Clinical evaluation of optic atrophy in patients with neurological disorders

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ABSTRACT

Objectives: Optic atrophy is a pathological term applied to optic nerve shrinkage from any process that produces degeneration of axons in the anterior visual system (the retino-geniculate pathway). The pathologist can make the diagnosis of optic atrophy by direct observation of the histopathological changes in the optic nerve. The clinician is restricted to indirect evidence by observing the optic nerve as it enters the eye and through testing its function.

Methods: Fifty patients with bilateral or unilateral optic atrophy, were collected randomly from several teaching hospitals in Baghdad, Iraq, between August 1998 and June 1999. Those patients included in this study had ophthalmoscopic abnormalities of the optic disc in addition to defective visual function that could be localized to the optic nerve.

Results: The defects in visual function varied between patients according to the disease process and duration of illness. Eight-seven percent of patients had visual acuity impairment, 74.4% had visual field defect, 58.5% had impairment in color perception, 64% had defective pupillary response to light and 88.4% had prolonged visual evoked potential (VEP) responses.

Conclusion: Patients who met the criteria for optic atrophy have different and unequal changes in optic nerve functions, ranging from 58.5% for color saturation test to 88.4% for VEP. Forty percent of patients with optic atrophy were discovered accidentally.

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Optic atrophy is a morphologic sequel, classified as any disease that causes damage to ganglion cells and axons with overall diminution in size of the optic nerve.[1] The term optic atrophy is applied to optic nerve shrinkage from any process that produces degeneration of axons in the anterior visual system (the retino-geniculate pathway), including ischemia, inflammation, compression, infiltration and demyelination.[1] When the visual axon is severed, its ascending (to the brain) segment disintegrates and disappears in approximately 7 days. The portion of the axon still connected to the ganglion cell body remains viable for 3 to 4 weeks, but then rapidly degenerates by 6 to 8 weeks, followed by optic disc pallor.[2] The usual symptom of optic atrophy is one of slow progressive visual failure in one or both eyes depending upon the cause, however when it is the result of vascular occlusion, trauma or severe optic neuritis, the onset may be abrupt.[3] Many patients are unable to give a precise history of the duration and course of their visual loss. In such patients, the examiner may have to rely upon the appearance of the fundus, especially if the visual fields are not reliable.[4]

The clinical diagnosis of optic atrophy is based on: 1. Ophthalmoscopic abnormalities of color and structure of the optic disc with associated changes in the retinal vessels and nerve fiber layer. 2. Defective visual function that can be localized to the optic nerve, which include:[1,2] a. Clinical tests – visual acuity, pupillary light reflex, clinical and formal visual fields including blind spots and color

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saturation test. b. Electrophysiological tests (visual evoked potentials [VEPs]).[4-8]

Methods. Between August 1998 and June 1999, 50 patients with the clinical diagnosis of optic atrophy were enrolled in this study conducted in the Neurological and Neurosurgical Departments at 4 sites, namely, the University Teaching Hospital, Baghdad Teaching Hospital, Al-Yarmouk Teaching Hospital and Al-Shaheed Adnan Teaching Hospital, Iraq. Visual function was assessed by: examining visual acuity (using Snellen's eye chart) and visual fields including the blind spot by white- and red-head pins, 10 mm in diameter, any restrictions in the field or scotoma were considered as field defects; pupillary responses to light; color saturation test, by using red objects and comparing its color and brightness in both eyes; neurophysiological tests (VEP) mainly the full-field examination and the hemi-field test were used whenever possible. The waves obtained were reproducible. The upper limit of the normal values (94-107.25) is the mean of the P100 latency of the full field is 100.65 $\pm$ 6.6 msecs; the upper normal acceptable latency equals 107 msec. Investigations were carried out for all patients including complete blood picture, erythrocyte sedimentation rate, fasting blood sugar, blood biochemistry, electrocardiogram and chest x-ray. Other investigations were selectively ordered and affected by factors such as availability and cost including computerized tomography scanning, magnetic resonance imaging, lumbar puncture and bone marrow aspirate.

Results. Fifty patients with optic atrophy (24 males and 26 females) were included in this study. The age of patients ranged between 1-68 years. Thirty-seven patients had primary optic atrophy and 13 patients had secondary optic atrophy. Bilateral optic nerve involvement was found in 25 patients out of the 37 patients with primary optic atrophy and in 12 patients out of the 13 patients with secondary optic atrophy (**Table 1**). Patients in our study were classified into 3 groups according to the presence of visual complaint. Visual disturbance was the chief complaint in 38% of patients, 22% presented with other problems but had, in addition, visual symptoms. Forty percent of patients had no visual complaint (**Table 2**). Changes in the disc appearance was divided into: just pallor in 36%; pallor with blurring in the margin and tortuous vessels in 20%; pale disc with attenuation of the main vessels entering into the disc in 12%; and pale disc with reduced vessels at periphery in 32%. Visual acuity measurement was divided into 4 groups: normal acuity was noticed in 12.7%, moderate affection in 14.8% and severe reduction in acuity to blindness in 51.7% (**Table 3**). Visual field examination was carried out in 47 patients; 74.4% had affected field and in 25.6% the visual field was normal. Color saturation test was affected in 58.5% and pupillary response to light in 64%. Visual evoked potential response test was offered for 26 patients and hemifield examination was offered for 3 patients. It was prolonged in 80.7% for the full field and in another 2 patients for the hemifield examination; this totals VEP abnormalities in 88.4% (**Table 4**).

Discussion. Recent studies have clarified the diagnosis, pathophysiology, natural history and treatment of several diseases affecting the optic nerve. Optic disc pallor with impaired visual acuity, visual fields, or the pupillary reactivity are associated with a wide variety of disorders that affect the optic nerve: including, inflammatory conditions, toxic nutritional, vascular and herido-degenerative diseases.[9,10]

The cases in this study were collected randomly from the outpatient neurological referral clinic and from inpatient neurological and neurosurgical wards and all non-neurological cases of optic atrophy were excluded. This resulted in multiple sclerosis and brain tumor being the most common causes, and other well-known causes of optic atrophy such as glaucoma and ischemic optic neuropathy being rare or not present. We found that the symptoms of optic atrophy are those of slowly progressive visual failure in one or both eyes depending upon the cause; as a result 40% of patients had no visual complaint and were discovered accidentally, and 22% of patients presented complaining of other symptoms but mentioned visual symptoms during historic interview. When optic atrophy results from vascular occlusion, trauma or optic neuritis, this can cause abrupt loss of vision or even blindness as noticed in 38% (**Table 2**).[3] The normal color of the disc is dependent upon its composition, the relationship of the components to each other and to the light that strikes them and is either reflected or refracted from the disc surface.[1] Quigley and Anderson postulated that in the atrophic disc rim, the axonal bundles have been destroyed and the remaining astrocytes are arranged at right angles to the entering light thus, little light passes into the disc substance to traverse the capillaries, while still present, are surrounded by layers of astrocytes. This postulation was based on the observation that disc capillaries are still present and appear to be functional.[11-14] Retinal vessel affection, including main vessel attenuation and reduction of the small vessels at the periphery of the disc, was observed in 44% of patients. These were observed in ischemic optic neuropathy. Kestenbaum introduced a "capillary number test", in which he observed and counted the small vessels on the disc margins. The small vessels usually number 9-10, but with diffuse optic atrophy, these vessels are said to be reduced.[1,2]

Table 1

Diseases	Primary optic atrophy (37)		Secondary optic atrophy (13)		Total (%)
	Bilateral (25)	Unilateral (12)	Bilateral (12)	Unilateral (1)	
Multiple sclerosis	10	4	-	-	**14 (28)**
Brain tumor	2	3	5	-	**10 (20)**
Hereditary causes	4	1	-	-	**5 (10)**
Hydrocephalus	-	-	5	-	**5 (10)**
Diabetes mellitus	2	2	-	-	**4 (8)**
Optic neuritis	-	-	2	1	**3 (6)**
Vitamin B_{12} deficient	1	-	-	-	**1 (2)**
Devic disease	1	-	-	-	**1 (2)**
Ischemic optic neuropathy	-	1	-	-	**1 (2)**
Central retinal artery occlusion	1	-	-	-	**1 (2)**
Trauma	-	1	-	-	**1 (2)**
Unidentified cause	4	-	-	-	**40 (8)**
					50 (100)

Table 2

Diseases	Presented with visual symptoms Group A	Recognize visual symptoms Group B	No visual symptoms Group C
Multiple sclerosis	3	3	8
Brain tumor	6	3	1
Hereditary causes	2	-	3
Hydrocephalus	-	2	3
Diabetes mellitus	2	1	1
Optic neuritis	3	-	-
Vitamin B_{12} deficient	-	-	1
Devic disease	-	-	1
Ischemic optic neuropathy	-	1	-
Central retinal artery occlusion	1	-	-
Trauma	1	-	-
Unidentified cause	1	1	2
Total (%)	**19 (38)**	**11 (22)**	**20 (40)**

Table 3

Normal acuity	Male	Female	Total (%)
Normal vision 6/6	1	5	**6 (12.8)**
Mildly impaired 6/9 - 6/12	5	5	**10 (21.3)**
Moderately affected 6/18 - 6/24	4	3	**7 (14.9)**
Severe affection - blind	13	11	**24 (51)**
Cannot be determined	1	2	**3 -**

Table 4

Diseases	VEP response		
	Normal P_{100} (94 - 106)	Prolonged P_{100} (107 - 130)	Severely prolonged P_{100} (131 - 175)
Multiple sclerosis	3	4	4
Hereditary	-	2	1
Optic neuritis	-	-	3
Diabetes mellitus	-	1	1
Hydrocephalus	1	-	-
Ischemic optic neuropathy	-	1	-
Devic disease	1	-	-
Trauma	-	1	-
Undetermined causes	-	2	1
Total (%)	**5 (19.2)**	**11 (42.3)**	**10 (38.5)**

VEP - visual evoked potential

Table 1 - Distribution of patients (n-50) according to the causes of optic nerve atrophy.

Table 2 - Visual complaints in patients (n-50) with optic atrophy.

Table 3 - Visual acuity in 47 patients with optic atrophy.

Table 4 - Visual evoked potential responses in 26 patients with optic atrophy “full-field stimuli”.

Mild affection of visual acuity occurs in 21.2%, and 12.7% had normal visual acuity (**Table 3**). These results correlate with a study carried out by Frisen and Frisen, giving some insight into loss of acuity in terms of structural changes. Their findings, in patients with abnormal photoreceptor separation, predict that a normal neural substrate should allow approximately 20/13 (6/3.9) acuity, but 20/20 (6/6) requires no more than 44% of the normal complement of foveocortical neural channels and 20/70 (6/21) no more than 5%.[1,15,16]

Visual field defects varied according to the disease process, most commonly the temporal field was found to be involved, and patients with bitemporal hemianopia had additional severe impairment of visual acuity. Acuity appears to remain normal as long as either the crossing or non-crossing outflow from the retinal foveola remains intact. Acuity fails only when both the crossing or non-crossing outflows are compromised especially, in sellar and suprasellar tumors. Impairment of visual acuity is a common finding in patients with visual field defects apparently restricted to the temporal fields.[15] This was noticed in 8 patients while, only 2 patients had affected temporal field with mildly affected visual acuity. Acquired defects in color vision frequently result from disease of the macula or optic nerve.[17] This was found in 58.5% of patients with either unilateral or bilateral involvement, and we found that the color saturation test is helpful in correlating rather than in establishing a diagnosis. Measurement of pupillary reactivity is not an easy task, as the amount of constriction varies with the starting size of the pupil, with the age of the patient and the inhibitory influences on the sphincter nucleus in the midbrain vary from moment to moment with mental activity. However, it is possible to compare one eye with the other and measure the relative impairment of pupillary function, whatever the cause, the involvement must be asymmetric in the 2 eyes in order to produce this pupillary defect.[4,18]

In this series, pupillary response to light was assessed and showed 64% in the form of poor reaction, Murcus-Gunn pupil and total loss of reaction. The symptoms of visual disturbances are not uncommon problems for the neurologist and VEPs can be of significant help if the eye examination is normal or equivocal. Visual evoked potential abnormalities are not specific for a particular optic nerve disease.[19] **Table 4** shows that VEP examination was offered for 26 patients, and found to be prolonged in 80.7% for full-field, an additional 2 patients had abnormalities in conduction in one of the hemifields. This shows that, only 11.5% had normal VEP and 88.4% had abnormal response; thus, VEP provides a sensitive extension of the clinical examination and commonly used clinical test, visual acuity, pupillary responses, clinical and formal visual field, fundoscopic examination and red color saturation.[19-21]

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