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Case report

Successful long-term treatment of paraneoplastic optic neuropathy with mycophenolate mofetil, prednisone, and plasmapheresis

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ABSTRACT

Purpose: To report long-term follow-up of a case of paraneoplastic optic neuropathy (PON) successfully treated with combination therapy.
Observations: We present a confirmed case of PON from cutaneous melanoma with nearly six years of meticulous follow-up in which vision was preserved and disease remission was successfully induced with combination mycophenolate mofetil, prednisone, and plasmapheresis therapy.
Conclusions and importance: Treatment of PON and long-term follow-up are not well described in the literature. In our case of PON, vision was preserved and disease remission was achieved with mycophenolate mofetil, prednisone, and plasmapheresis. Such information may be useful for future cases of PON.

1. Introduction

Paraneoplastic optic neuropathy (PON) is a rare condition that has been associated with cutaneous melanoma.[1] Increasing incidence of cutaneous melanoma along with improved recognition of this disease entity may result in higher prevalence rates. Optimal treatment of PON has not been well-described in the literature, and despite removal of inciting lesions, this vision-threatening disease entity can progress rapidly.[2] Several treatment regimens including corticosteroids, plasmapheresis, and intravenous immunoglobulin have been used, but clinical responses have been disappointing with no published long-term follow-up.[2,3] We provide herein six year follow-up of a confirmed case of PON from cutaneous melanoma in which disease remission along with visual field recovery was successfully achieved with combination mycophenolate mofetil, prednisone, and plasmapheresis therapy.

2. Case report

A 67-year-old female presented in July 2010 with photopsias and floaters in her right eye (OD). Visual acuity (VA) was 20/30 OD and 20/20 left eye (OS) with a brisk afferent pupillary defect OD and only 3 of 13 Ishihara color plates correctly identified (13 of 13 were identified OS). Vitritis, venous sheathing, and optic disc leakage were present (Fig. 1). Findings were normal on the following: complete blood cell count, metabolic panel, erythrocyte sedimentation rate, chest radiography, and magnetic resonance imaging of the head and orbit. Serologies were negative for hepatitis, syphilis, Lyme disease, and toxoplasmosis, and polymerase chain reaction testing of aqueous fluid was negative for herpes simplex virus, cytomegalovirus, and varicella-zoster virus.[1] Tuberculin purified protein derivative testing results were negative. Full-field electroretinogram (ERG) findings were unremarkable. A paraneoplastic panel including collapsing response mediator protein 5 IgG were negative. Visual evoked testing (VEP) demonstrated delayed conduction latencies. Optical coherence tomography of the retina was unremarkable. Despite treatment with oral corticosteroids, visual field loss continued. The patient underwent positron emission tomography-computed tomography scanning which demonstrated an active right groin lymph node. Subsequent biopsy revealed metastatic cutaneous melanoma. In the setting of metastatic melanoma with brisk APD, loss of color vision, reduced conduction latency on VEP testing, rapid visual field loss, and unremarkable ERG, a diagnosis of PON was made.[1]

Despite complete removal of the inciting lesion, the patient's visual field loss continued (Fig. 2). Consequently, the patient was started on mycophenolate mofetil 2 grams/daily and 60 mg oral prednisone (tapered to 10 mg over 3 months). Progressive bilateral visual field loss continued (Figs. 2 and 3) and mycophenolate was

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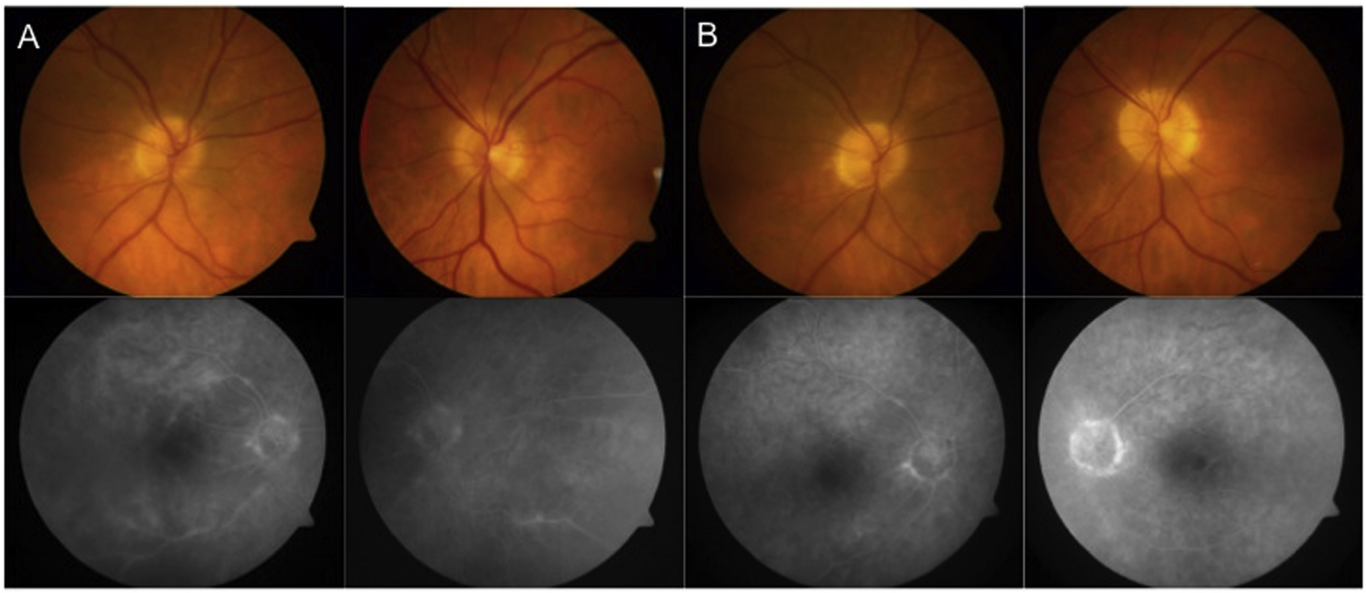

Fig. 1. Color fundus photographs and fluorescein angiography of both eyes at A) initial presentation demonstrating optic disc hyperemia and extensive vascular leakage, and B) most recent follow-up after stopping plasmapheresis demonstrating resolved optic nerve hyperemia and vascular leakage. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

increased to 3 grams/daily. Due to persistent visual decline, five months after initiation of immunosuppressive agents, plasmapheresis was implemented initially at every 4 weeks and then increased to every 2 weeks.

The patient's clinical course stabilized and subjective VA and mean deviation (MD) improved on serial visual field testing during the first year of combination treatment (Fig. 2). During the 2nd year of treatment, with continued improvement in MD on serial visual

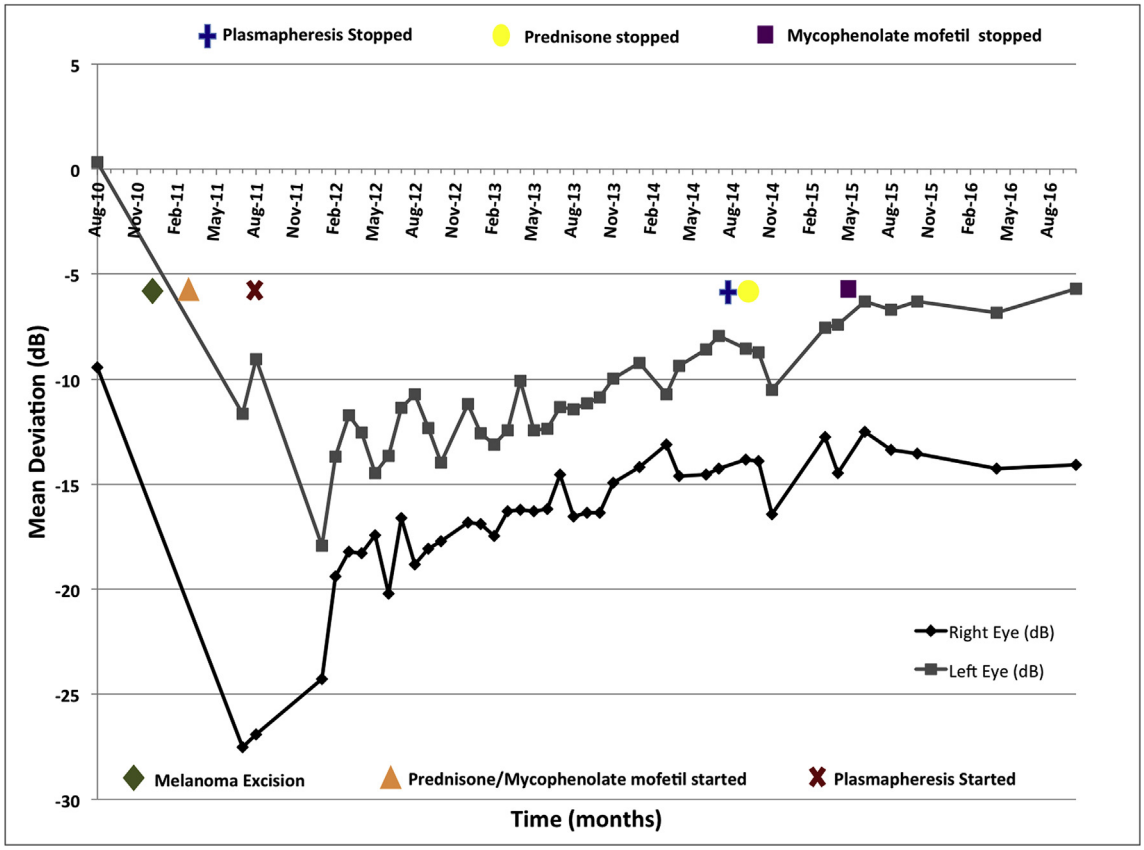

Fig. 2. Graph of mean deviation (MD) changes on serial 10-2 Humphrey visual fields (HVF) from initial presentation (August 2010) through completion of plasmapharesis (April 2014), to last follow up examination. MD improved from −27.52 dB OD (July 2011) to −14.06 dB OD (October 2016) and from −17.93 dB OS (January 2012) to −5.71dB OS (October 2016).

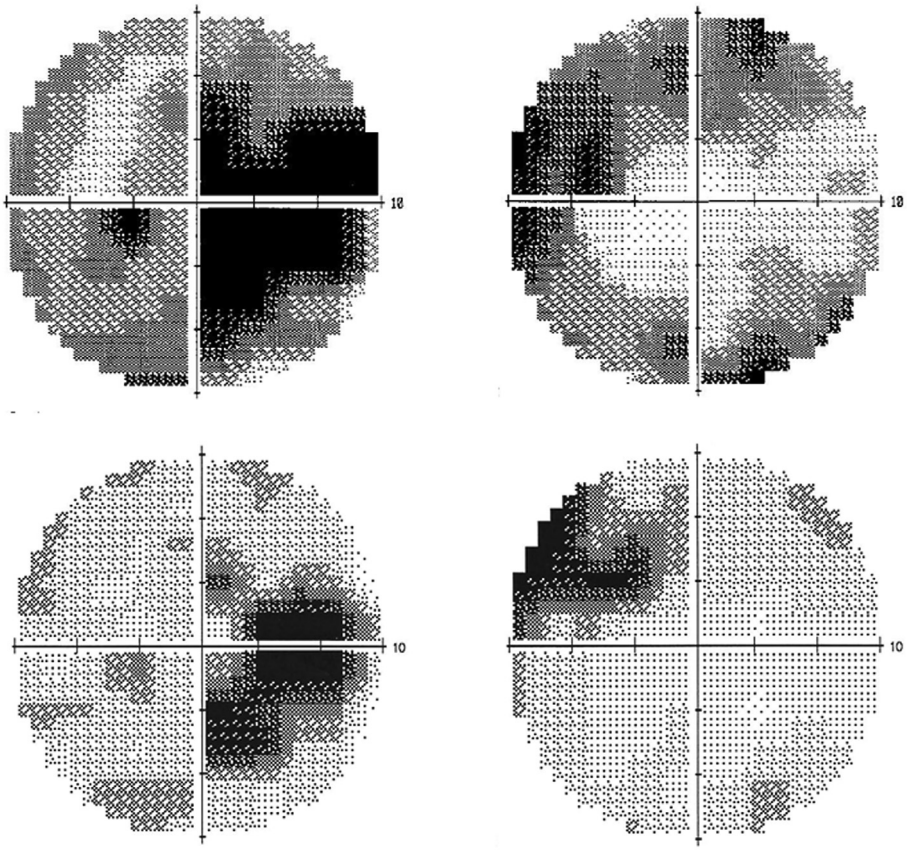

Fig. 3. Representative 10–2 automated Humphrey visual fields taken on 2-13-12 (top row) and 1-6-15 (bottom row) at the same location with the same machine. Mean deviation improved from −19.40 to −11.97 in the right eye (left side) and from −13.69 to −7.60 in the left eye (right side) with treatment.

field testing, the frequency of plasmapheresis was reduced to monthly and prednisone was tapered to 5mg/daily. During the 3rd year of treatment, plasmapheresis was stopped and mycophenolate mofetil and prednisone were continued. Prednisone was later discontinued 5 months after cessation of plasmapheresis, and mycophenolate mofetil was discontinued one year thereafter. Visual acuity remained stable at 20/40 OD and 20/25 OS with no evidence of recurrent visual field loss after more than 1 full year off treatment (Figs. 2 and 3).

3. Discussion

PON remains a rare disease entity in ophthalmology, however, heightened clinical suspicion of PON may allow for more timely intervention and subsequently improved morbidity and mortality.[4] Unfortunately, despite complete surgical removal of inciting lesions, relentless vision loss and clinical deterioration can continue. To date, there exists no consensus regarding optimal treatment for PON, but the authors describe a case of successful clinical remission with aggressive combination therapy.

The pathogenesis of PON is poorly understood, but the best available evidence suggests that it results from the production of autoantibodies to neuronal proteins such as collapsin response-mediator protein-5 (CRMP-5) with consequent inflammation.[2,3] Thus, combination treatment that employs various mechanisms of action remains appealing due to synergistic potential; this strategy is frequently employed in recalcitrant uveitis as well as autoimmune disease cases.[5]

Prednisone is a strong inhibitor of inflammatory mediators such as prostaglandins and leukotrienes. Inhibition of these molecules may facilitate reestablishment of the blood-brain barrier, which is imperative in restoring central nervous system immune privilege. Mycophenolate mofetil is an antimetabolite that inhibits guanosine nucleotide synthesis, which is required for cellular proliferation. This drug is often utilized due to its proven efficacy in preventing transplant rejection and controlling autoimmune disease. Thereby, mycophenolate mofetil's inhibition of proliferating B-cells may explain a potential therapeutic effect in PON. Plasmapheresis is a form of therapeutic apheresis in which plasma is removed and replaced with donor plasma or normal saline and albumin. It is hypothesized to remove autoantibodies, circulating immune complexes, and cytokines contributing to autoimmune processes. While we cannot rule out the possibility that plasmapheresis alone may have been effective, it was not until the administration of these three treatments in concert that the clinical course and visual symptoms appeared to stabilize.

4. Conclusions

In summary, the authors describe a case of PON successfully treated with combination mycophenolate mofetil, prednisone, and plasmapheresis therapy. Greater awareness of this potential therapeutic regimen may help guide treatment in future cases.

Patient consent

Written consent to publish the report was obtained from the patient.

Acknowledgments and disclosures

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Conflict of interest

None of the authors have any financial disclosures.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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