Annals of Clinical Case Reports

Case Report
Published: 11 Apr, 2019

Optic Neuritis as the First Sign of MGUS - Clinical Presentation

Zavoreo Iris, Miljenka-Jelena Jurašić and Bašić Kes Vanja*

Department of Neurology, Sestre Milosrdnice University Hospital, Croatia

Abstract

Monoclonal gammopathies are a heterogeneous group of disorders, ranging from the subclinical Monoclonal Gammopathy (MGUS) to malignant systemic disorders. The majority of these paraproteins are IgG with less than 15% being IgM. In patients with peripheral neuropathy, particularly those with demyelinating neuropathies IgM monoclonal gammopathy are much more common. Optic neuritis is an inflammatory, demyelinating condition that causes acute, usually monocular, visual loss. Optic neuritis is the presenting symptom in 15% to 20% of multiple sclerosis patients, but it can also be a secondary presentation of some other disorders. We will describe the case of 37 year old woman who presented with retrobulbar pain and visual field disturbances of the left eye. Spinal tap revealed oligoclonal bands type 5 suggesting haematological disorder. Serum protein electrophoresis showed IgG kappa paraprotein. After diagnostic workup, diagnosis of subclinical Monoclonal Gammopathy (MGUS) was established. Retrobulbar neuritis was treated with corticosteroid therapy (methylprednisolonum, 1 g) for 3 days with significant regression of pain and visual loss.

Keywords: Optic neuritis; Visual evoked response; IgG gammopathy; MGUS; Diagnostic workup

Introduction

Monoclonal gammopathies are caused by proliferation of monoclonal plasma cells or B lymphocytes. Clinical picture varies from the subclinical Monoclonal Gammopathy of Uncertain Significance (MGUS), to malignant systemic disorders [1,2]. IgM Monoclonal Gammopathy is much more common in patients with peripheral, particularly demyelinating neuropathies. Peripheral neuropathy associated with multiple myeloma can be due to perineural or perivascular IgG kappa deposition [3]. Optic neuritis is an inflammatory, demyelinating condition that causes acute, usually monocular, visual loss. It can be a secondary presentation of ischemic optic neuropathy, infections, inflammation, genetic disorders, neoplasms, local compression, or a consequence of toxic/metabolic disorders or the first symptom of multiple sclerosis (15% to 20% patients) [4].

Case Presentation

We would like to present the case of a 37 year old woman who was admitted to our department due to almost constant retrobulbar pain and visual field disturbances of the left eye. She noticed the first symptoms six months prior to overt clinical presentation. They were most conspicuous in the morning with regressive dynamic during the day. Her neurological examination showed no alterations apart from intermittent pain of the left eye, most prominent behind the eye, with decreased visual acuity and change in colour perception. In her personal history she reported occasional migraines associated with menstrual cycle from childhood that responded well to non-steroid analgesics. From family history: patient's mother died due to uterine cancer, her father died due to pancreatic cancer, and her daughter had already established MGUS diagnosis.

Standard laboratory workup was performed. Complete blood count and biochemistry analysis showed normal findings. MRI of the brain showed slight increase of signal in coronal STIR (short T1 inversion recovery) sequence of the left optical nerve suggesting optic neuritis of the left eye (Figure 1). There was no gadolinium contrast enhancement. MRI of the cervical spine showed normal finding. Thyroid hormones and tumor markers were within the normal range. Spinal tap showed neither pleocytosis nor protein elevation, and oligoclonal bands were type 5 suggesting hematological disorder. Serum electrophoresis and immunofixation, serum free light chain assay, and quantification of immunoglobulins were performed to identify them as IgG kappa paraproteins.

OPEN ACCESS

Correspondence:
Miljenka-Jelena Jurašić, Department of Neurology, Sestre Milosrdnice University Hospital, Vinogradska 29, 10000, Zagreb, Croatia; Tel: 38513787740; Fax: 38513768282; E-mail: mjjurasic@gmail.com

Received Date: *15 Mar 2019*
Accepted Date: *05 Apr 2019*
Published Date: *11 Apr 2019*

Citation:
Iris Z, Jurašić M-J, Vanja BK. Optic Neuritis as the First Sign of MGUS - Clinical Presentation. Ann Clin Case Rep. 2019; 4: 1646.

ISSN: 2474-1655

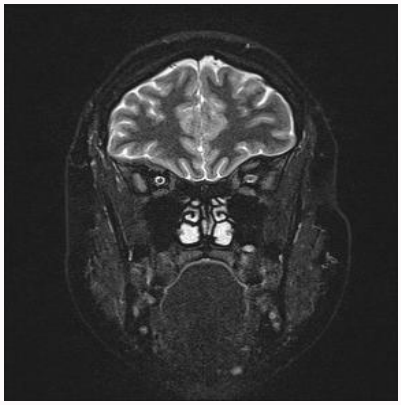

Figure 1: MRI, STIR sequence, showing optic neuritis of the left eye.

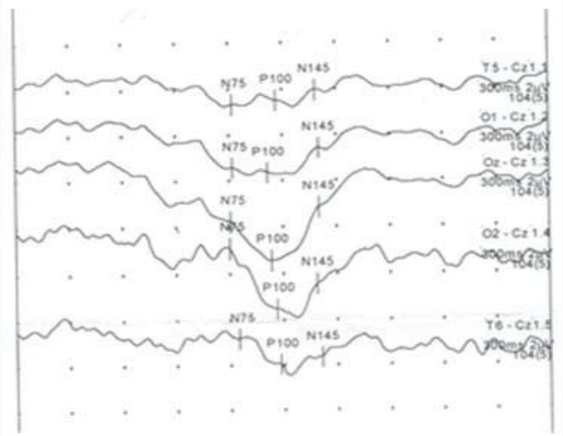

Figure 2: VER of the left eye showing delay in P100 component.

Consequentially, abdominal ultrasound, breast ultrasound and chest X-ray was performed and showed normal findings. Metastatic bone survey was performed by means of X-ray and finding was highly suspicious for bone lesions in the neck region of the right femur as well as parietal region on craniogram. Therefore MRI of the pelvis and both femurs was performed and it did not prove any lytic bone lesions. MRI of the head, also, showed no bone lesions. Visual Evoked Response (VER) showed a delay in P100 response component (Figure 2) that is a manifestation of slowed conduction of the left optic nerve as a result of demyelination. Lastly, aquaporin-4-specific serum antibodies were negative.

After hematological workup, diagnosis of subclinical Monoclonal Gammopathy (MGUS) was established. Optic neuritis was treated with corticosteroid therapy (methylprednisolonum, 1g) for 3 days with significant regression of pain and increase in visual acuity. At further follow up, 6 months after, our patient had no signs of visual disturbances. Visual field showed normal findings. Hematologic disorder was, also, under control requiring no active treatment. Control VER detected a normal finding (Figure 3).

Discussion and Conclusion

Monoclonal Gammopathy are heterogeneous group of disorders, ranging from MGUS, to malignant systemic disorders such as multiple myeloma, amyloidosis, Waldenstrom's macroglobulinemia and POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M-spike or monoclonal gammopathy and skin changes) [2].

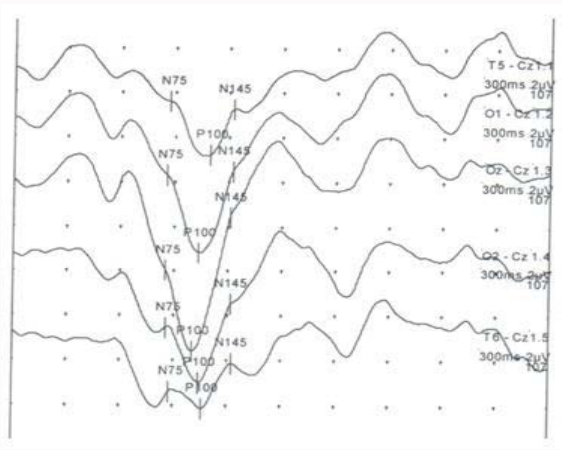

Figure 3: Control VER after six months – delay in normal finding.

Monoclonal Gammopathy are caused by proliferation of monoclonal plasma cells or B lymphocytes, they are characterized by the proliferation and deposition of M proteins or paraproteins that are formed by a single heavy chain (M, G or A) and a light chain (kappa or lambda) [2]. Monoclonal Gammopathy occur in 1% of healthy individuals older than 25 years, without an associated plasma cell disorder [5,6]. The majority of these paraproteins are IgG with less than 15% being IgM. In patients with peripheral neuropathy, particularly those with demyelinating neuropathies IgM monoclonal gammopathy are much more common [5]. Peripheral neuropathy associated with monoclonal gammopathy is rare, but important cause of neuropathy because of serious, yet treatable underlying disease [3]. IgG monoclonal gammopathy (35% of patients) and IgA monoclonal gammopathy (15% of patients) are rarely associated with specific neuropathies. However, usually IgM Monoclonal Gammopathy of uncertain significance (MGUS) is the most commonly found Monoclonal Gammopathy associated with neuropathy (50% of patients) [6]. Peripheral neuropathy associated with multiple myeloma can be caused by either perineural or perivascular IgG kappa deposition [7]. Underlying etiology of peripheral neuropathy in patients with monoclonal gammopathy is not well understood [3]. Some evidence suggests that the M protein cross-reacts with a neural antigen, such as 4-Methylumbelliferyl β-D-galactopyranoside (MUG)- a glycoprotein found in the myelin sheath of both the central and peripheral nervous systems, sulfurizing glucuronyl paragloboside and sulfatide resulting in activation of complement and nerve damage. Also, there is possible secondary toxic or metabolic influence on nerve damage, but this is still unclear [3]. Additionally, the risk of developing MGUS appears to be higher among individuals with first degree relatives with either multiple myeloma (RR 2.0) or MGUS (RR 3.3) [6,8]. Diagnosis of monoclonal gammopathy is usually incidental and it is commonly established during evaluation of another disorder such as unexplained proteinuria, bone loss, elevated total protein in blood or peripheral neuropathy of undefined etiology [8,9]. In evaluation of patients suspected for having monoclonal gammopathy, the following work up should be performed: complete blood count, serum and urine electrophoresis and immunofixation, serum free light chain assay, quantification of immunoglobulin's, metastatic bone survey (X-ray, computerized tomography-CT or magnetic resonance imaging-MRI evaluation and positron emission tomography-PET/CT) [9]. According to the results of aforementioned workup, it is important to distinguish MGUS from more advanced plasma cells

dyscrasia such as multiple myeloma (smouldering or symptomatic), Waldenstrom's macroglobulinemia (smouldering or symptomatic), idiopathic Bens Jones proteinuria or primary amyloidosis [10].

Optic neuritis is an inflammatory, demyelinating condition that causes acute, usually monocular, visual loss. Optic neuritis is the presenting symptom in 15% to 20% of MS patients, but it can be also be the presentation of ischemic optic neuropathy, infections, inflammation, genetic disorders, neoplasms, local compression, various demyelinating CNS disorders or a consequence of toxic/metabolic disorders. Visual deficits can present as changes in visual acuity, decrease in contrast sensitivity, colour vision reduction or various defects of the visual field [4]. In general, optic neuritis is a clinical diagnosis based on medical history, and examination findings including ophthalmologic evaluation as well as MRI of the brain and orbits with gadolinium contrast. Spinal tap is not an essential diagnostic test in optic neuritis, but it should be performed in atypical cases. Patients with acute optic neuritis in 60% to 80% can have abnormalities in the Cerebrospinal Fluid (CSF) finding including elevated lymphocyte count (10-100) and elevated protein, and also myelin basic protein elevation in about 20% of patients, IgG synthesis can be found in 20% to 36% patients and oligoclonal bands in 56% to 69% of patients [4]. Other testing includes fluorescein angiography, visual evoked responses, optical coherence tomography, and aquaporin-4-specific serum antibodies [4].

From this case we have learned that optic neuritis can be the first sign of multiple sclerosis, but also a rare complication of a hematological disorder. In such cases wide diagnostic workup should be performed in order to establish the true diagnosis.

References

1. Rajkumar SV, Kyle RA, Buadi FK. Advances in the diagnosis, classification, risk stratification, and management of monoclonal gammopathy of undetermined significance: Implications for recategorizing disease entities in the presence of evolving scientific evidence. Mayo Clin Proc. 2010;85(10):945-8.
2. Bird J, Behrens J, Westin J, Turesson I, Drayson M, Beetham R, et al. UK Myeloma Forum (UKMF) and Nordic Myeloma Study Group (NMSG): Guidelines for the investigation of newly detected M-proteins and the management of monoclonal gammopathy of undetermined significance (MGUS). Br J Haematol. 2009;147(1):22-42.
3. Kelly JJ. Peripheral neuropathies associated with monoclonal gammopathies of undetermined significance. Rev Neurol Dis. 2008;5(1):14-22.
4. Toosy AT, Mason DF, Miller DH. Optic neuritis. Lancet Neurol. 2014;13(1):P83-99.
5. Therneau TM, Kyle RA, Melton LJ 3rd, Larson DR, Benson JT, Colby CL, et al. Incidence of monoclonal gammopathy of undetermined significance and estimation of duration before first clinical recognition. Mayo Clin Proc. 2012;87(11):1071-9.
6. Wadhera RK, Rajkumar SV. Prevalence of monoclonal gammopathy of undetermined significance: A systematic review. Mayo Clin Proc. 2010;85(10):933-42.
7. Rajabally YA. Neuropathy and paraproteins: Review of a complex association. Eur J Neurol. 2011;18(11):1291-8.
8. Greenberg AJ, Rajkumar SV, Vachon CM. Familial monoclonal gammopathy of undetermined significance and multiple myeloma: Epidemiology, risk factors, and biological characteristics. Blood. 2012;119(23):5359-66.
9. Vrethem M, Cruz M, Wen Xin H, Malm C, Holmgren H, Ernerudh J. Clinical, neurophysiological, and immunological evidence of polyneuropathy in patients with monoclonal gammopathies. J Neurol Sci. 1993;114(2):193-9.
10. Kyle RA, Durie BG, Rajkumar SV, Landgren O, Blade J, Merlini G, et al. Monoclonal gammopathy of undetermined significance (MGUS) and smouldering (asymptomatic) multiple myeloma: IMWG consensus perspectives risk factors for progression and guidelines for monitoring and management. Leukemia. 2010;24(6):1121-7.