Case Report: GcMAF Treatment in a Patient with Multiple Sclerosis

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Abstract. *Background/Aim: Gc protein-derived macrophage-activating factor (GcMAF) has various functions as an immune modulator, such as macrophage activation, anti-angiogenic activity and anti-tumor activity. Clinical trials of second-generation GcMAF demonstrated remarkable clinical effects in several types of cancers. Thus, GcMAF-based immunotherapy has a wide application for use in the treatment of many diseases via macrophage activation that can be used as a supportive therapy. Multiple sclerosis (MS) is considered to be an autoimmune disorder that affects the myelinated axons in the central nervous system (CNS). This study was undertaken to examine the effects of second-generation GcMAF in a patient with MS. Results: This case study demonstrated that treatments of GcMAF in a patient with MS have potent therapeutic actions with early beneficial responses, especially improvement of motor dysfunction. Conclusion: GcMAF shows therapeutic potency in the treatment of MS.*

The group-specific component (Gc) protein, also known as vitamin D-binding protein (DBP), is a human plasma glycoprotein (1). Inflammation results in the hydrolysis of terminal galactose and sialic acid of the Gc protein and this is mediated by both membrane-bound β-galactosidase present on activated B-cells and sialidase on T-cells to produce Gc protein-derived macrophage-activating factor (GcMAF) (2). GcMAF has been shown to possess several biological activities, such as macrophage activation, anti-angiogenic activity and antitumor activity (3-7). It is conceivable, therefore, that GcMAF is an immunomodulatory factor potentially useful for the treatment of immune diseases. In this regard, we report that second-generation GcMAF prepared from human serum shows remarkable therapeutic effects in multiple sclerosis (MS) (8, 9).

MS is considered to be an autoimmune, inflammatory and demyelinating disease of the central nervous system (CNS). Typically, MS begins as a relapsing-remitting disease and evolves over time to a chronic secondary progressive condition that can lead to severe disability and even death (10). The number of patients affected with MS has increased to more than two million in 2013 across the world (11). The central role of T cells in the pathogenesis of MS has long been established (12). In addition, B cells also play an important role in the pathogenesis of MS (13). These findings support that abnormal interactions between T cells and B cells are involved in the immunopathogenesis of MS (14).

Since there were limited effective treatment options available for the patient, we performed this case study to elucidate whether GcMAF and oral colostrum MAF is therapeutically effective in the treatment of MS (15).

Case Report

An Australian male developed MS confirmed by lumbar puncture and magnetic resonance imaging (MRI) scan of the brain in 1989 at the age of 45. Thereafter, he was confined to

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Key Words: Immunotherapy, macrophage activating factor (MAF), GcMAF, colostrum MAF, multiple sclerosis, motor dysfunction.

a wheelchair for four years. In 1991, he was treated with pulse steroid therapy to manage symptoms, such as increasing weakness, sensory disturbance, numbness and tingling paresthesia. In 1999, a further episode occurred and then he again received pulse steroid therapy. In 2004, MRI scans showed extensive lesions in the brain and spinal cord, indicating secondary progressive MS. From February 2011, he again became wheelchair-bound and was no longer able to work. At the time, he presented with chronic urinary tract infection, urinary incontinence, severe muscle weakness, muscle pain, head fullness, tinnitus, poor memory, irritability and constipation.

From September 17, 2014, he received 0.5 ml GcMAF (1,500 ng/0.5 ml) intramuscularly or subcutaneously twice weekly. After three weeks of treatment with GcMAF, the following beneficial responses and changes were observed; (a) He slept through the night and got up at 7 am to use the bladder. (b) All medications for pain and urinary bladder control and antibiotics had been discontinued. (c) He had more energy and was able to drive an adapted car. (d) He went to work every day. However, he still had some confusion. By October 31, 2014, the responses to GcMAF treatment after six weeks were observed as follows (Figure 1); (i) The patient was able to walk with assistance for the first time after four years being wheelchair-bound, although, as shown in Figure 1c, leg muscles were small and weak due to being confined to a wheelchair for four years. Moreover, he could also go up and down stairs. (ii) He had complete urinary bladder control without medication, even for bladder infections. (iii) Brain fog was much better and he was animated and happy. Subsequently, the patient was continuing treatment with second-generation GcMAF 0.5 ml, three times weekly and daily oral colostrum MAF.

Discussion

This case study demonstrated that treatment with the second-generation GcMAF markedly improved the motor disability in a patient with MS, suggesting the possibility that GcMAF, an immunomodulator, is useful for the treatment of this disease.

MS is an immune-mediated disorder affecting the CNS that is thought to result from destruction of myelin by autoreactive T cells (16, 17). Several studies, regarding the imbalance of the immune system in both MS and its animal model, have largely focused on $CD4^+$ T-cells as mediators and regulators of this disease. In this regard, $CD4^+$ T cells secreting interferon (IFN)-γ and interleukin (IL)-17 are considered to be key players in MS pathogenesis. In addition, forkhead box P3 $(FoxP3)^+$ regulatory T cells and type 1 regulatory cells secreting IL-10 are also involved in the pathogenesis of MS because of controlling effector T cell activity (18-21). Therefore, MS disease activity and relapse development are ultimately attributed to the imbalance between effector and regulatory cell actions (17). Furthermore, the findings that $CD8^+$ T-cells represent the predominant T-cell population in human MS brain lesions and are oligoclonally expanded at the site of pathology support a pathogenic role for CNS-specific $CD8^+$ T-cells. Furthermore, B cells can produce pro-inflammatory cytokines and are potent antigen presenting cells being involved in the activation of pro-inflammatory T cells. $CD4^+$ T cells are important for the activation of B cells in secondary lymphoid tissues and a relationship between increased T-cell and B-cell activation in blood from patients with MS was reported to be involved in the immunopathogenesis of MS (15). From these viewpoints, the majority of current therapies approved for MS are aimed against the immune system activity and the entry of immune cells into the CNS in order to reduce disability and relapse rates.

MS exhibits chronic destruction of the myelin sheath surrounding axons that leads to degeneration of axons and, eventually, loss of neurons. B cells produce autoantibodies directed against myelin and cause complement-mediated attack on the myelin sheath (14). Then, re-myelination is postulated to restore neuronal function and prevent further neuronal loss and clinical disability in MS, although little is known on the molecular and cellular mechanisms regulating myelination.

MS is associated with several emotional comorbidities, including a high incidence of depressive symptoms. The depressive disorders in MS exacerbate the manifestations of the disease and make its management challenging (18). Although our understanding of the underlying mechanisms that are responsible for the emotional disorders in MS patients is limited, it is important to provide a neurorehabilitative framework. In addition, patients with MS suffer from pronounced physical and cognitive disabilities that are due to focal brain lesions and diffuse demyelination (19).

In this case study, GcMAF, as the modulator of the immune system, exhibited potent therapeutic activity for MS. In particular, physical disability in MS was drastically improved following the administration of GcMAF, indicating that the treatment of GcMAF promoted the incentive of physical rehabilitation in MS with emotional disorders as mentioned above. Moreover, although, at this time, it is not clear how GcMAF precisely modulates the immune system and what the therapeutic mechanism of GcMAF is, it seems likely that GcMAF may influence the imbalance of the immune system and emotional comorbidities. Furthermore, a large-scale clinical study and experimental studies using the animal model of experimental autoimmune encephalomyelitis for MS would be required to clarify the definitive efficacy of GcMAF in MS and the probable mechanism(s) for the pathophysiological actions of GcMAF. Moreover, the examination of brain MRI, physical activity and neuropsychological evaluation will help elucidate further information on therapeutic efficacy of GcMAF in MS.

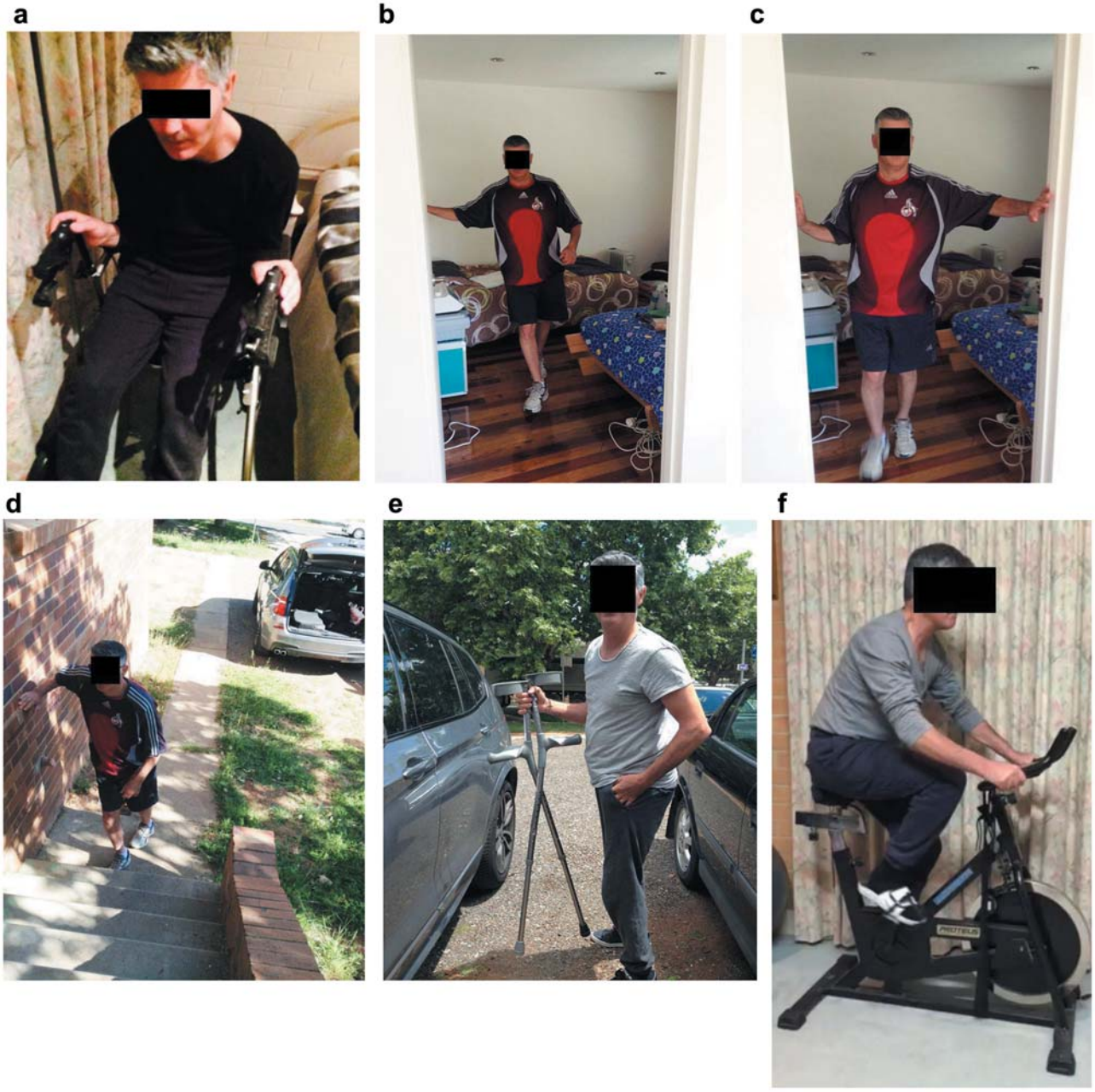

Figure 1. *Effects of GcMAF in a patient with MS. (a): Prior to treatment (September 17, 2014). Wheelchair-bound for 4 years. (b), (c) and (d): After 6 weeks of treatment (October 31, 2014). The patient was able to stand up, walk and climb stairs with assistance for the first time. (e): After 3 months of treatment (December 12, 2014). He was undergoing walking rehabilitation and using walking sticks. (f): At the present time, he was able to peddle on an exercise bike.*

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Received April 5, 2016
Revised May 11, 2016
Accepted May 12, 2016