. The existence of dysphonia in FSHD connected with vocal folds edema was confirmed in GRBAS scale and acoustic examination of voice. Articulation disorders observed in FSHD were connected with severe reduction of articular muscles tension. Voice, speech, and hearing disorders may indicate the need for systematic, objective phoniatric and audiological as well as comprehensive speech-language (logopedic) assessment in children with FSHD type 1.

Ethics Approval and Informed Consent

Institutional approval was not required to publish case details. The patient's guardians had given written informed consent for the publication of case details and accompanying images.

Disclosure

The authors report no conflicts of interest in this work.

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