Safety and efficacy of granulocyte colony stimulating factor in a patient with tetraplegia caused by cervical hyperextension injury: a case report

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ABSTRACT

The authors present the case of a 17-year-old boy who suffered a cervical spinal injury as a result of the sharp bending of the head after slipping (without falling). After about 30 minutes, he began to feel tingling in the limbs and he developed tetraparesis. He went through physical rehabilitation, psychological rehabilitation, occupational therapy, and periodic catheterization. Additionally, we introduced to him a low dose of analog granulocyte colony-stimulating factor (G-CSF). G-CSF 5 μg/kg was given subcutaneously daily for 5 days per month for 3 months, again after 6 months, and again after 10 months. The boy could sit indecently and walk with assistance. A significant increase in muscle strength in this patient with tetraplegia after 10 months of treatment may indicate beneficial effects of G-CSF in this disorder.

Key words: Cervical hyperextesniosn, spinal cord injury, tetraplegia, male

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INTRODUCTION

Hyperextension-dislocation of the cervical spine is an enigmatic injury because of the absence of gross displacement on lateral radiographs, and the failure of conventional imaging techniques to demonstrate ligament damage [1]. The cervical spine is the most mobile part of the spine, which is a result of the construction of the vertebrae, the joint system, and the muscular tendons. The specific structure and function of the spine causes a constant load, exposing the emergence of various kinds of damage [2]. The trauma of the cervical spine (cervical spine injury [CSI]) is very rare in children, occurring in less than 1% of them [3]. Younger children tend to have upper cervical spine injuries, while children in the older age group are much more prone to lower cervical spine injuries [4].

In Poland, approximately 1200 cases of SCI occur annually [5]. For children under 16 years of age, SCIs account for about 0.2% of all injuries. In the pediatric population, the overall incidence of SCI is 5.99 per 100,000 people, mostly in the cervical region. So far, there is no effective treatment for patients with SCI.

Case Report

A 17-year-old male was admitted to the department of pediatric neurology due to tetraplegia. After accidentally slipping (without falling), resulting in excessive hyperextension of the cervical spine backwards, he felt neck pain, but without difficulty, he went back home. After 30 minutes, he began to feel tingling in the limbs and developed tetraparesis, predominantly in the lower limbs. Neurological examination showed a complete paralysis of upper and lower limbs with sensory deficits from Th3 levels.

According to the international standards for neurological and functional classification of spinal cord injury (American Spinal Injury Association [Asia]), the patient was rated by the degree of damage to the incomplete B: lack of physical activity below the level of injury, while sensivity was the preserved (this includes the range of segments S4-S5).

CT showed abolition of the physiological cervical lordosis, bones, and joints without fracture and damage; spinal canal width was preserved and small hyperintensive areas in the spinal cord at the level of C1-C5 suggested bleeding.

MRI demonstrated a central disc prolapse at C5-C6 and increased intramedullary zone edema at C4-Th1 as a result of ischemia. Angio-CT was normal. After performing neuroimaging studies, the patient was transferred to our department for rehabilitation.

As a patient without indication for surgery, he was treated conventionally (cervical collar, cytoprotective, nootropic, and anti-edema therapies). He also underwent physical therapy, respiratory kinesiotherapy, and intermittent catheterization.

After three weeks, we observed a small improvement in muscle strength of the patient's upper and lower limbs. Muscle strength was better on the left side.

The control MRI revealed in front of the spinal cord C4-Th1 an area of ischemia-oedema with less swelling.

After obtaining the approval of the bioethics committee of the Medical University of Białystok for therapy with granulocyte colony-stimulating factor (G-CSF), we administered G-CSF in this patient. G-CSF is a glycoprotein. This cytokine promotes survival, proliferation, and differentiation of cells in the neutrophil lineage [6,7]. Currently, G-CSF is used to treat neutropenia, stimulating the bone marrow to increase production of neutrophils during chemotherapy and bone marrow transplantation [8]. It was also demonstrated that G-CSF promoted the restoration of damaged spinal cord tissue and the recovery of neural function [9].

G-CSF (5μg/kg/body/d) was sub-cutaneously administered for five consecutive days during the first, second, and third months. Laboratory tests were performed. Blood was sampled before G-CSF administration on day five of each treatment cycle. The measurement of CD34+ cells was performed using flow cytometry.

Functional assessment made after three cycles of treatment showed that the patient could turn from side to side. He could perform active movements in the joints of the lower limbs and arms, and could sit in a wheelchair.

At six months after the accident, the patient was able to sit, stand, and walk a few steps with assistance. He was classified at level V of the GMFCS (Gross Motor Function Classification System*)* and to ASIA C. We demonstrated that more than half of his muscles had the strength of a 3 score on the Lovett scale.

After 10 months, the patient was classified at level III of the GMFCS, and to ASIA D. He could sit and walk with assistance. More than half of his muscles had the strength equal to or greater than a 3 on the Lovett scale. MRI of the spinal cord revealed thinner cervical spine (around 4–4.5 mm) at the levels of C4-C7. The urodynamic investi-gation also demonstrated an improvement of bladder function: bladder was stable, with a clear feeling of urgency and incomplete voiding.

DISCUSSION

Our findings are in accordance with previous reports [10–14]. Sakuma et al. [10] administered G-CSF for 15 adult patients'

worsening symptoms of compression myelopathy in a clinical trial. Neurological improvements in motor and sensory functions were obtained in all patients after the administration of G-CSF.

Kato et al. [12], in an open label single-center prospective clinical trial, treated 17 patients with compression myelopathy. All patients underwent intravenous administration of G-CSF (10 μg/kg/day) for five consecutive days. In 14 of the 17 patients, pain was relieved within several days after G-CSF administration. No adverse events occurred during or after G-CSF administration. Inada et al. [13] in an open-labeled multicenter prospective non-randomized controlled clinical trial treated 41 patients with acute spinal cord injury (SCI). G-CSF (10 μg/kg/d) was intravenously administered for 5 consecutive days. They evaluated motor and sensory functions using the ASIA impairment scale at 1 week, 3 months, 6 months, and 1 year after onset. They found beneficial effects on neurological recovery in patients with acute SCI compared to the control group. .

In our pervious study [14], we also examined the safety and effectiveness of a low dose of G-CSF in a 15-year-old boy presented with congenital kyphoscoliosis, along with spastic paraparesis. G-CSF 5 μg/kg was given subcutaneously each day for five days per month over the course of three months. Clinical examination revealed an increase of muscle strength in the upper limbs and a decrease of spasticity in the lower limbs between baseline and day 90 and day 180. We found no serious adverse event. G-CSF was safe and well tolerated by the patient.

In oncology and hematology, a recombinant form of G-CSF is used with cancer patients to accelerate recovery from neutropenia after chemotherapy, allowing higher-intensity treatment regimens [15]. G-CSF is a growth factor which stimulates the bone marrow to produce granulocytes and stem cells and release them into the bloodstream. It is a cytokine and a hormone, and it is produced by a number of different tissues [16]. Besides the effect it has on the hematopoietic system, G-CSF can also act on neuronal cells as a neurotrophic factor. Indeed, its receptor is expressed by neurons in the brain and spinal cord. The action of G-CSF in the central nervous system is to induce neurogenesis, to increase the neuroplasticity, and to counteract apoptosis [7,9].

In conclusion, a significant increase in muscle strength and motor functioning in this patient with tetraplegia after treatment may indicate beneficial effects of G-CSF in this disorder. Low-dose G-CSF was safe and well tolerated by the patient. We found no serious adverse effects during the therapy. We think that the cytoprotective and anti-inflammatory effects of G-CSF had a positive impact on the acceleration of regeneration of spinal cord functioning and improved the patient's clinical status.

Conflicts of interest

The authors declare that there are no conflicts of interest of this paper.

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