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Clinical profile and aetiology of optic atrophy in Malaysia

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马来西亚视神经萎缩的临床特点及病因

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摘要

目的:研究在马来西亚非青光眼视神经萎缩的病因及临床特点。

方法:一系列回顾性的研究分析马来西亚理科大学校医院眼诊所在 2007/2011 年间被诊断为非青光眼视神经萎缩的患者。至少随访 1a。评估这些患者的医疗记录及汇编调查结果。

结果:100 例患者符合选择标准,56% 的患者双眼都参与研究。主要症状为视力模糊(61%),除了视力模糊外还出现神经方面病症(18%),视野狭窄(9%)。大多数患者(63%)患眼视力下降到 3/60 以下。主要的病因是颅内占位性病变(26%),先天性疾病(13%),脑积水(12%),创伤(12%)及血管因素(12%)。对大多数患者(67%)采用保守治疗。不管其病因,视神经萎缩都伴有不同程度的视功能障碍。随访 1a 后,50% 的患者出现不同程度的视觉障碍。

结论:视神经萎缩主要的病因是颅内占位性病变,其次分别是先天性疾病,创伤和血管疾病。在诊断之前常常就出现视觉和神经上的症状,而疾病显著地影响着视力的变化。为了早期诊断视神经萎缩,当视力模糊的主诉为非特异性时,应该高度怀疑本病。

关键词:视神经萎缩;病因;视神经疾病;失明;脑瘤;马来西亚

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Abstract

• AIM: To describe the aetiology and clinical profile of non-glaucomatous optic atrophy in a tertiary hospital in Malaysia.

• METHODS: A retrospective case series was conducted on patients diagnosed with non-glaucomatous optic atrophy who presented to the Eye Clinic of Hospital Universiti Sains Malaysia from 2007 until 2011 with a minimum of one year follow-up. Medical records of these patients were reviewed and the findings compiled.

• RESULTS: Of the 100 patients who met the selection criteria, 56% had bilateral involvement. The chief presenting symptom was visual blurring (61%), followed by visual blurring with neurological symptoms (18%) and visual field constriction (9%). Most patients (63%) had a presenting visual acuity worse than 3/60 in the affected eye. The main aetiologies were space-occupying intracranial lesions (26%), congenital/hereditary diseases (13%), hydrocephalus (12%), trauma (12%), and vascular causes (12%). The majority of cases (67%) were managed conservatively. Regardless of aetiology, optic atrophy was associated with variable degrees of visual dysfunction. At the end of one year, 50% of the patients had some degree of visual impairment.

• CONCLUSION: The main aetiology of optic atrophy was space-occupying intracranial lesions, followed by congenital/hereditary, trauma and vascular problems. Visual or neurological symptoms usually preceded the diagnosis, and visual acuity was significantly affected by the disease. A high level of suspicion is required in order to make an early diagnosis of optic atrophy, as the main complaint of visual blurring is usually non-specific.

• KEYWORDS: optic atrophy; aetiology; optic nerve diseases; blindness; brain neoplasms; Malaysia
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INTRODUCTION

Optic atrophy is the final common morphologic endpoint of any disease process that causes axon degeneration in the retino-geniculate pathway. Clinically, optic atrophy manifests as changes in the colour and the structure of the optic disc, associated with variable degrees of visual dysfunction[1].

Optic atrophy has traditionally taken a back seat to more well-known causes of visual impairment[2-4]. However, it has nevertheless been shown to be one of the leading causes of blindness, contributing up to 25.4% of blindness, depending on the sample population[5-8].

The irreversibility of this condition, as well as the fact that it cannot be attributed to a single cause, but rather, is the end result of a motley assortment of diseases[9-12], may be just some of the factors underlying the relative scarcity of epidemiological studies in this field. In the past, the aetiology of optic atrophy was unknown in approximately 25%-50% of the cases studied[13-15]. In Malaysia, there have yet to be reported any studies regarding the aetiology of optic atrophy. The objective of this study, therefore, was to identify the causes of optic atrophy in this country, as well as document the clinical profile of patients with this condition.

SUBJECTS AND METHODS

Patients who were diagnosed with optic atrophy in Hospital Universiti Sains Malaysia from 2007 - 2011 and met our selection criteria were included in the study. The inclusion criteria were patients with non-glaucomatous optic atrophy with a minimum of one year follow-up. Any patient with concomitant glaucoma was excluded from the study. Patients were all evaluated by an ophthalmologist, and work-up encompassed visual acuity using a Snellen chart or Cardiff acuity test with best corrected refraction where relevant, slit-lamp biomicroscopy, fundus examination, perimetry and tests of optic nerve function including Ishihara colour vision, red saturation, light brightness and visual evoked potential where necessary. Additional investigations where necessary included blood tests like full blood count, erythrocyte sedimentation rate and infective screening (*e. g.* Mantoux test, treponema pallidum serology), as well as radiological investigations like computed tomography or magnetic resonance imaging of the brain and orbit. Diagnosis of optic atrophy was made based on the presence of visual loss with impaired optic nerve function and a pale optic disc. Visual acuity was classified according to the World Health Organization proposed revision of categories of visual impairment[16]. Data was compiled and analysed using SPSS version 20.0.

RESULTS

Of the 100 patients who met our selection criteria, mean follow up was quarterly up to one year, except in 3 patients; two defaulted after 3 months and came back only at the end of a year, and the last one defaulted completely after the 6th month of follow up. There were 61 males (61%) in the sample. In both genders, bilateral eye involvement occurred in 56% (Table 1). In unilateral cases, no predilection for either eye was demonstrated. Figure 1 shows the distribution of cases according to the age groups. The age of the patients ranged from 1 month to 74 years old. The mean age was 30 years old, while the peak age group (21%) was those aged 11-20 years of age.

Table 1 Demographic characteristics and clinical profile of patients with optic atrophy Cases(%)

Variable	M (*n*=61)	F (*n*=39)	Total (*n*=100)
Laterality			
Unilateral right	14 (23.0)	7 (17.9)	21 (21.0)
Unilateral left	13 (21.3)	10 (25.6)	23 (23.0)
Bilateral	30 (49.2)	20 (51.3)	50 (50.0)
Unilateral then bilateral	4 (6.6)	2 (5.1)	6 (6.0)
Presenting symptom			
Visual blurring	42 (68.9)	19 (48.7)	61 (61.0)
Visual blurring+neurological sx	8 (13.1)	10 (25.6)	18 (18.0)
Visual field constriction	4 (6.6)	5 (12.8)	9 (9.0)
Isolated neurological symptoms	2 (3.3)	3 (7.7)	5 (5.0)
Post-trauma	3 (4.9)	-	3 (3.0)
Squint	2 (3.3)	-	2 (2.0)
Others	-	2 (5.1)	2 (2.0)
Relative afferent pupillary defect	33 (54.1)	21 (53.8)	54 (54.0)
Macula abnormality	6 (9.8)	5 (12.8)	11 (11.0)
Vessel abnormality	14 (23.0)	5 (12.8)	19 (19.0)
Aetiology			
Space-occupying intracranial lesions			
-With hydrocephalus	6 (9.8)	4 (10.3)	10 (10.0)
-Without hydrocephalus	10 (16.4)	6 (15.4)	16 (16.0)
Congenital/Genetic	10 (16.4)	3 (7.7)	13 (13.0)
Hydrocephalus	6 (9.8)	6 (15.4)	12 (12.0)
Trauma	9 (14.8)	3 (7.7)	12 (12.0)
Vascular	6 (9.8)	6 (15.4)	12 (12.0)
Inflammatory/Infection	6 (9.8)	2 (5.1)	8 (8.0)
Others	2 (3.4)	1 (2.5)	3 (3.0)
Unknown	6 (9.8)	8 (20.5)	14 (14.0)
Treatment			
Conservative	43 (70.5)	24 (61.5)	67 (67.0)
Surgical	18 (29.5)	15 (38.5)	33 (33.0)
Visual outcome			
Worse	18 (29.5)	18 (46.2)	36 (36.0)
Static	42 (68.9)	18 (46.2)	60 (60.0)
Improved	1 (1.6)	3 (7.7)	4 (4.0)
Final visual acuity(based on better eye)			
6/6 to 6/18	32 (52.5)	18 (46.2)	50 (50.0)
<6/18 to 6/60	3 (4.9)	6 (15.4)	9 (9.0)
<6/60 to 3/60	6 (9.8)	2 (5.1)	8 (8.0)
<3/60 until 1/60 or counting fingers(CF)	12 (19.7)	6 (15.4)	18 (18.0)
<1/60 until perception to light(PL)	4 (6.6)	3 (7.7)	7 (7.0)
No perception to light (NPL)	4 (6.6)	4 (10.3)	8 (8.0)

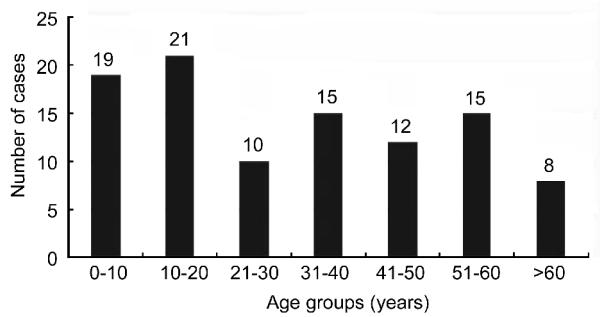

Figure 1 Distribution of cases according to age groups.

The chief presenting symptom was visual blurring (61%), followed by visual blurring associated with neurological symptoms (18%), and visual field constriction (9%) (Table 1). The majority of patients (63%) presented with a visual acuity worse than 3/60 in the affected eye (Table 2). A relative afferent pupillary defect (RAPD) was present in all the unilateral cases (54%). Upon fundoscopy examination,

Table 2 Presenting and final visual acuity of patients with optic atrophy at one year follow-up *n*(%)

WHO classification category	Distance VA	Initial VA(*n*=100)	Final VA(*n*=100)
Mild or no VI (0)	6/6 until 6/18	12 (12.0)	50 (50.0)
Moderate VI (1)	Worse than 6/18 until 6/60	19 (19.0)	9 (9.0)
Severe VI (2)	Worse than 6/60 until 3/60	6 (6.0)	8 (8.0)
Blindness (3)	Worse than 3/60 until 1/60 or CF	20 (20.0)	18 (18.0)
Blindness (4)	Worse than 1/60 or CF until PL	19 (19.0)	7 (7.0)
Blindness (5)	NPL	17 (17.0)	8 (8.0)
(9)	Undetermined	7 (7.0)	-

VA: Visual acuity; VI: Visual impairment; CF: Counting fingers; PL: Perception to light; NPL: No perception to light.

macula was normal in 89%, and vessels likewise in 81%. Optic disc pallor was only noted in 45% of patients upon first presentation.

In most patients (67%), the treatment was conservative. The visual outcome was not affected by treatment. In 50% of patients, the final visual acuity at one year follow-up was 6/18 and better (Table 2). In cases of bilateral optic atrophy, final visual acuity was based on better eye. A final visual acuity worse than 3/60 was documented in 33% of patients. The commonest cause of optic atrophy in our series was a space-occupying intracranial lesion (26%). This was followed by congenital/genetic diseases (13%) (Table 1). In 14 patients, the cause was unknown. The most common intracranial neoplasm identified was meningioma (9 patients; 34.61%), followed by pituitary/parasellar tumours (7 patients; 26.92%) (Figure 2).

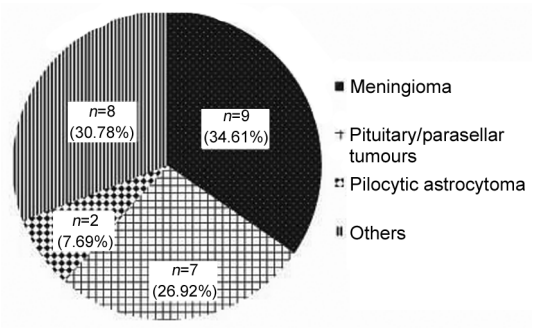

Figure 2 Type of space-occupying intracranial lesions.

DISCUSSION

Optic atrophy has a substantial effect on vision. The visual implications of optic atrophy are made even greater by the fact that it tends to be bilateral; as in other studies, more than half of our patients had bilateral optic atrophy[13,17,18]. Previous studies have documented a slight male preponderance; ours was no exception[13,15]. Most studies did not document the common presenting symptoms of patients with optic atrophy. In our patients, blurring of vision with or without neurological symptoms was the most common presenting complaint. A relative afferent pupillary defect (RAPD) was only noted in about half of the sample on initial presentation. This may be attributed to the fact that in cases of bilateral optic atrophy, both the pupils may react sluggishly to light. This data suggests that a high level of suspicion is required in order to make an early diagnosis of optic atrophy, as the main complaint of visual blurring is usually non-specific.

The aetiology of optic atrophy varies between studies, and may be related to the standard of healthcare in different countries. In our study, space-occupying intracranial lesions were the main cause of optic atrophy (26%). This differs from the findings of Chaddah *et al*[15] (India) and Loh *et al*[14] (Singapore), in which the majority of cases (35% and 31% respectively) were secondary to inflammatory causes (Table 3). Conversely, inflammatory causes, which included infective causes and demyelinating disease, formed a relatively small percentage of our sample, comprising 8% of the total cases. This difference may reflect the changing demographics in our world today, in which cancer has become the leading cause of death in adults aged 40 - 79 years old[19]. A recent epidemiological study on cancer statistics showed that in children, brain and other nervous system cancers comprise 25% of malignancies, thus making it the second most common cancer type after acute lymphocytic leukemias[19].

Congenital/hereditary causes formed the second largest cause of optic atrophy in our study. This is similar to the percentage noted by Chaddah *et al*[15], who noted that 13% of cases were secondary to congenital/genetic factors. Among our patients with congenital/genetic causes of optic atrophy, the majority had cerebral visual impairment secondary to various malformations of the central nervous system. Interestingly, we also had a few patients, all from the same family, who were diagnosed to have Leber's hereditary optic atrophy, which is a rare inherited mitochondrial disease that affects only about 15 in 100000 people[20].

This was followed by vascular and traumatic causes, which were also main causes in the study by Loh *et al*[14]. Table 4 shows the age-distributed causes of optic atrophy in our series compared with that of Loh *et al*[14], with numbers converted to percentages to facilitate comparison. The total sample size in our study was 100 patients, while in the study by Loh *et al*[14], the sample size was 160 patients. Interestingly, the age distribution of causes varies between the study by Loh *et al*[14] and the current study. We found that the age group most affected by space-occupying intracranial lesions was the group of patients aged 51-60 years old, while according to Loh *et al*[14], the peak age occurred earlier, in those who were 41-50 years of age.

Table 3 Aetiology of optic atrophy in different countries %

Cause	Malaysia (n=100)	Nigeria (2005)[1] (n=100)	India (1971)[2] (n=100)	Singapore (1968)[3] (n=160)
Space-occupying intracranial lesions	26	8	12	21
Congenital/Genetic	13	3	13	–
Hydrocephalus	12	7	1	–
Trauma	12	8	7	16
Vascular	12	–	2	18
Inflammatory	8	2	35	31
-Infective	7		28	21
-Demyelinating disease	1		7	3
-Others				7
Others	3	10	3	–
Unknown	14	62	27	24
Total	100	100	100	100

Table 4 Aetiology of optic atrophy by age in Malaysia *vs* Singapore %

Age groups	Space-occupying lesions		Trauma		Vascular		Inflammatory		Unknown		Hydro-cephalus	Congenital	Others
	My	Sg	My	Sg	My	Sg	My	Sg	My	Sg	My	My	My
0-10	11.5	3.0	–	7.7	–	–	–	12.2	7.1	–	75.0	46.2	33.3
11-20	15.4	9.1	41.7	26.9	8.3	–	25.0	8.2	35.8	8.3	8.3	15.4	66.7
21-30	7.7	21.2	8.3	34.6	–	3.6	12.5	6.1	14.3	–	8.3	7.6	–
31-40	19.2	27.3	25.0	11.6	8.3	–	37.5	14.3	7.1	20.9	–	15.4	–
41-50	19.2	39.4	16.7	15.4	25.0	17.9	–	14.3	7.1	45.8	8.4	–	–
51-60	23.1	–	8.3	3.8	33.4	32.1	–	34.7	14.3	12.5		15.4	–
>60	3.9	–	–	–	25.0	46.4	25.0	10.2	14.3	12.5		–	–

My: Malaysia; Sg: Singapore.

In our series, inflammatory causes of optic atrophy were mostly seen in patients in their thirties, while in the study by Loh *et al*[14], all age groups were generally affected, especially patients aged of 51 to 60 years old. However, since our number of those with inflammatory causes of optic atrophy was small, this data may not be entirely significant. The higher proportion of older patients noted within this group in other studies may be due to the fact that optic atrophy may not develop until the later stages of inflammatory diseases[21].

Trauma as a cause of optic atrophy mostly affected teenagers, followed by those in their thirties, while Loh *et al*[14] in Singapore found that teenagers came second to young adults as the largest age group with trauma-related optic atrophy. Among those with trauma-related optic atrophy, the male to female ratio was 3:1. In the series by Loh *et al*[14], males outnumbered females 25:1. Our data is consistent with that study also in that patients with vascular causes of optic atrophy were usually aged more than 50 years old[14]; in our series, the bulk of vascular causes occurred in the age group of patients aged 51-60 years old. Hydrocephalus was another noteworthy cause of optic atrophy in our study, with 12% of cases being secondary to isolated hydrocephalus. In this age group, three-quarters of the patients were aged 10 years and below. Contrary to expectations, where hydrocephalus is generally malleable to treatment in view of its early detection and relatively straightforward approach to management, our patients likely developed permanent optic nerve damage due to delayed presentation and socioeconomic factors.

The category 'others' included patients with miscellaneous causes like nutritional, drug-related and radiation-induced optic atrophy. The categories of hydrocephalus, congenital optic atrophy, and others were not included in the study by Loh *et al*[14], which only involved patients with acquired optic atrophy.

The cause of optic atrophy may in certain conditions be obscure, and has been postulated to be related to dysfunction of autoregulatory mechanisms[22]. In our study, unknown causes contributed to 14% of cases. In other studies, the aetiology of optic atrophy was likewise unknown in a significant proportion of cases, with this group forming 62% of the sample in a study by Oluleye *et al*[13-15]. These studies are comparable in that they included a similar number of sampled cases; the largest sample size being that of by Loh *et al*[14].

The visual outcome remained static in most of our patients, while about 1/3 of them experienced a deterioration in vision. This is consistent with the pathological basis of optic atrophy, in which the damage to the nerve fibre layer is usually irreversible. For the purpose of assessing the overall visual disability, we based our final visual acuity on that of the better eye. In 50% of patients, the final visual acuity was 6/18 and better. A final visual acuity worse than 3/60 in the better eye was noted in 1/3 of patients, who were subsequently referred for visual aids. Although the outlook for optic atrophy may

appear bleak, innovative approaches to the treatment of optic atrophy offer a ray of hope to these unfortunate patients[23,24]. Among others, a recent meta analysis of thirteen randomized controlled trials of acupuncture for treatment of optic atrophy showed promising results[25].

We are fortunate that the availability of diagnostic equipment and clinical expertise in our centre enabled us to determine most of the causes of optic atrophy. However, in view of the unfeasibility of performing a prospective study to determine the aetiology of optic atrophy, our series is naturally bound by some of the limitations which afflict studies of a retrospective; among others, we were wholly dependent on the accuracy and availability of the medical records, and thus had to exclude cases where the medical records were unavailable. Also, due to insufficient documentation, we were generally unable to determine the duration of symptoms prior to first presentation.

To sum up our findings, the main aetiology of optic atrophy was space - occupying intracranial lesions followed by congenital/hereditary, trauma and vascular problems. Visual or neurological symptoms usually preceded the diagnosis, and visual acuity was significantly affected by the disease. A high level of suspicion is required in order to make an early diagnosis of optic atrophy, as the main complaint of visual blurring is usually non-specific.

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