Guillain Barre Syndrome and Matrix Metalloproteinases

Dash S1, Kamath U1, Pai A2 and Rao P3*
1Department of Biochemistry, Melaka Manipal Medical College, Manipal Campus, Manipal University, India
2Department of Neurology, Kasturba Medical College, Manipal, Manipal University, India
3Department of Biochemistry, Kasturba Medical College, Manipal, Manipal University, India

Abstract

Guillain Barre Syndrome (GBS) is an autoimmune inflammatory neuropathy. It affects all age group of both sexes and can lead to morbidity if untreated. It is usually preceded by an infection and has a fast progression. There are two treatment modalities practiced primarily, plasmapheresis and intravenous immunoglobulin therapy. Matrix metalloproteinases have been indicated to play a role in pathogenesis of GBS by mediating inflammation and disrupting blood nerve barrier. Greater focus needs to be put on these MMP’s as marker enzymes for early detection and/or diagnosis and as targets for therapy.

MMP-9: It is also known as gelatinase B and type IV collagenase. MMP-9 is secreted from neutrophils, macrophages and other transformed cells. It is important in protease and cytokine modulation. MMP-2 and 9 have an intricate relation in the cell where MMP-2 has an important role in protease and cytokine modulation. MMP-9 is secreted from neutrophils, macrophages and other transformed cells. It is important in protease and cytokine modulation. MMP-2 and 9 have an intricate relation in the cell where MMP-2 has an important role in protease and cytokine modulation.

Role of MMP’s in GBS: An ideal model to study GBS has been the EAN or Experimental Autoimmune Neuritis. It has been observed in EAN models that beta-dystroglycans, located at the outermost layer of myelin sheath, is associated with demyelination of the peripheral nerves. This neuritis and beta-DG disruption has been shown to be associated with increased production of MMP-2 and MMP-9 [6]. In another study, MMP-9 levels were correlated with rise in F-wave.

Keywords: Guillain Barre syndrome; Polyneuropathy; Hyporeflex

Introduction

Guillain Barre Syndrome (GBS) is an autoimmune polyneuropathy. There is ascending paralysis seen in this and the onset is rapid, many a times preceded by an infection. Hyporeflex is observed and if respiratory component is involved can lead to death. Both sensory and autonomic nerve involvement is seen [1]. Matrix metalloproteinase (MMP’s) are the biggest family of extra cellular matrix degrading enzymes. They are zinc dependent proteases which have a role in general physiology, development and in pathological processes like acting as mediators of inflammation [2]. MMP’s participate in physiological processes like inflammation, immunity, neurite growth, through pro-neurotropic factors and chemokines/cytokines. In the Central Nervous System (CNS), their role in neurogenesis, axonal guidance and learning and memory has been delineated [3]. A central role of MMP’s and cytokines in mediating inflammatory demyelinating diseases of Central Nervous System (CNS) and Peripheral Nervous System (PNS) has been indicated, with GBS being an example of the latter.

MMP – Role in Development and Normal Physiology

MMP’s were discovered owing to their collagenolytic properties in amphibian metamorphosis. MMP’s are Zn and Ca dependent endopeptidases, active at neutral pH which are involved in many developmental processes like branching morphogenesis, angiogenesis, wound healing, and extracellular matrix degradation. Synthesized as propeptide, a removal of peptides from amino-terminal end activates them. About 23 families of MMP’s, which share common functional domains and activation mechanism have been found (Figure 1) [4].

MMP’s associated with GBS

MMP-2: Matrix metallopeptidase-2 is also known as gelatinase A and a 72 kDa type II collagenase. Other than its role in degrading and remodelling extra cellular matrix, its role has been identified in multiple sclerosis. Not only does monocyte express MMP-2, astrocytes, microglia and macrophages produce it too. MMP-2 has a role in blood brain barrier disruption, which helps in movement of immune cells into the CNS [5].

MMP-7: Matrix metalloproteinase 7 is also called as matrilysin. Its expression has been found to be increased during upregulation of microglia and macrophage cells. The mechanism by which it induces lesions is mediated by its induction in infiltrating macrophages.

*Corresponding author: Dr. Pragna Rao, Department of Biochemistry, Kasturba Medical College, Manipal, Manipal University, India, Tel: 08202922532; E-mail: drpragnarao@gmail.com

Received May 13, 2015; Accepted May 26, 2015; Published May 29, 2015


Copyright: © 2015 Dash S, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
Estimating MMP2, 7 and 9 could serve as an early indicator. It has and findings. MMP's by the virtue of them playing an important role in the pathogenesis of GBS [9].

These abnormalities cause immune cells to adhere and migrate across the endothelium of immune cells. This phenomenon has been indicated in human model [8].

Cellular immune reaction in GBS Cellular is intricately linked with a rise in TNF-alpha, a proinflammatory cytokine, a decrease of TGF-B1, an anti-inflammatory cytokine and an increase in MMP-9 levels. These abnormalities cause immune cells to adhere and migrate across the endothelium of immune cells. This phenomenon has been indicated in pathogenesis of GBS [9].

Future Direction

It is highly imperative that detection of Guillain Barre Syndrome occurs early. The progression of the disease is fast and differential diagnosis is a challenge because of non-specificity of nerve Conduction Studies and the various other disorders that manifest similar symptoms and findings. MMP's by the virtue of them playing an important role in pathogenesis of GBS could be candidate diagnostic markers. Estimating MMP2, 7 and 9 could serve as an early indicator. It has also been suggested that MMP9: TIMP-1 (Tissue Inhibitors of Metallo Proteinases) levels would be a suitable and easily measurable marker of inflammation [10].

The treatment modality of GBS currently involves two choices plasmapheresis and intravenous immunoglobulin (IVIg) therapy. However the damage caused if the progression of disease is fast cannot be reversed. MMP's can be candidate markers for treatment. Inhibition of these MMP's could slow down the inflammatory process in peripheral nervous system. In the past, Captopril, a MMP inhibitor has been used to inhibit MMP 2 and 9 and has shown improvement in clinical signs [11,12]. Further research needs to be carried out to come up with new drugs that alter the MMP induced process of neuropathy and thereby reduce the quick progression of GBS.

References