

## Granulocyte colony-stimulating factor therapy for facioscapulohumeral dystrophy: a case report

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### ABSTRACT

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We examined the safety and effectiveness of a low dose of analog granulocyte-colony stimulating factor in a 15-year-old boy with facioscapulohumeral dystrophy. The onset of disease was noted at 12 years of age. The physical examination noted general muscle atrophy more pronounced at left side of the body. He was able to walk 300 meters within 6 minute walk test. Granulocyte colony-stimulating factor 5 µg/kg was given subcutaneously daily for 5 days/month for 1, 2, 3, 6 and 12 months. Clinical examination, laboratory tests including blood, biochemical tests, and CD34+ cells were performed. A significant increase of muscle strength in the lower and upper limbs between baseline, and after 3 months of treatment, after 6, and after 12 months was found. He was able to walk 480 meters within 6 minutes

after 12 months. Electromyography demonstrated increase of amplitude in the examined in upper and lower limbs after six months compared to baseline. Leukocyte levels remained below 25000/µL. CD34+ increased significantly at day 5 of granulocyte colony-stimulating factor administration. It was safe and well tolerated by the patient. A significant increase in muscle strength in this patient with facioscapulohumeral dystrophy after 3 months of treatment, after 6, and after 12 months since the first treatment course was completed may indicate beneficial effects of granulocyte colony-stimulating factor in this disorder.

**Key words:** Facioscapulohumeral dystrophy, granulocyte colony-stimulating factor, muscle strength

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## INTRODUCTION

Facioscapulohumeral dystrophy (FSHD) is an autosomal dominant disorder that is clinically defined as progressive asymmetric muscular weakness, typically of the face, scapular stabilizers, and proximal arm and leg [1]. A partial deletion of an integral number of 3.3 kb polymorphic repeats, identified as D4Z4, within the subtelomeric region of chromosome 4q is the cause of FSHD [2]. In FSHD, patients' cells have demonstrated a defect in the myogenic differentiation program and the deregulation of genes related to oxidative stress, vascular smooth muscle, and endothelial cells [3].

Many growth factors, and platelet-derived growth factors as well as cytokines have been identified as causing proliferation of satellite cells, with subsequent transformation into myotubes and muscle fibers, to regulate myoblast proliferation and differentiation, and to promote muscle regeneration or repair [4,5].

Besides the function of hematopoietic effects, Granulocyte-colony stimulating factor-(G-CSF) acts as a neurotrophic factor, induces neurogenesis, exerts anti-apoptotic effects in neurons and muscles, and has anti-inflammatory properties [6]. Recent studies have indicated that G-CSF can potentially be used for the treatment of spinal cord injury, stroke, and neurodegenerative diseases [7-9].

To our knowledge, no therapeutic options have been suggested for patients with FSHD. We used Filgrastim analog G-CSF as therapy for the weakness in the muscles of a 15-year-old boy with FSHD.

## CASE STUDY

A 15-year-old male with FSHD has been under the care of our department for three years. Disease onset was noted at 12 years of age, after which the patient reported weakness in his right hand and difficulties running. In the DNA of our patient genetic testing found deletions on chromosome

4q35 so FSHD1 was confirmed. The physical examination noted facial weakness (asymmetrical smile) and general muscle atrophy that was more pronounced on the left side of the body. The Gower's sign was positive. Manual muscle testing the patient demonstrated: hip extension 3, knee flexion/extension 4/3.5, shoulder abduction 4, and elbow flexion/extension 4/4 at the left side; hip extension 4, knee flexion/extension 4/4, shoulder abduction 5, and elbow/flexion 3/3 at the right side.

Hand grip strength was measured with the hand dynamometer. Hand grip force was measured bilaterally for hand-muscle actions. The force determination carried out before and after each two-week rehabilitation stay. The patient got active rehabilitation during each treatment cycle. The patient had decreased muscle strength of the upper (left hand 16 kg, right hand 13 kg by dynamometer) and lower extremities: (left 17 kg, right 23 kg by Leg Tensor-AC International East. He was able to walk 300 meters within 6 minute walk test. EMG demonstrated findings consistent with a myopathic disorder. Hematological data from the treated patient was analyzed. The measurement of CD34+ cells was carried out using flow cytometry.

G-CSF (5µg/kg/day) was administered subcutaneously for 5 consecutive days during the first, second, third, sixth, and twelfth months. Adverse events were also evaluated.

The ethic committee of the Medical University of Białystok approved the study, and written informed consent was obtained from patient and parent.

## RESULTS

The patient reported increased muscle strength in the upper and lower limbs after two months of G-CSF treatment. We confirmed the increase in muscle force of the upper and lower extremities in an objective assessment using a dynamometer and leg tensor (Table 1).

**Table 1.** The patient's muscle strength in the upper and lower extremities before and after 3 months, 6 and 12 months of granulocyte colony-stimulating factor treatment

	Before treatment		After 3 months of G-CSF treatment		After 6 months of G-CSF treatment		After 12 months of G-CSF treatment	
Hand	Left	Right	Left	Right	Left	Right	Left	Right
Isometric force/kg	16	13	22	21	26	22	30	27
Leg	Left	Right	Left	Right	Left	Right	Left	Right
Isometric force/kg	17	23	23	32	24	34	25	36

G-CSF- granulocyte colony-stimulating factor

The patient was able to walk 420 meters within 6 minutes after 3 months, 450 meters after 6 months, and 480 after 12 months. The patient did not report any side effects following G-CSF administration. White blood cell count increased at 5 days after G-CSF administration. White blood cell count increased 19,600 during the first cycle, 21,000 during the second cycle, and 20,000 during the third. CD34+ cell counts increased up to 13,000 cells/ml during the first cycle, 11,000 during the second cycle, and 10,000 during the third. EMG demonstrated increase of amplitude about 30% in the left biceps and left gastrocnemius after six months compared to baseline.

## DISCUSSION

We observed the beneficial effects of G-CSF treatment in a patient with FSHD after three, six, and twelve months. EMG demonstrated increase of amplitude in the examined in upper and lower limbs after six months compared to baseline. This patient has been under our care for several years, and we did not observe an increase in muscle strength. Significant increase in muscle strength in this patient after 3 months of treatment, after 6 and after 12 months of the treatment may indicate beneficial effects of G-CSF in this disorder. In the present study, no serious adverse events occurred during or after the administration of G-CSF.

The results indicated improvements in muscle strength and motor functions after three months of therapy, after six, and after twelve months of observation therapy. The patient continues under our care, and we are going to administer G-CSF at 24 month.

## Conflicts of interest

The authors declare that they have no conflicts interests.

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