

Bilateral Optic Neuritis after Inactivated Influenza Vaccination

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KEY WORDS: bilateral optic neuritis, influenza vaccination, optical coherence tomography (OCT), retinal nerve fiber layer (RNFL), H1N1

IMAJ 2012; 14: 705-707

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Adult optic neuritis is usually a monocular condition. The presentation of bilateral optic neuritis suggests a systemic cause. We present a case of bilateral optic neuritis following the H1N1 trivalent influenza vaccination.

PATIENT DESCRIPTION

An 18 year old white male presented to our department with a progressive visual loss that had emerged 2 weeks earlier. The visual complaints were associated with headache and pain upon ocular movements. The patient's past medical history was negative and no history of any preceding illness was reported. He was not taking any medication and did not smoke or drink alcohol. There was no history of allergy or cat bite.

One month prior to his admission he had received inactivated influenza vaccine trivalent types A and B – Vaxigrip® (Sanofi Pasteur, Lyon, France). The strains for the 2010–2011 season included: A/California/7/2009 (H1N1)-like strain, A/Perth/16/2009 (H3N2)-like strain and B/Brisbane/60/2008. The vaccine did not contain an immunologic adjuvant but only thimerosal, formaldehyde, triton

X-100, and trace amounts of neomycin as preservatives and stabilizers.

Upon admission best corrected visual acuity in his right eye was 6/60 and in his left eye 6/30. A trace right relative afferent pupillary defect with full range of extraocular movements and decreased saturation for red were noted in the right eye. Anterior segments were normal in both eyes. Optic disks were swollen in both eyes with congestion of retinal veins as well as blurring of disk margins. Other than those retinal findings, examination was within normal limits. The patient was put on intravenous Solu-Medrol® (methylprednisolone) 250 mg four times a day for 3 days followed by prednisone tablets 1 mg/kg a day.

Medical investigations included antinuclear antibody/anti-neutrophil cytoplasmic antibody, erythrocyte sedimentation rate, complete blood cell count, prothrombin time, partial thromboplastin time, hepatitis B and C viruses, human immunodeficiency virus, cytomegalovirus, immunoglobulins G, A and M, herpes simplex virus 1+2, varicella zoster virus, complement C3 and C4, anti-citrullinated protein antibody, anti-dsDNA antibody, anti-cardiolipin antibody, angiotensin-converting enzyme, *Treponema pallidum* hemagglutination, rapid plasma regain, toxoplasma IgG+IgM, creatinine, blood urea nitrogen, glucose, sodium, inorganic phosphate, alanine and aspartate aminotransferases, bilirubin, alkaline phosphatase, albumin, creatine kinase, cholesterol, C-reactive protein, amylase, lactate dehydrogenase – all of which were within normal limits. Epstein-Barr virus

IgG was found positive. Magnetic resonance imaging of the brain and orbits on admission with and without gadolinium enhancement showed no sign of demyelination plaques but revealed thickening of the intracranial portion of both optic nerves, more so on the right. Optical coherence tomography of the retinal nerve fiber layer showed increased thickness in both eyes due to edema of the inflamed optic nerves.

Follow-up OCT-RNFL performed 6 months later demonstrated subtle signs of optic atrophy in the superior and inferior quadrants in the right eye, and in the superior quadrant only in the left [Figure]. Visual field with excellent reliability indexes was normal except for slight enlargement of the blind spot in both eyes. Follow-up visual fields were normal.

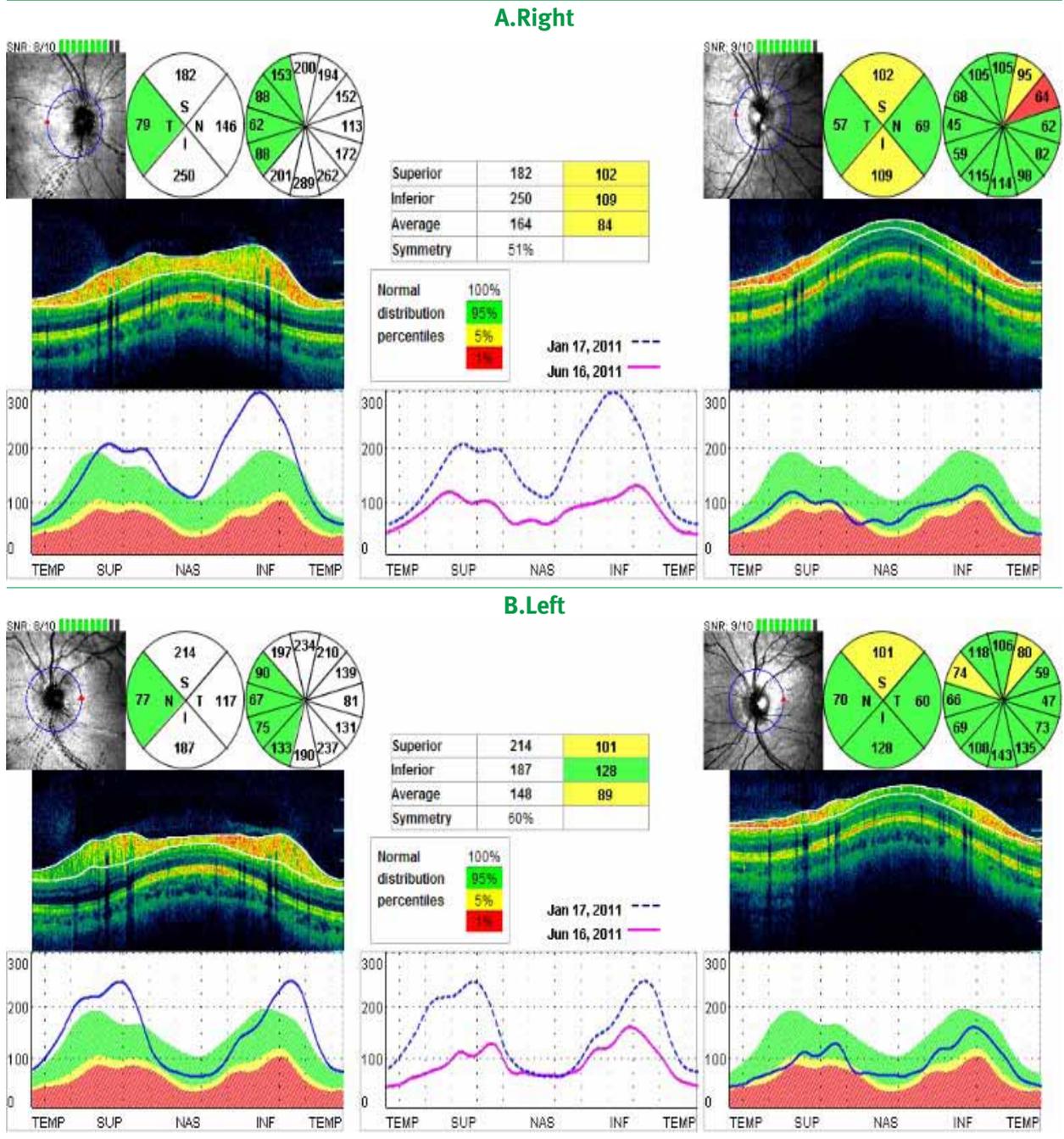
Treatment with intravenous Solu-Medrol led to complete resolution of headache and eye movement-associated pain, along with visual acuity improvement to 6/12 in the right and 6/7.5 in the left eyes. During 3 months of follow-up the patient's vision improved to 6/6 in each eye and treatment was gradually tapered off.

COMMENT

Vaccination-associated neuropathy is known to occur in approximately one in 100,000 cases. [1]. Influenza vaccination-associated optic neuropathy is a rare occurrence and its diagnosis is one

IgG = immunoglobulin G
OCT-RNFL = optical coherence tomography-retinal nerve fiber layer

Serial OCT-RNFL showing swelling of RNFL upon admission and subsequent thinning 6 months later, as shown in the comparative central graph for both eyes [A and B]. Thinning is more pronounced on the right [A]. RNFL thickness is given in micrometers for the respective parts of the optic disk



of exclusion. The patient reported here did not have any signs of preceding or concurrent bacterial, parasitic or viral illness, and comprehensive screening for connective tissue disease was negative.

While compressive or infiltrative lesion was excluded by the findings of the MRI scan, slight enlargement of both optic nerves was demonstrated. Optic neuritis was not reported in the Vaxigrip

clinical trials, but reports of vaccination-associated optic neuritis were included in product monograph post-marketing data. Since 1971, 17 cases of influenza vaccination-associated optic neuropathy

thy have been reported in the literature, including 2 associated with swine influenza vaccine and 1 recent case associated with trivalent influenza vaccine [2]. To the best of our knowledge the present case is the first adult case reported for the 2010–2011 season suffering from trivalent influenza vaccine-associated optic neuropathy. The mean time between vaccination and onset of neuropathy is 10 days [3]. Clinical symptoms (deterioration of vision) in our patient occurred 14 days after the trivalent influenza vaccination, supporting the temporal relationship between the vaccination and the optic neuropathy.

The cause of post-infectious and post-vaccination neuropathy is not known. Several authors have proposed an autoimmune response elicited due to distinct sequence homologies of myelin basic protein and the proteins of several viruses. It seems unlikely that this sequence homology is solely responsible, however, given the relative infrequency of post-viral and post-vaccination neuropathy [4].

In recent years there has been growing evidence regarding the role of immunological adjuvants such as pristane, which are used to increase the protec-

tive and lasting immune response to the infectious antigen, in the formation of autoimmune/autoinflammatory diseases [5]. In our case, however, the vaccine did not contain an adjuvant. Allergic reactions to preservatives and other stabilizers of the vaccination formula have also been reported [5]. According to the hypothesis presented by Westfall and Root-Bernstein in 1986, three requirements need to be met in order to induce such a neuropathy: a) one antigen must be homologous with an active fragment of myelin basic protein, P2 protein, or another component of the central or peripheral nervous system; b) the second antigen must be a chemically complementary component analogous to bacterial adjuvants; and c) both antigens must be present and immunologically active in the host simultaneously. The hypothesis requires that the two agents interact before they are immunoprocessed. The probability of acquiring two complementary infections meeting the specifications listed above are very low, which is the reason why neuropathy does not develop in every person with viral or bacterial infection or after vaccination [1]. This hypothesis supports the practice not to vaccinate a patient showing signs

of illness, because of a well-known linkage between immunization during illness and post-vaccinational neuropathy.

The present case provides strong evidence for a causal relationship between influenza vaccination and optic neuritis. We believe that in any case of unusual presentation of optic neuritis with no cause found on thorough clinical investigation, attention should be directed to the possibility of post-vaccination neuropathy.

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