THE CORRELATION BETWEEN ANTERIOR ISCHEMIC OPTIC NEUROPATHY THE NON-ARTHRITIC FORM, AND THE TREATMENT INVOLVING $\alpha$-INTERFERON

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THE CORRELATION BETWEEN ANTERIOR ISCHEMIC OPTIC NEUROPATHY THE NON-ARTHRITIC FORM, AND THE TREATMENT INVOLVING $\alpha$-INTERFERON (Abstract). The Anterior Ischemic Optic Neuropathy is an uncommon complication of $\alpha$-Interferon treatment, characterized by the either temporary or permanent diminishing in visual acuity. We are hereby presenting the clinical case of an Anterior Ischemic Optic Neuropathy (non-arteritic form) complicating interferon therapy for Chronic Hepatitis C. In such cases we recommend ophthalmological examinations and if severe ophthalmologic complications occur antiviral treatment should be stopped immediately. **Keywords:** ANTERIOR ISCHEMIC OPTIC NEUROPATHY, $\alpha$-INTERFERON, VIRUS C PERSISTENT CHRONIC TOXIC HEPATITIS

Interferons are glycoproteins that have multiple antiviral, antiproliferative and immunomodulatory activities and can be effective in the treatment of hepatitis B and C, malignant melanoma, follicular lymphoma, *condyloma acuminata* (1,2).

Ophthalmologic complications with interferon therapy are rare, generally mild and transient(3).Optic neuropathy, retinopathy with cotton wool spots, hemorrhages, macular edema, trombotic microangiopathy occur in less than 1% of the patients (3).

The ocular complications are reported at the individuals with predisposing risk factors: diabetes, arterial hypertension, dyslipidemia(4).Systemic side effects due to interferon use are: flu-like syndrome, myalgia, rash, hypotension, thrombo-cytopenia, depression, anemia, peripheral neuropathy(1,3).

**CASE**

We’ve examined patient B.E, aged 64, a retiree, living in Iași. The patient was admitted on March 23rd, 2013, for the following symptoms: a progressive diminishing in visual acuity at R.E. for approximately two weeks, and the peripheral narrowing in her visual field at the O.U. The patient men-
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mentioned that she had been diagnosed some 36 months prior to her admission, with virus C persistent chronic toxic hepatitis, and then she had been under treatment with α-Interferon (IFN-PEG 2α, 180 mcg/ml/weekly) for 2 months and with Ribavirin (1.200 mg/daily). Her general pathological history was: Virus C Persistent Chronic Toxic Hepatitis, High Blood Pressure Stage III, Chronic Vestibular Syndrome, Multiple Lacunar Cerebral Infarctions. The patient had no previous visual problem. The biomicroscopic exam: normal. Visual acuity R.E. 1/3, L.E.1. Cromatic sense: R.E. red-green axis dyscromatopsia, L.E. normal. R.E. relative afferent pupillary defect, L.E. normal. The ophthalmoscopic exam: R.E. diffuse hyperemic optic nerve papilla, indefinite contour, edematous, peripapillary hemorrhages, “flaming”, of small dimensions in the inferior temporal zone, narrowed arteries, veins dilated, Salus-Gunn sign, testing positive for foveolar reflex macula; L.E. optic nerve papilla of clear contour, temporally pale, narrowed arteries, veins dilated, Salus-Gunn sign, testing positive for foveolar reflex macula. The intraocular pressure: P.R.E. 14 mmHg; P.L.E. 16 mmHg. The anamnesis data, the general and the overall ophthalmologic clinical exam are pointing to the following probable diagnosis: O.U. Anterior Ischemic Optic Neuropathy Non-Arteritic Form, Secondary α-Interferon.

Other complementary explorations were: visual field, M.R.I., carotid and temporal arteries Doppler ultrasonography.

At the M.R.I. native exam (M.R.I. Nr.725/30.05.2013), no suggestive M.R.I. modifications were shown, on either M.A.U, P.E.I.C, A.V.C. or cerebral edema. The orbit, the optic chiasm, the optic strips were found to be within normal limits. Some cerebral atrophy, more prominent in the frontal-temporal area, bilateral, asymmetric.

Fig. 1a. V.F.R.E. lower and upper arcuate scotoma, with a narrowing in the visual field fixed at 10º in the nasal sector, and 15º temporal ocular fixations

Fig.1 b. V.F.L.E. lower paracentral scotoma, upper arcuate scotoma

Laboratory investigations: VSH 90 mm/h, CRP 64 mg/l, Erythrocytes
3.08.10^3.10^3/µL, Hemoglobin 10.2 g/dl, Haematocrit 31.5 %, Average Erythrocytes volume 102/fl., Average Erythrocyte Hemoglobin 33/pg, Lymphocyte 1 x 10^3/µL, mean Platelet volume 7.6/fl, Lymphocyte 23.8%, Urea 75.8 mg/dl. The internal medicine exam established the following diagnoses: C Virus Chronic Persistent and Toxic Hepatitis, Hypertension in the 3rd degree with great additional risk, Macrocytic Hypochromic Anemia, Multiple Lacunar Cerebral Infarctions, 1st degree Obesity, Sequel Pulmonary Tuberculosis. It was recommended: low in lipids and low in soda diet, treatment with Metoprolol 100 mg/dayly, Indapamide 1.5 mg/dayly, Ribavirin 1.200 mg/dayly, α-Interferon 180 mcg/ml/weekly, Acetylsalicylic Acid 75 mg/daily. The patient refused the temporal artery biopsy (no clinical sign of irregularly enlarged and ropey appearance of the temporal arteries was noticed).

The carotid and temporal arteries Doppler ultrasonography did not highlight any obstructive modifications at the carotid and temporal artery levels, indicative of a carotid obstructive syndrome and for the Anterior Ischemic Optic Neuropathy the Arteritic Form. The Otorhinolaryngology exam did not highlight neither acute nor chronic inflammatory process in the vicinity.

Following every investigation, the visual loss was decided to be due to α-Interferon therapy and the positive diagnosis takes shape: O.U. Anterior Ischemic Optic Neuropathy Non-Arteritic Form, Secondary α-Interferon; C Virus Persistent Toxic Chronic Hepatitis; Macrocytic Hypochromic Anemia; Multiple Lacunar Cerebral Infarctions, Atherosclerotic Hypertension in the 3rd degree, of very high risk; 1st degree Obesity; Sequel Pulmonary Tuberculosis. The diagnosis is being backed up by: the visual loss, the ophthalmoscopic exam (hyperemic disc edema), the visual field changes, the chronic treatment with α-Interferon, the risk factors (arterial hypertension, obesity), M.R.I., carotid and temporal Doppler ultrasonography.

The differential diagnosis

The papillary edema differential diagnosis is by the ischemic optic neuropathy arteritic form, non-arteritic form, toxic, optic neuritis, pseudo-syndrome Foster Kennedy.

Treatment

Throughout hospitalization, the patient was administered the following: systemic corticosteroids and antibiotics, vitamin therapy (B1, B6), aspirin, neurotrophics.

EVOLUTION

One month later, the evolution under treatment was favorable: V.A.R.E. 2/3, V.A.L.E.1, the optic disc edema partially resolved, resorption of the peripapillary hemorrhages, but the visual field did not improve. The prognostic under treatment: cautious. It was recommended a treatment with peripheral vasodilators, neurotrophic, aspirin, antihypertensive and the interruption of α-Interferon treatment immediately.

The antiviral treatment (α-Interferon 180 mcg/ml/weekly and Ribavirin 600 mg/daily) was not stopped and the patient experienced seven months later a relapse of optic neuropathy of controlateral eye. Ophthalmologic examination showed: the visual acuity L.E. 1/500, R.E. 2/3; L.E., hyperemic optic disk edema with peripapillary hemorrhages, R.E. optic nerve papilla of clear contour, temporally pale, L.E. relative afferent pupillary defect, O.U. red green dyschromatopsia. Laboratory investigations: VSH= 48 mm/1h, RBC=
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3.68/10^3x10^3/µl, TGP= 93 U/L, TGO= 42 U/L, Fibrinogen= 351µg/dl, CRP = 1,1 mg/L. IgM, IgG for Borrelia, Toxoplasma, Toxocara was negative. Complementary explorations were: L.E. constricted visual field at 5⁰ ocular fixations, R.E. constricted visual field at 5⁰ in the nasal sector and at 10⁰ in the temporal ocular fixation; fluorescein angiography (fig. 2).

![Fluorescein angiography](image)

**Fig. 2.** Fluorescein angiography revealed: L.E. blocking retinal flouerescence flame-shaped hemorrhages; O.U. hiperflourescent papillary growing in intensity until the late phase

The treatment was: intravenously metilprednisolone therapy, followed by oral metilprednisolone one mg per kilogram body weight for ten days, followed by tapering, vitamin therapy (B1,B6), aspirin, neurotrophics. The recommendation was the rapid cessation of α-Interferon therapy. One month later, the ophthalmologic examination showed: visual acuity L.E. 1/8, R.E. 2/3, L.E. optic disk edema partially resolved, O.U. red-green dyschromatopsia.

**DISCUSSION**

The Anterior Ischemic Optic Neuropathy is either a idiopatic or secondary ocular condition. The World Health Organization criteria recommends that AION (non-arteritic form) associated with α-Interferon therapy is “possible” (1).

The literature reports few cases of AION (non-arteritic form) during antiviral treatment for chronic hepatitis C (2 cases), cancer (2 cases), treatment of primary trombocytemia (1 case), malignant melanoma (1 case), amyotrophic lateral sclerosis (5).

The mechanism for how α-Interferon could cause AION (non-arteritic form) is unknown(1); the underlying immunologic mechanism has been suggested. It has been proposed that interferon is able to produce auto antibodies leading to the depositions of immune complexes in the small retinal or optic arteries (6).

The α-Interferon is causing the formation of cryoglobulin, rheumatoid factor, anticardiolipins antibodies (7).

Interferon has immunomodulatory properties capable of stimulating the production of various interleukins that can cause an inflammatory response affecting the blood vessels, leading to ischemia (8).

**CONCLUSIONS**

AION (non-arteritic form) secondary α-Interferon therapy may occur in rare cases, but the clinicians should be aware of the possible association and recommend interruption of the antiviral treatment.

Our patient received corticosteroids, with favorable course of visual function; the interferon therapy was stopped immediately after the relapse.
We suggest that the patients who would receive interferon therapy should have ophthalmologic examinations before starting and during the treatment and to discontinue or stop the α-Interferon treatment, if serious ocular implications occur.

REFERENCES


LASER TREATMENT OF ONYCHOMYCOSIS

The efficacy of 1064nm Nd:YAG laser for the treatment of onychomycosis was investigated by Noguchi et al. The study included 12 patients with onychomycosis caused by *Trichophyton rubrum* and *T. mentagrophytes*, confirmed by fungal culture and/or real-time PCR. The laser therapy was applied in 3 sessions at 4-week intervals, to a single hallux nail, with thickness at baseline <3mm and turbidity affecting <75% of the surface of the nail. The efficacy of the therapy was evaluated 6 months after the first treatment: the nail turbidity significantly improved in 3 cases (>70%), while in 2 cases turbidity improved 50-70%, in one case it was slightly improved (30-50%) and in 5 cases there was no change in turbidity (<30% improvement); in one case, the turbidity was worse. Overall, there was a decrease in the turbidity of the total lesion area from 664.4mm to 481.0mm and a 27.6% improvement. The study concluded that the 1064nm Nd:YAG laser therapy is well tolerated and can be used as an alternative for treatment of mild onychomycosis (Noguchi H, Miyata K, Sugita T, Hiruma M et al. Treatment of Onychomycosis Using a 1064nm Nd : YAG Laser. *Med Mycol J.* 2013;54(4):333-9).