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Case Report
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Recurrent Optic Neuritis as the First Presentation of Monoclonal Gammopathy of Undetermined Significance (MGUS): A Case Report

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Abstract

Monoclonal Gammopathy of Undetermined Significance (MGUS), which can be asymptomatic, is a premalignant proliferative disorder of plasma cells. The peripheral nervous system may be involved in MGUS, causing a monoclonal gammopathy associated peripheral neuropathy. However, involvement of the Central Nervous System (CNS) in MGUS was rarely reported. Here we report a rare case of recurrent optic neuritis, as the first clinical presentation of MGUS, in an otherwise healthy male patient. He was treated with intravenous high-dose methylprednisolone for acute attacks and Rituximab as maintenance therapy. The patient's vision was recovered, and he did not experience any other attack in one year of follow-up.

Keywords: MGUS; Optic neuritis; Rituximab

Introduction

Monoclonal Gammopathy of Undetermined Significance (MGUS), which can be asymptomatic, is a premalignant proliferative disorder of plasma cells. It is defined by the presence of serum monoclonal immunoglobulin <3 g/dL, plasma cells in the bone marrow <10%, and absence of end-organ damage. There are three distinct types of MGUS based on the involved immunoglobulin: Non-IgM, IgM, and light-chain, each with a risk of progression to a malignant plasma cell dyscrasia or lymphoproliferative disorder. It is not rare for MGUS to be an incidental finding, but it can be correlated with shorter life expectancy even in the absence of malignancy [1].

Previous studies showed some associations between MGUS and increased fracture risk, renal impairment, secondary immunodeficiency, infections, thromboembolism, and cardiovascular diseases. The peripheral nervous system may be involved in MGUS, causing a monoclonal gammopathy associated peripheral neuropathy [2,3]. However, involvement of the Central Nervous System (CNS) in MGUS was rarely reported. Here we report a rare case of recurrent optic neuritis, as the first clinical presentation of MGUS, in an otherwise healthy male patient.

Case Presentation

A 54-year-old man was presented to the neurology clinic with a headache and Blurred vision in his left eye. The patient's symptoms had begun following psychological stress. Headache was generalized and oppressive in nature and blurred vision was progressive and accompanied by eye pain. The patient underwent LASIK Eye Surgery four months ago due to hyperopia. He recovered from surgery and had normal visual acuity (10/10). He did not mention any other medical or surgical history. In fundoscopy papilledema was evident. Other neurological examinations were normal.

Magnetic Resonance Imaging (MRI) of the brain and cervical spine and Positron Emission Tomography (PET) scans were normal. Increased latency of Visual-Evoked Potentials (VEPs) was found after stimulation of the left eye. All performed blood investigations and vasculitis panels were normal. Cell-based antibody assays for anti-Aquaporin-4 Antibody (AQP4-Ab) and antibody against Myelin Oligodendrocyte Glycoprotein (anti-MOG-Ab) were also reported negative. The patient underwent a diagnostic lumbar puncture which determined a normal opening pressure of Cerebrospinal Fluid (CSF). CSF examination showed albumin 28.2 mg/dl (normal values <30 mg/dl), IgG index 1.43 (normal values <0.65), no pleocytosis and no elevated protein level. The

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oligoclonal band assay detected no heterologous band in CSF.

The patient was diagnosed with left optic neuritis and treated with three days of intravenous high-dose methylprednisolone (1000 mg daily). We performed serum protein electrophoresis and immunofixation for further investigation. Serum protein electrophoresis revealed a peak in the gamma-globulin region. Serum Fractions levels were as follows: Albumin 4.8 g/dl (4 g/dl to 4.8 g/dl), Alpha-1 0.2 g/dl (0.2 g/dl to 0.4 g/dl), Alpha-2 0.6 g/dl (0.5 g/dl to 0.9 g/dl), Beta-1 0.4 g/dl (0.3 g/dl to 0.5 g/dl), Beta-2 0.3 g/dl (0.2 g/dl to 0.5 g/dl), Gamma 1.6 g/dl (0.8 g/dl to 1.4 g/dl). In immunofixation, the Gamma-globulin band was highlighted in Kappa and IgG region that is compatible with monoclonal Kappa IgG. A Bone Marrow Aspiration (BMA) and Biopsy (BMB) showed the presence of normocellular marrow with trilineage hematopoiesis and 6% to 7% polyclonal plasma cells. IHC staining showed CD138, Kappa, Lambda, and Pax5 positive. BMA immunophenotyping revealed a population in monocytes gates which express CD138, CD38, negative CD19, CD45 (Myeloma cell) about 1% to 1.5% of all nucleated cells. There was no increase in myeloblast and B-lymphoblast. There was no clinical manifestation associated with plasma cell myeloma such as lytic bone lesions, and the amount of monoclonal component was <3 g/dl. According to these results, he was diagnosed with optic neuritis with MGUS. The patient's vision improved after high-dose methylprednisolone therapy. Rituximab was started as maintenance therapy at a dosage of two intravenous infusions (2 weeks apart) of 1,000 mg. Within one week of Rituximab induction, the patient had another optic neuritis attack in the opposite eye. Intravenous high-dose methylprednisolone therapy was repeated for acute attack and then Rituximab has been continued every six months upon results of CD19 flow-cytometry. After 12 months of starting rituximab, the patient had no new symptoms.

Discussion

The neurologic complications of MGUS have been reported rarely. Subclinical optic neuropathies with increased latencies of Visual Evoked Potentials (VEPs) were reported in MGUS patients with monoclonal anti-MAG M-protein antibodies [4], MAG is a component of both central and Peripheral Nervous System (PNS) myelin. Hence, both CNS and PNS involvement in MGUS may be induced by monoclonal antibodies against anti-MAG M proteins. On the other hand, brain imaging abnormalities were also reported in some patients with MGUS associated Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [5].

The CNS involvement of MGUS in form of a chronic disseminated demyelinating disorder was previously described. Monoclonal IgM/λ gammopathy, with anti-myelin and anti-nuclear reactivity [6], and IgG/λ monoclonal gammopathy [7] were reported in patients with MGUS and MS. Earlier reports showed that some MGUS patients with CNS involvement fulfill the latest diagnostic criteria of MS [8], Acute Disseminated Encephalomyelitis (ADEM) [8], or Neuromyelitis Optical [9]. Other studies have reported MGUS patients with CNS disorders such as cerebellar atrophy [10], Parkinson's disease [11], and multiple system atrophy [11]. However, optic neuritis as the only presentation of an undiagnosed MGUS is very rare.

Conclusion

In this report, we presented a patient with recurrent optic neuritis diagnosed with MGUS. He was treated with intravenous high-dose methylprednisolone for acute attacks and Rituximab as maintenance therapy. The patient's vision was recovered, and he did not experience any other attack.

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