eNeurologicalSci 21 (2020) 100284

Contents lists available at ScienceDirect

eNeurologicalSci

journal homepage: www.elsevier.com/locate/ensci

Case report

A case of type 1 facioscapulohumeral muscular dystrophy (FSHD) with restrictive ventilatory defect and congestive heart failure

Nobutoshi Morimoto [a,*], Mizuki Morimoto [a], Yoshiaki Takahashi [a], Motonori Takamiya [a], Ichizo Nishino [b], Koji Abe [c]

[a] Department of Neurology, Kagawa Central Prefectural Hospital, Japan
[b] Department of Neuromuscular Research, National Institute of Neuroscience, National Center of Neurology and Psychiatry (NCNP), Japan
[c] Department of Neurology, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Japan

ARTICLE INFO

Keywords:
Facioscapulohumeral muscular dystrophy (FSHD)
Restrictive ventilatory defect (RVD)
Congestive heart failure (CHF)

ABSTRACT

[Background] Facioscapulohumeral muscular dystrophy (FSHD) is an autosomal dominant muscle disease characterized by asymmetric involvement of muscles in the face, upper extremity, trunk, and lower extremity regions, with variable severity. It was recently reported that restrictive respiratory involvement is more frequent and severe than previously recognized, while cardiac dysfunction other than arrhythmia is still considered extremely rare in FSHD. [Case report] A 59-year-old man presenting with marked muscle atrophy in the trunk and asymmetrical muscle atrophy in the legs was hospitalized because of dyspnea and edema in the face and limbs. Shortness of breath with body movement started from approximately 40 years of age. Muscle biopsy revealed myopathic change with mild to moderate variation in fiber size. The diagnosis of FSHD was made by D4Z4 contraction to three repeats on genetic testing. A pulmonary function test revealed a decline of forced vital capacity (FVC) and a preserved FEV1/FVC indicating restrictive ventilatory defect (RVD). Ultrasonic echocardiogram (UCG) showed diffuse left ventricular hypokinesis, ventricular septum thickening, pericardial effusion, and decreased ejection fraction (LVEF 30%). [Conclusion] Although restrictive ventilatory defect and congestive heart failure are uncommon in FSHD, respiratory and cardiac evaluation may be necessary in patients with FSHD.

1. Introduction

Facioscapulohumeral muscular dystrophy (FSHD) is an autosomal dominant myopathy characterized by asymmetric involvement of muscles in the facial, upper extremity, trunk, and lower extremity regions with variable severity. In over 95% of patients, deletion of a 3.3 kb tandem repeat, D4Z4, on chromosome 4q35 is present (type1 FSHD) [1]. It was recently reported that respiratory involvement in FSHD is more frequent and severe than previously recognized [2]. However, cardiac dysfunction other than arrhythmia is considered extremely rare in FSHD [3]. We present a case of type 1 FSHD with restrictive ventilatory defect (RVD) and congestive heart failure (CHF).

Case report.

A 59-year-old man was admitted to hospital because of dyspnea and edema of the extremities and face. At the age of 12, he first noticed difficulty in raising his arms, but he was able to work and live independently until the age of 50. Shortness of breath with body movement started from approximately 40 years of age. At 55 years of age, he noticed muscle weakness in his upper arms. Regarding his medical history, hypertension had been noted in the past but was not treated. He had no smoking habits and was drunk on occasion. There were no obvious myopathic cases in his family. He was born to non-consanguineous parents.

On physical examination, the patient was 75.1 kg in weight, 158 cm in height, and 30.4 kg/m^2 in body mass index (BMI). Blood pressure was 135/89 mmHg and heart rate was 73 beats/min, with a resting respiratory rate of 18 breaths/min. Edema was observed in the limbs and the eyelids. No obvious heart murmurs and no pulmonary crackles were heard on auscultation. Asymmetric muscle weakness was observed in the left and proximal dominant upper limbs, but the trapezius and deltoid muscles were hypertrophic. The patient's grip strength was 16.1 kg in the right and 18.3 kg in the left, respectively. Asymmetrical muscle weakness was observed in his lower limbs and gluteus muscles. The facial and abdominal muscle tone reduced. Beevor's sign was positive.

* Corresponding author at: Department of Neurology, Kagawa Prefectural Central Hospital, 1-2-1 Asahimachi, Takamatsu 760-8557, Japan.
E-mail address: morinobu@cc.okayama-u.ac.jp (N. Morimoto).

https://doi.org/10.1016/j.ensci.2020.100284
Received 14 June 2020; Received in revised form 25 September 2020; Accepted 13 October 2020
Available online 15 October 2020

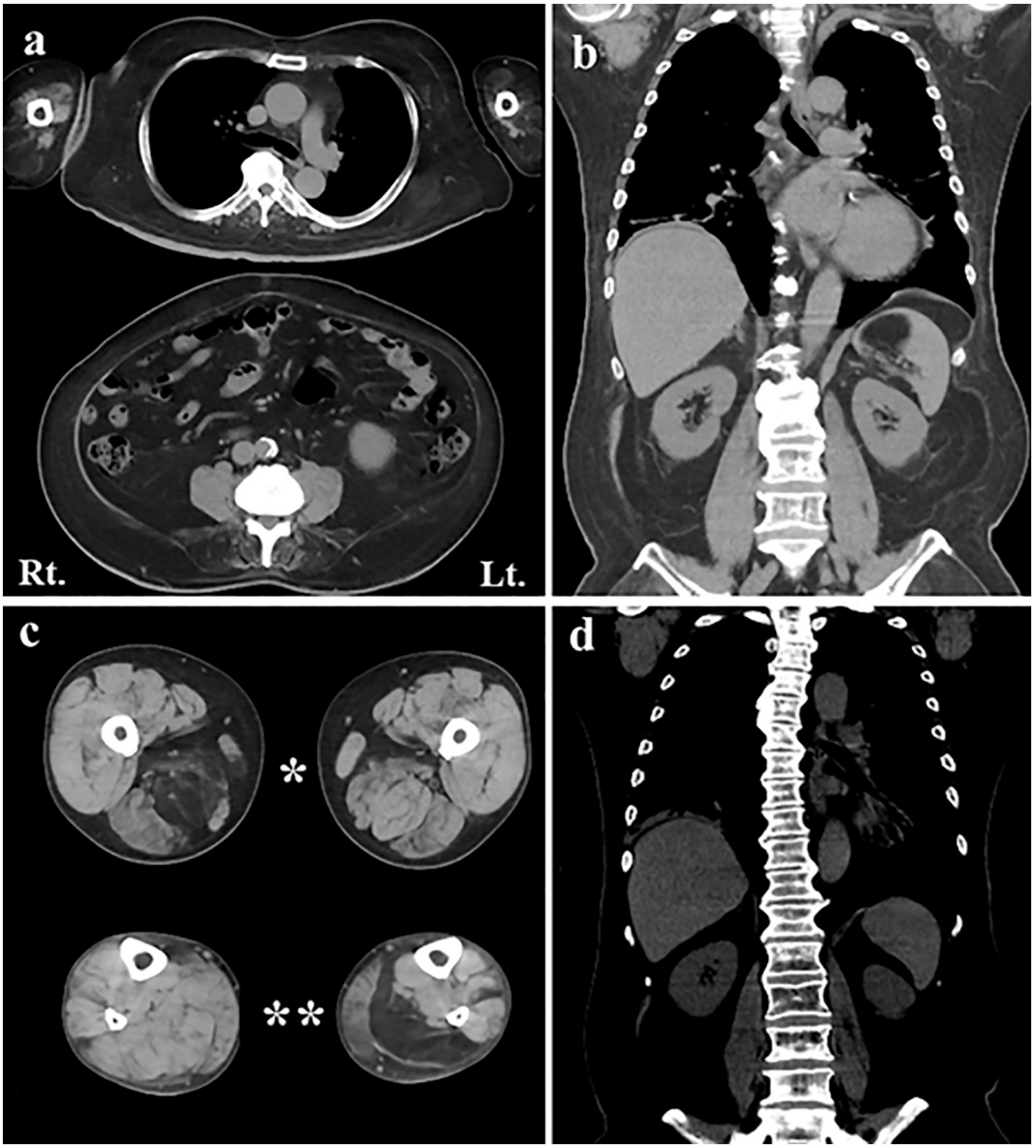

Fig. 1. a. Muscle CT scan axial images of the thorax (upper), abdomen (lower). Note severe muscle atrophy in the thorax, left abdomen, paravertebral muscles asymmetrical muscle atrophy in the thighs and lower legs. **b**. Muscle CT scan coronal image of the thorax, abdomen. Note elevation of the right diaphragm. **c**. Muscle CT scan axial images of the thighs (asterisk) and the lower legs (doble asterisks). Note sever muscle atrophy in the right hamstring and left lower leg. **d**. CT scan of the vertebral column. Scoliosis is not obviously observed.

Deep tendon reflexes, sensation, coordination and cognitive functions were normal. There was no hearing loss or clear visual loss. Scoliosis was not apparent (Fig. 1d).

Needle electromyography (nEMG) displayed myopathic changes with polyphasic potentials, especially in proximal muscles. Muscle CT revealed marked muscle atrophy in the thorax, abdomen, paravertebral muscles, left upper arm, right hamstrings, and left lower leg (Fig. 1 a–c). A muscle biopsy from the patient's right biceps brachii revealed myopathic changes with mild to moderate variation in fiber size and remarkable adipose tissue infiltration. Genetic testing revealed that the patient carried a D4Z4 reduced allele with three repeats. A chest X-ray showed an enlarged cardiac outline with cardiothoracic ratio (CTR) of 60% without apparent pulmonary opacity. The electrocardiogram (ECG) showed regular sinus rhythm with findings of left ventricular hypertrophy. The pulmonary function test showed a declined forced vital capacity (FVC) of 1.16 L (33.9% predicted) and a preserved FEV1/FVC of 0.86 (0.83 L/1.16 L). Serum creatine phosphokinase (CPK) was

Table 1
Blood test results.

CBC		Biochemical tests		ABG	
WBC	7300 /μL	AST	43 IU/L	pH	7.423
RBC	$476*10^4$/μL	ALT	86 IU/L	pO_2	81.8 mmHg
Hb	14.7 g/dL	γGTP	54 IU/L	pCO_2	52.2 mmHg
Plt.	$28.8*10^4$/μL	LDH	236 IU/L	HCO_3^-	33.4 mEq/L
		CPK	145 IU/mL	B.E.	7.7
		BUN	15.0 mg/dL	SaO_2	92%
		Cr	0.61 mg/dL		
		UA	4.7 mg/dL		
		Na	145 mEq/L		
		K	4.0 mEq/L		
		Cl	105 mEq/L		
		BS	118 mg/dL		

CBC: complete blood count; ABG: arterial blood gas

145 IU/mL. Other blood tests were largely normal (Table 1, left and middle lines). Room air arterial blood gas showed elevated partial pressure of carbon dioxide ($PaCO_2$ 52.2 mmHg) (Table 1, right line). The electrocardiogram showed regular sinus rhythm with findings of left ventricular (LV) hypertrophy. The ultrasonic echocardiogram (UCG) showed diffuse LV hypokinesis, ventricular septum thickening, pericardial effusion, and decreased LV ejection fraction (LVDd 57 mm, LVDs 49 mm, LVEF 30%). UCG showed normal right ventricular diameter of 29 mm.

After admission, continuous intravenous infusion of furosemide and carperitide, and oxygen administration, improved CHF. Non-invasive positive pressure ventilation (NPPV) was recommended, but was not accepted by the patient.

2. Discussion

We examined a case of FSHD with slowly progressive muscle weakness for approximately 40 years with severe RVD and CHF. Symptoms of respiratory involvement began around the age of 40, and emergency treatment was required for exacerbation of CHF after the age of 50.

RVD was generally defined as an FEV1/FVC >0.70 and an FVC <80% predicted. In the present case, the result of pulmonary function test corresponded to RVD. Previous studies reported that respiratory involvement occurs in 1.25% to 9.6% of patients with FSHD [4,5]. However, a recent report suggested that approximately 40% of FSHD patients exhibited reduced respiratory function with a predominantly restrictive pattern [2]. Patients with neuromuscular-related RVD generally have no subjective symptoms. Therefore, it is recommended to obtain baseline pulmonary function tests from all patients with FSHD.

Previous electrocardiographic studies reported that approximately 50% of patients experienced cardiac anomalies and the most frequent cardiac complication was incomplete right bundle branch block (iRBBB) (25%) [3]. However, UCG studies in FSHD patients suggest that structural abnormalities, including heart failure or LV dysfunction, are extremely rare [6,7]. The only case we identified was a 38-year-old FSHD patient with biopsy-proven cardiomyopathy, reported by Tsuji et al. [8]. In the present case, despite the subjective symptoms, the patient had no opportunity to check for respiratory or cardiac function, and finally required urgent hospitalization for CHF. He had several cardiovascular risks, such as hypertension, obesity, and sleep apnea, therefore it must be considered that his heart failure may be caused by factors other than FSHD. Although cardiac dysfunction other than arrhythmia is rare, patient should be evaluated for cardiac function if they develop apparent signs or symptoms of cardiac dysfunction in FSHD.

Sources of support

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

None.

Acknowledgments

We thank Benjamin Knight, MSc., from Edanz Group (https://en-author-services.edanzgroup.com/) for editing a draft of this manuscript.

References

[1] R.J. Lemmers, P.J. van der Vliet, R. Klooster, S. Sacconi, P. Camano, J.G. Dauwerse, et al., A unifying genetic model for facioscapulohumeral muscular dystrophy, Science. 329 (2010) 1650–1653.
[2] S. Moreira, L. Wood, D. Smith, C. Marini-Bettolo, M. Guglieri, G. McMacken, et al., Respiratory involvement in ambulant and non-ambulant patients with facioscapulohumeral muscular dystrophy, J. Neurol. 264 (2017) 1271–1280.
[3] F. Labombarda, M. Maurice, J.P. Simon, D. Legallois, L. Guyant-Marechal, A. L. Bedat-Millet, et al., Cardiac abnormalities in type 1 Facioscapulohumeral muscular dystrophy, J. Clin. Neuromuscul. Dis. 18 (2017) 199–206.
[4] M.A. Scully, K.J. Eichinger, C.M. Donlin-Smith, R. Tawil, J.M. Statland, Restrictive lung involvement in facioscapulohumeral muscular dystrophy, Muscle Nerve 50 (2014) 739–743.
[5] M. Wohlgemuth, E.L. van der Kooi, R.G. van Kesteren, S.M. van der Maarel, G. W. Padberg, Ventilatory support in facioscapulohumeral muscular dystrophy, Neurology. 63 (2004) 176–178.
[6] R. Tawil, J.T. Kissel, C. Heatwole, S. Pandya, G. Gronseth, M. Benatar, et al., Evidence-based guideline summary: evaluation, diagnosis, and management of facioscapulohumeral muscular dystrophy: report of the guideline development, dissemination, and implementation Subcommittee of the American Academy of neurology and the practice issues review panel of the American association of neuromuscular & electrodiagnostic medicine, Neurology. 85 (2015) 357–364.
[7] G.P. van Dijk, E. van der Kooi, A. Behin, J. Smeets, J. Timmermans, S. van der Maarel, et al., High prevalence of incomplete right bundle branch block in facioscapulohumeral muscular dystrophy without cardiac symptoms, Funct. Neurol. 29 (2014) 159–165.
[8] M. Tsuji, M. Kinoshita, Y. Imai, M. Kawamoto, N. Kohara, Facioscapulohumeral muscular dystrophy presenting with hypertrophic cardiomyopathy: a case study, Neuromuscul. Disord. 19 (2009) 140–142.