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DIFFERENTIAL DIAGNOSIS OF OPTIC NEURITIS

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Abstract: Optic neuritis is inflammation of the optic nerve, which in a single or repeated attacks can severely and permanently damage visual function. Errors in diagnostic are daily and usually occur because of incomplete diagnostic procedure performed. This manuscript presents a series of 19 patients reffered with optic neuritis diagnosis. The diagnosis was confirmed in 15, while four had other changes in the optic nerve or macula. We analyzed the diagnostic specificity of the basic parameters of optic neuritis diagnosis and afferent pupillary defect showed the highest sensitivity. The spectrum of differential diagnoses is shown within this finding. Optic neuritis diagnosis should be established carefully, using usual and available diagnostic methods in ophthalmologic and neurological practice, and if necessary, refer patients to neuro-ophthalmologist, as well as to electrophysiological evaluation and other methods that help fifferentiate disease.

Key words: optic neuritis, papillitis, retrobulbar neuritis, relative afferent pupillary defect, differential diagnosis.

INTRODUCTION

Optic neuritis (ON) is a demyelinating inflammation of the optic nerve. His finding is frequently associated with multiple sclerosis, in which it can be the first clinical manifestation of the disease. It occurs in the optical neuromyelitis Devic, but also as an isolated entity during or after systemic viral and bacterial infections and during several systemic autoimmune diseases (1, 2). Not only in the multiple sclerosis, but also as a monosymptomatic, optic neuritis is the result of an autoimmune reaction. In the histological findings dominate perivascular lymphocytic infiltration and focal demyelination. Optic neuritis is classified as an inflammatory optic neuropathy.

According to statistics of Western European countries and the United States, the incidence of the diseases is 1 to 6,4 (1). Significantly more often the disease affects members of white race (Caucasians) and women (1). Most often they are young people, ages between 18 and 45. Neuritis has acute or subacute clinical course. It lasts two to three weeks, after which begins a spontaneous recovery. In adults only one eye is mostly affected and may have a tendency to recurrence. If appears in childhood, the diseases occurs after a viral infection, usually in both eyes and has a good prognosis. According to the anatomical localization, it can be at the level of the retina, when in a form of papillitis includes optic nerve head, or as a retrobulbar neuritis, when we cannot see signs of inflammation by ophthalmoscope.

Classic phrase for the presence of retrobulbar neuritis “neither the patient nor the doctor does not see anything” has long been shattered. Detailed history and comprehensive eye examination can detect retrobulbar neuritis even in patient with normal visual acuity, but also can reject this diagnosis, when only visual loss or inflammation of the papilla indicate its presence.

The patient most often complains of sudden decrease or loss of vision in one eye, pain while moving eyeball, less frequently on disturbance on the quality of color perception. Some patients can refer phosphenes during eye movement or sudden noise, worsening of symptoms related to the body temperature increase (Uthoff phenomenon), the disturbance in the space perception (Pulfrich effect), better vision in dim light and neurological symptoms (headache, weakness of extremities, paresthesia) (2). If optic neuritis is suspected, the patient should be asked separately about quality and duration of each of these symptoms. Ophthalmic examination, in such cases, involves the color vision, visual filed and pupillary reaction to light testing.

OBJECTIVE

The aim of this paper is to evaluate the validity of generally available ophthalmic diagnostic techniques in the differential diagnosis of optic neuritis.

METHOD

Patients, diagnosed with optic neuritis, referred by an ophthalmologist or neurologist to Neuro-ophthalmology cabinet of Clinic for children neurology and psychiatry in Belgrade, during period January-December 2007 were analyzed. After taking the history of disease, patients were checked for visual acuity (Snellen 6 meters distance chart), ocular fundi were examined by direct ophthalmoscopy, the pupillary response by swinging-flashlight test, color vision by Ishihara plates, visual field tested at Goldman perimeter and possible macular disease was tested by photo-stress test. After data collecting, the sensitivity of diagnostic tests, defined as the proportion of patients that the test marked as diseased and specificity of diagnostic test, defined as the proportion of healthy marked as diseasesed, were analyzed.

RESULTS

The study included 19 patients, 13 (68,4%) female and 6 (31.6%) male. The average age of the patients at the time of examination was 29.16 ± 5.7 years, range 19 to 40. 14 patients were reffered with diagnosis of rebulbar neuritis and 5 with the diagnosis of papillitis. Their most common complaints were decreased or blurred vision, and more rarely, pain in the eye movements. In all, except in one patient, it was the first and unilateral attack of the disease. That one female patient had admission diagnosis of repeated bilateral neuritis, and it was confirmed. The diagnosis of optic neuritis was confirmed in 15 (78.9%), while four of them or even one-fifth (21%) had other ophthalmic diagnoses: posterior scleritis, central serous choroidopathy, optic nerve druse and layer macular rupture.

Blurred or unclear vision or sudden visual loss observed in last few days before the examination referred all patients. Decline of visual acuity was verified in 10 (66.6%) patients with neuritis and Snellen visual acuity varied between 6/30 and 6/7.5. Changes in color vision were found in 12 patients with neuritis (80%), valued at 8/24 to 16/24 Ishihara plates and in two patients with other diagnoses, in whom the test is less valid (20/24). In one patient with neuritis and visual acuity 6/30 color vision testing was possible only by comparing the intensity impression of red objects in front of each eye, respectively. Scotoma in the visual field werecentrocecal (8 patients with neuritis) and central (4 patients with neuritis and two with macular changes), while in one patients with neuritis we obsereved diffuse and extensive changes. Retrobulbar pain noticed 7 patients with neuritis and one patient with diagnosed posterior scleritis.

Among patients directed to cabinet with the diagnosis of papillitis, the diagnosis was confirmed in three of them (Table 1, Edema d.n.o.). In addition to a loss of vision, disturbance of color vision and central scotoma in the visual field, three patients with papillitis had a positive relative afferent pupillary defect (RAPD, Marcus-Gunn pupil) in affected eye. In one patient in whom the referral diagnosis was rejected, we found optic disc druse and in the second one we discovered posterior scleritis, which resembled papillitis (visual loss, retrobulbar pain, papilloedema, centrocecalscotoma). Her diagnosis of scleritis was confirmed by ultrasound examination of eye.

Among the 14 patients reffered with a diagnosis of retrobulbar neuritis diagnosis was confirmed in 12 of them (85.7%). The diagnosis was rejected in a case in which there was a central serous choroidopathy and in one patient with a ruptured layer of the macula. These are, at the same time, only patients who had a positive photo-stress test, which is characteristic of the macular area diseases (Table 1).

Table 1. *Number of patients with positive findings of the performed tests in patients with optic neuritis (ON) and in whom this diagnosis was rejected (Other)*

Test	ON: positive*/tested	Other: positive/tested
Visual acuity	10/15	3/4
Color vision	13/15	2/4
Visual field	13/15	2/4
Marcus-Gunn	14/15	0/4
Optic disc edema	3/15	2/4
Photo-stress test	0/15	2/4

*Positive findings for the visual acuity means decrease below the normal or usual acuity on Snellen distance chart for a patient; for color vision means inability to detect all tables in Ishihara test; for visual field means scotoma appearance; for Marcus Gunn pupil means positive test; for optic disc edema means finding of edema of optic nerve disc; for photo-stress means positive test (prolonged recovery time after macular light stimulation).

When examining the specificity and sensitivity of the tests used in the diagnosis (Table 2), it is seen that testing swinging-flashlight test for afferent pupillary defect (APD), or Relative APD (RAPD), or Marcus Gunn pupil) shows the highest sensitivity, i.e. the ability to identify patients with optic neuritis. Then, there are changes in color vision, and disorders of the visual

Table 2. *Sensitivity and specificity of the test used in diagnosis of optic neuritis*

Test	**Sensitivity**	**95%CI**	**Specificity**	**95%CI**
Visual acuity	66.67%	(38.41%–88.05%)	25.0%	(4.12%–79.66%)
Color vision	86.67%	(59.51%–97.95%)	50.00%	(8.30%–91.70%)
Visual field	86.67%	(59.51%–97.95%)	50.00%	(8.30%–91.70%)
Marcus-Gunn	93.33%	(67.98%–98.89%)	100.0%	(40.23%–100.0%)
Edem d.n.o.	20.00%	(4.57%–48.09%)	50.00%	(8.30%–91.70%)
Foto-stress test	0.00%	(0.00%–21.97%)	50.00%	(8.30%–91.70%)

field, while decrease in visual acuity has high sensitivity, although lower than the previous two, and understandable, clearly lower specificity, as one nonspecific ophthalmologic symptom. Photo stress test is not an element of diagnosis of neuritis, but is very useful in differentiating in the presence of suspected macular process, which was confirmed in two cases, Hence its sensitivity is 0% and specificity in this not homogenous group 50%, when is related to optic neuritis diagnosis.

DISCUSSION

Worsening of visual acuity without noticeable or with discrete or uncertain retinal changes and decrease in visual acuity with papilloedema are the most common reasons for ophthalmologists and neurologists suspect the existence of optic neuritis. If the patient, at the same tame, is a female of younger age, many will consider this diagnosis certain.

Sudden decrease or loss of vision that develops and lasts a few days can be isolated symptom in more than half of the patients with neuritis (1, 3). It cannot be altered with stenopeic hole, the most prominent is one week after the onset of the disease, and then begins his spontaneous recovery. According to the literature, approximately 11% of patients with optic neuritis have normal visual acuity (1, 2). In our group this percentage was higher (this paper is one-year cross-section of patients, more representative in terms of differential diagnostic dilemmas of optic neuritis), although all the patients referred visual disturbances. They really exist, but they are not always related to the decrease in visual acuity which can be measured by Snellen chart. In such cases it is useful to examine the contrast sensitivity, which shows higher sensitivity, but the necessary equipment has a negligible number of clinics. The degree of impairment of visual acuity is a key element in assessing the need for clearly defined treatment protocols (1, 4, 5).

Retrobulbar pain, deep orbital pain, pain with eye movements exists in two thirds of patients. Develops during the second and third day of the disease and rarely persists. Other subjective symptoms, such as photosphenes and spatial perception disorder patientsrecoreded less frequently. The existence of Uthoff phenomenon may have prognostic value (1, 3, 5).

Each of valid diagnostic signs and symptoms of optic neuritis has its own characteristics that define it further. The classic clinical signs of optic neuritis are defects in the visual field (usually centrocekalscotoma), impaired color vision (dishromatopsy in the form od color desaturation), and abnormal pupillary response (3). In our circumstances, the examination of these characteristics is often overlooked, as evidenced by misdiagnosis in up to one-fifth of our respodents. Their prevalence and characteristics are similar to those in our series and the literature (1, 3, 5). Ishihara color vision plates test is sufficient for testing of suspected optic neuritis, but visual acuity for this test should be at least 6/12. Farensworth Hue panels have greater diagnostic significance. To test scotoma in the visual field sufficient is Goldman perimetry, but static methods in computerized perimeters provide better and more clearly defined diffuse decreased sensitivity, which exists in nearly all patients with neuritis.

Testing of pupillary response can be made by ophthalmoscope or a flashlight, which are standard parts of diagnostic equipment of each ophthalmologist and neurologist. Relative afferent pupillary defect (RAPD) or Marcus Gunn pupil manifests by isocoria and both sides wakened pupillary reaction when affected eye pupil is illuminated and normal pupillary response at highlighting the healthy eye. It is the sign of delayed or interrupted transfer of visual impulses in afferent fibers of optic nerve. Our investigation has confirmed its high sensitivity (nearly 100%) in the diagnosis of optic neuritis. May be absent or insufficiently persuasive in cases of bilateral neuritis, when losing his relativity in relation to the healthy eye (our patient with bilateral optic neuritis). Test is positive and in the presence of any optic neuropathy (traumatic, compressive, radiation, infiltrative, metabolic, toxic, diabetic, genetical, ischemic, in asymmetric neuropathy with advanced glaucoma, in other optic nerve atrophy and hypoplasia), but also in schemia and some other diseases of the retina, in which damage disrupted afferent part of the pupil-

lary reflex (central retinal artery occlusion, ischemic retinal vein occlusion, neuroretinitis, extensive retinal detachment) (4).

On the other hand, the decrease in visual acuity without positive RAPD with normal fundus appearance and inconspicuous changes should arouse suspicion to cerebral infarctions, tumours and inflammations or diseases of the macula (age-related and diabetic maculopathy, macular rupture, epiretinal membrane, central serous choroidopathy), retinal dystrophy, or functional blindness. Such result can be consequence of bilateral optic neuropathy, where RAPD loses its relativity (1, 4, 6). In differentiation of these diseases, in addition to other basic diagnostic elements, of great help is photo-stress test, which is positive in macular diseases. If the sensitivity of photo-stress test was analyzed in diseases of the macula, its sensitivity would amounted to 100%.

Papillitis account for less than one-third of cases of optic neuritis, similar to our findings. However, papilledema with a decrease in visual acuity can be seen in the posterior scleritis, perineuritis, optic nerve druse and pseudopapilledema, in which the positive RAPD is almost always absent (7), similar to our two out of five patients with the diagnosis of papillitis. Papilledema with positive RAPD could be seen in malignant hypertension, diabetic papillopathy, anterior ischemic neuropathy, neuroretinitis and neurouveitis, hemangioblastomas and hamartomas, multiple evanescent white dot syndromes (MEWDS) and chronic relapsing inflammatory optic neuropathy (CRION) (4, 8).

A number of other test methods can help in the diagnosis differentiation or confirmation and follow-up of patients with optic neuritis (visual evoked potentials, electroretinography, fluorescein angiography, ulatrasonography of eye and orbit, testing contrast sensistivity, optical coherence tomography, Heildeberg retinal tomography, magnetic resonance imaging) (5).

CONCLUSION

It is clear that the diagnosis of optic neuritis cannot be established on the basis of examination of one symptom or diagnostic use of only one method. Each element of the diagnosis requires the full attention and dedication, and medical history is of very great importance. In addition to patient complains characteristics and other elements of his history, a few simple diagnostic procedures can lead us to the right path. The correct diagnosis is important for proper therapeutic approach and because of the economy of other diagnostic procedures, but also has additional dimensions for optic neuritis prognosis and risk for development of serious neurological disease.

Sažetak

DIFERENCIJALNA DIJAGNOZA OPTIČKOG NEURITISA

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Optički neuritis je inflamacija optičkog nerva koja, tokom jednog ili ponovljenih ataka, može znatno i trajno da ošteti vidnu funkciju. Greške u postavljanju dijagnoze su svakodnevne i najčešće se dešavaju zbog nepotpuno sprovedene dijagnostičke procedure. U radu je prikazana serija od 19 pacijenata upućenih sa dijagnozom optičkog neuritisa. Dijagnoza je potvrđena kod 15, dok je četvoro imalo druge promene na optičkom nervu ili u makuli retine. Analizirana je specifičnost osnovnih dijagnostičkih parametara kod optičkog neuritisa, pri čemu aferentni pupilarni defekt pokazuje najveću senzitivnost. Spektar diferencijalnih dijagnoza prikazan je povezano sa ovom promenom. Dijagnozu optičkog neuritisa treba postaviti pažljivo, koristeći svakodnevno dostupne dijagnostičke metode u oftalmološkoj i neurološkoj praksi, a po potrebi, pacijente uputiti neurooftalmologu, kao i na elektrofiziološku evaluaciju i druge metode koje pomažu diferenciranje bolesti.

Ključne reči: optički neuritis, papilitis, retrobulbarni neuritis, relativni aferentni pupilarni defekt, diferencijalna dijagnoza.

REFERENCES

1. Beck RW, Trobe JD, Moke PS, et al. High- and low-risk profiles for the development of multiple sclerosis within 10 years after optic neuritis: experience of the optic neuritis treatment trial. Arch Ophthalmol 2003; 121(7): 944–9.

2. Martinelli V, Bianchi Marzoli S. Optic neuritis: differential diagnosis. NeurolSci 2001; 22: S52–4.

3. Ergene E, Machens NA, Roy H, Ing E, Law SK, Younge BR. Adult optic neuritis clical presentation. Medscape. Šupdated 2013 March 13; cited 2013 April 15]. Available from: http://emedicine.medscape.com/article/1217083-clinical.

4. Behbehani E. Clinical approach to optic neuropathies. ClinOphthalmol 2007; 183): 233–46.

5. Cleary PA, beck RW, Bourque LB et al. Visual symptoms after optic neuritis. Results from Optic neuritis treatment Trial. J neuroophthalmol 1997; 17: 18–23.

6. Voss E, Raab P, trebst C, Stangel M. Clinical approach to optic neuritis: pitfalls, red flags and differential diagnosis. TherAdvneurolDisord 2011; 4(2): 123–34.

7. Zoric L, Jaksic V, Mirkovic M, Elek-Vlajic S, Stevic S, Petrovic M. Some aspects of posterior scleritis differential diagnosis. SOE/AAO 2007, Vienna; Abstract book: EP-NEU-796.

8. Samra A, Rantahal J. Reccurentsubacute visual loss presenting in a 52-year-old woman with chronic relapsing inflammatory optic neuropathy. A case report. J Med Case Rep 2012; 6: 15.

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