Abstract: Optic neuritis are neuro-ophthalmic disorders of multiple causes: demyelinating, inflammatory infectious, toxic evolving towards the decrease of visual acuity, recoverable in 75% of patients, central scotoma, impaired color sense on the red/green axis, painful optic neuropathy associated in some patients with residual neurological signs. Optic neuritis affects the optic nerve behind the lamina cribrosa of the papilla until the crossing of the optic nerve in the chiasm. MRI is important in the positive diagnosis of MS. OCT may be useful in the positive diagnosis of optic neuropathy. The risk of developing multiple sclerosis in subacute optic neuritis increases up to 60% at the age of 40. Optic neuritis is: acute in methyl alcohol poisoning; subacute in demyelinating disorders, NRB associated with inflammatory and vasculitis, chronic in tobacco-alcohol intoxication.

Keywords: dyschromatopsia on the red/green axis, optic disc edema, MRI, ENP-Gun-Marcus reflex, optic neuropathy, viral infections, fungal infections, systemic inflammatory diseases, systemic vasculitis

Rezumat: Nevritele optice sunt afecțiuni neurooftalmologice de cauze multiple: demielinizantă, infecțios inflamatorie, toxică, care evoluează cu scăderea AV recuperabilă la 75% din pacienți, scotom central, tulburări de simț cromatic pe axul roșu-verde, neuropatie optică durerosă, asociată la unii pacienți cu semne neurologice reziduale. Nevritele optice afectează nervul optic în spatele laminei cribrosae de la papila până la încrucișarea NO în chiasmă. RMN este important în diagnosticul pozitiv al SM. OCT poate fi utilizat în diagnosticul pozitiv al neuropatiei optice. Riscul dezvoltării sclerozei multiple în nevrita optică subacută crește până la 60% la 40 de ani. Nevrita optică este: acută în intoxicația cu alcool metilic, subacută în afecțiunile demielinizante, NRB asociată cu boli infecțioase inflamatorii și vasculită sistemică, cronică în intoxicația alcool-tabagică.

Cuvinte cheie: discromatopsie pe axa roșu-verde, edem al discului optic, RMN, PEV, reflex Marcus-Gun, neuropatia optică în infectii virale, infectii fungice, boli inflamatorii sistemic, vasculită sistemică

Subacute optic neuropathy is accompanied by the reduction of the central visual acuity, impaired sense of colour and contrast sensitivity, Relative Afferent Pupillary Defect (RAPD) faulty visual field with central scotoma at light and colour and ophthalmoscopic changes or not (normal fundus, rarely papillary edema).

Subacute optic neuritis causes are multiple: idiopathic demyelination in multiple sclerosis, where RON can evolve with relapses, (3,4,5,6), optic neuritis associated with viral, bacterial, fungal infections, neuroretinitis, periretinitis, maculopie, optic neuritis in systemic inflammatory diseases (sarcoidosis, chronic inflammation, autoimmune optic neuritis, optic neuritis after vaccination, Devic’s disease, Behcet’s disease, celiac disease, inflammatory bowel disease, Vogt-Koyanagi-Harada syndrome) optic neuritis associated with systemic vasculitis (Systemic lupus erythematosus (SLE), Sjogren’s syndrome, scleroderma, rheumatoid arthritis, Churg-Strauss syndrome, Wegener’s granulomatosis, polyarteritis nodosa, giant cell arteritis).

The most common systemic diseases associated with optic neuritis are: multiple sclerosis, sarcoidosis, syphilis, Lyme disease, collagen vascular disease (Wegener granulomatosis, SLE).

Because of the multiple triggering pathology and maintenance of subacute RON, urgent investigations are necessary to detect the causal condition and the appropriate treatment.

Clinical signs:
The careful ophthalmological examination is mandatory and it shows:
- decrease of visual acuity, variable;
- visual field: central scotoma and of red/green colour with the peripheral extension of scotoma in any direction; altitude arcuate, deficits; nasal step; diffuse alterations of the visual field;
- colour sense: dyschromatopsia on the red/green axis may be more important than the decrease of the visual acuity; red saturation is low in RON and the affected eye sees the red colour darker;
- contrast sensitivity is abnormal in 98% of cases;
- afferent pupillary defect with slow photo-motor reflex;
- in bilateral cases, DPA is not visible.

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**Ocular signs:** (1,2,5)
Fundus of eye can be normal or in 35% of patients there is edema of the optic disc; disc edema degree is not correlated with the degree of visual acuity decline; a small number of patients may experience peripapillary bleeding; disc pale papillary disc may present a compressive lesion by aneurysm or mucocele; exudative changes of the vitreous with cell present in the vitreous may appear in sarcoidosis, Behcet’s disease, where retinal periphlebitis may exist; pars-planitits may precede the onset of the demyelinating disorders, many pars-planitits be associated to multiple sclerosis. Simultaneous bilateral optic neuritis is possible or not, immediately or later (after 3 months).

**Positive diagnosis:** (4,6) – is based on the clinical diagnosis and history of disease that establish the diagnosis of optic neuropathy

The laboratory examination helps in establishing the positive diagnosis:

Blood tests to identify the infection or inflammation: ESR, ACE - angiotensin converting enzyme C-reactive protein, antinuclear antibodies, Rapid Plasma Reagin. Analysis of LCR for the diagnosis of multiple sclerosis in 50-80% of cases; there is a moderate lymphocytosis with increased protein, IgG rise. Imaging examinations are useful for establishing an etiologic diagnosis. MRI is used to identify signs of multiple sclerosis (multiple sclerosis risk of about 90% after 10 years).

The optic nerve can be edematous, reduced in size with possible fatal optic atrophy.

Gadolinium MRI in order to highlight the inflammatory lesions of the optic nerve.

Visually evoked potentials (VEP) can be abnormal even in the presence of a normal MRI. VEP is useful for the differentiation of early neuropathy and allows the differentiation between inflammation and compression. In the acute phase of the optic neuritis, VEP amplitude diminishes and latency is extended. VEP is useful for the identification of the forms of optic neuropathy.

Electroretinogram (ERG) can help in differentiating macular and retinal lesions, in which P50 and N95 are abnormal in ERG. The P50 optic neuropathy tends to remain normal with reduced N95 amplitude.

**Optic neuropathy associated with infections:** (1,2,4,6)
Optic neuritis may complicate a wide variety of infections, in which optic neuritis can be isolated or associated with neurological and ophthalmic complications. Optic neuropathy in viral infections:

Viral infections are common in children, they are bilateral and may present concomitantly with optic neuritis, simultaneous neurological complications, such as ataxia, meningoencephalitis. The cephalohachidian fluid shows a slight increase in protein and lymphocytes.

**HIV infection:** It causes eye determinations and neurological complications through the existing immunosuppression.

At ocular level, the primary lesions are retinal microangiopathy and cotton wool spots, microaneurysms and retinal hemorrhages may occur; retinopathy progresses with the widening of the focal areas; optic neuropathy is given by the direct toxic effect of HIV-1 on retinal ganglion cells and optic nerve axons, slowly progressive lesions, which sometimes are unresponsive to treatment and are accompanied by a decline in the visual function, optic neuropathy immunodeficient patients can be produced and toxoplasma infections, cryptococcal, tuberculosis, chickenpox.

**Bacterial infections:**
These are the result of the direct infection of the optic nerve during a meningitis, abscess, endarteritis.

**Shigella, Salmonella, Francisella tularensis** can cause isolated unilateral, bilateral associated optic neuritis.

**Mycoplasma** infection may be associated with neurological complications and bilateral neuritis: disseminated encephalomyelitis, meningitis, encephalitis, polyradiculoneuropathy.

**Brucella** infection may present optic neuropathy associated with meningoencephalitis, radiculopathy. **Syphilis** can be accompanied by neuro-ophtalmologic complications including acute optic neuritis, neuroretinitis, papilledema, chorioretinitis and meningitis in the secondary stage of the disease and in congenital syphilis.

Other spirochetes - *Borelia burgdorferi* that causes the Lyme disease, presents in 5% of cases, neurological complications with cranial nerves isolated paralysis, meningitis, and ocular polyradiculoneuropathies: optic neuropathy, neuroretinitis.

**TB, in which optic neuropathy is the result of the infiltration of the optic nerve or of chiasm in the granulomatous inflammatory process or through the compression of a tuberculum.**

**Leptospires – may present isolated optic neuritis.**

*Bartonella henselae* (cat scratch disease) associates pars-planitits, retinal vasculitis with regional lymphadenopathy, pneumonia, meningitis, encephalitis, isolated cranial nerve neuropathies.

**Fungal infections:**
Optic neuropathy may complicate meningitis, the most severe lesions being in the immunocompromised patients, immunosuppressed with diabetes, AIDS patients. Meningitis or brain abscess may be caused by mucormycosis, histoplasmosis, Candida, Aspergillus, cryptococcal.

**Systemic inflammatory diseases:**
*Sarcoidosis:* it is a granulomatous inflammation of tissues of unknown origin. It is frequently present in African-Americans. The most commonly affected are: lungs, skin, joints, eyes, CNS (10%) with meningeal inflammatory lesions along with neuroopathies, brain, spinal canal, peripheral musculature.

**Ocular complications:** (2,5) uveitis (frequently previously) lachrymal gland damage, conjunctivitis, keratitis, scleritis, optic neuropathy with or without edema and inflammation adjacent granulomatous masses, adjacent small granulomas in the skin, lung, conjunctiva, vitritis panuveitis complicated with cataract, glaucoma.

**Neurological complications:** meningeval masses at the tip of the orbit, cavernous sinus, sphenoid ridge, involving the neighbouring structures including the optic nerve; systemic and intracranial hydrocephalus are possible that can give compression neuropathy.

**Optic neuropathy in chronic inflammation:** Debut by eye pain, periocular pain preceding the decrease of the visual acuity, when the pain is more intense than in the demyelinating disorders. Initially, the evolution can be dramatic with blindness in 2-3 weeks, but the treatment should be continued for a long period of time.

**Devic’s syndrome** – Ophthalmo-neuromylitis: It is a serious form of the disease, in which the optic neuropathy with severe bilateral abrupt onset is associated with transverse myelitis occurring simultaneously or rapidly in evolution. Regressive evolution is possible. Clinical phenotype can be seen in a variety of immune-mediated diseases, such as: SLE, Sjogren Sd, antiphospholipid antibodies, Antineutrophil cytoplasmic autoantibodies (ANCA), viruses, tuberculosis, mycosplasm. It is
more common in women at any age. Unilateral, bilateral sequential neuropathy with synchronous development. The decrease of vision is acute and severe and is accompanied by defects of visual field. Fundus of eye has a variable optical disc from normal to severe edema with peripapillary bleedings and optic atrophy in time. If the acute episode of optic neuritis is repeated, the patient remains with permanent visual impairment.

**Positive diagnostic criteria in Devic’s syndrome:** optic neuromyelitis, optic neuritis, acute myelitis, IRM lesions extended to 3 vertebral segments, brain MRI – multiple sclerosis diagnosis.

**Behçet’s syndrome:** syndrome of unknown etiology, characterized by mouth, recurrent genital ulcers and panuveitis.

General symptoms: fatigue, weight loss, malaise.

General signs: skin (erythema nodosum, rash pustular, Pseudofolliculitis) joint knee damage, hip, pulmonary impairment, gastrointestinal tract, kidney - rarely, thrombosis and vasculitis frequently associated with arterial aneurysms, frequently in the Mediterranean area, Japan, genetically HLA BS1 positive.

Eye disease in 70% of cases: anterior uveitis with hypopyon, retinal vasculitis, cystoid macular edema, glaucoma, optic atrophy, optic neuropathy.

Neurological complications in 5-10% of cases are by inflammations in the brain, spinal cord, nerve roots, sometimes the consequence of cavernous sinus thrombosis. The complications are progressive and may be followed by neurological sequelae and disabilities. Isolated optic neuropathy is rare, but in many cases subacute optic neuropathy is present, unilaterally moderate associated with defects of the visual field, disc edema or retinal vasculitis. In many forms of the Behçet’s syndrome, the early manifestations are neurological. There is no relationship between optic neuropathy and neurological complications.

**Celiac disease:** associates the neurological complications with anti-gliadin antibodies in the absence of gastrointestinal disorders.

Neurological complications: peripheral neuropathy, myopathy, cerebellar ataxia, encephalitis and encephalopathies and fissure calcifications,(1,5,6) At ocular level, bilateral optic neuritis may occur.

**Sd. Vogt-Koyanagi-Harada:** rare disease present in Africans and Asians, viral prodrome with meningitis aspect, hearing loss, tinnitus. It is produced by immune-mediated attack of the cells containing melanin, the cochlea.

At ocular level: previous granulomatous uveitis associated with vitritis, disc edema, serous retinal detachment, patchy - vitiligo, alopecia, poliosis eyelids, hair. Fundus of eye: multiple Dalen Fuchs nodules in the periphery of the retina, optic neuropathy by inflammation and / or ischemia.

**Systemic vasculitis**

*Systemic lupus erythematosus*(1,2,4) It is a multisystem disease associated with ANA and anti-DNA antibodies with damage at skin, joints, kidneys, eyelids, eyes, the presence of antiphospholipid antibodies.

20% with neurological complications: encephalopathy (sometimes psychosis) vascular damage; lamb optic neuropathy, headache.

**Ocular disorders:** are predominantly retinal, with cotton wool spots associated with arterial retinal dilations and intraretinal hemorrhages, venous and arterial occlusions with progressive extensive bleeding and NVSR, sclera, orbital inflammation, uveitis - rarely, optic neuropathy can be acute or chronic, progressive.

**Sjogren’s syndrome:**(2,5) It is a syndrome with lymphocytic infiltration of the lachrymal glands and salivary glands associated with dry eye. Is an association between disorders of SS-A (Ro) autoantigen and SS-B (La). The syndrome may be associated with: LES, rheumatoid arthritis, scleroderma.

**Neurological symptoms:** Isolated neuropathy and ganglionopatia of the cranial nerves; myositis, transverse myelitis, encephalomyelitis.

**Rheumatoid arthritis** - optic neuropathy may be present. Neurological - pahimeningitis.

**Wegener’s granulomatosis**

It is a small vessel vasculitis associated with the C-ANCA (cytoplasmic) pattern antibodies (cANCA) with necrotizing vasculitis with granuloma formation in the lungs, kidneys, nervous system.

**Ocular manifestations:** conjunctivitis, dacryocystitis, keratitis, episcleritis, scleritis, uveitis, retinal vasculitis, impaired optic nerve by inflammation or compression (optic neuropathy can be bilateral, retinal vasculitis).

**Giant cell arteritis** - present in the middle-aged people. It is characterized by enlargement of blood vessels and the branches of the aortic arch. It is a granulomatous vasculitis with infiltration of lymphocytes, histiocytes and giant cells, accompanied by adventitial edema and necrosis of the internal elastic lamina.

The visual symptoms are secondary to thrombotic occlusion of arteries and NOT to the direct inflammation.

**Ischemic optic neuropathy** occurs via short ciliary artery occlusion. The papillary disc may be pale or edematous with hemorrhage, retinal cotton-wool spots in adjacent retina.

### REFERENCES