



Clinical Characteristics and Treatment Outcomes of Cases Diagnosed with Pediatric Optic Neuritis

Çocukluk Çağı Optik Nörit Tanılı Olguların Klinik Özellikleri ve Tedavi Sonuçları

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ABSTRACT

Objective: Optic neuritis (ON) is a condition that causes vision loss usually in one eye, often due to multiple sclerosis (MS). In this study, we aim to examine the clinical course, diagnostic tests, and treatment outcomes of patients presenting with acute or subacute ON.

Method: In this retrospective study, we examined the medical records of pediatric patients aged 3-18 years who were evaluated for acute ON in our neurology department between January 2015 and January 2021.

Results: Our study population of 18 participants consisted of female (55.6%), and male (44.4%) patients with an overall mean age of 13.8±2.3 years at admission. During the follow-up period, patients received the diagnosis of isolated ON (n=10), MS (n=7), and acute disseminated encephalomyelitis (n=1). The most common complaints at initial presentations were blurred vision and visual loss. ON was unilateral in 83.7% and bilateral in 16.7% of the patients. Color vision was initially impaired in 11 of 18 patients. Cranial magnetic resonance imaging (MRI), orbital MRI and spinal MRI revealed demyelinating lesions at different rates.

Conclusion: It is crucial to consider ON as one of the potential causes of vision loss in patients. The possibility of other demyelinating diseases, including MS, which can be present or may develop in patients with ON either during the initial presentation or follow-up should be kept in mind.

Keywords: Optic neuritis, demyelinating diseases, vision loss, children

ÖZ

Amaç: Optik nörit (ON) genellikle akut ve subaküt monooküler görme kaybına neden olan demiyelinizan bir hastalıktır. Yüksek oranda multiple skleroz (MS) ile ilişkilendirilmiştir. Bu çalışmada akut veya subaküt ON ile başvuran hastalardaki klinik seyir, yardımcı tanı testleri ve tedavi uygulamaları sonuçlarını değerlendirmeyi amaçladık.

Yöntem: Bu çalışmada Ocak 2015-Ocak 2021 yılları arasında akut ON ile çocuk nöroloji bölümünde değerlendirilen 3-18 yaş arası ON hastaların tıbbi kayıtları retrospektif olarak incelendi.

Bulgular: Çalışmamıza 18 hasta dahil edildi. Hastaların %55,6'sı kız, %44,4'ü erkekti. ON'nin ilk başlangıç yaşı ortalama 13,8±2,3 yıldır. Takip sürecinde hastalardan 10'u (%56) izole ON, 7'si (%39) MS, 1 hasta akut dissemine ensefalomyelit (%5) tanısı aldı. Hastalarımızda ilk başvuruda en sık görülen şikayetler bulanık görme ve görme kaybıydı. ON hastaların %83,7'sinde (16 hasta) unilateral ve %16,7'sinde bilateral (2 hasta) idi. Görme alanı muayenesi yapılan 11 hastanın 10'un da başlangıçta görme alanı etkilenmişti. İncelenen 18 hastanın 11'inde başlangıçta renkli görmede bozulma mevcuttu.

Sonuç: Çalışmamız neticesinde görme kaybı bulguları ile gelen hastalarda ON'nin ayırıcı tanılarda düşünülmesi gerektiği, bununla birlikte ON'li hastalarda ilk başvuru sırasında veya izlemlerde MS başta olmak üzere diğer demiyelinizan hastalıkların olabileceği veya gelişebileceği akıldan tutulmalıdır.

Anahtar kelimeler: Optik nörit, demiyelinizan hastalıklar, görme kaybı, çocuk

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INTRODUCTION

Optic neuritis (ON) is a condition that develops due to an inflammatory process involving the optic nerve. ON is among the most common causes of acute and subacute vision loss and can be characterized by many ophthalmic symptoms^(1,2). The main features of ON can be listed as decreased visual acuity, visual field defects, dyschromatopsia (abnormal color vision, especially red color desaturation)⁽³⁾. Since ON may be seen in many disease states, as a critically important issue, specific causes of ON should be identified at admission to prevent development of relapses and complications. An initial clinical history and detailed examination are required to narrow the list of differential diagnosis and make a diagnostic evaluation^(4,5). Although ON is often considered an isolated pathology or a part of another disease, imaging exams, and laboratory tests still play a significant role in confirming its diagnosis⁽⁶⁾. During follow-up, clinical progression, as well as changes in laboratory variables, can sometimes lead to a revision of the initial diagnosis of ON. Utilizing diagnostic tools is essential to aid in making the differential diagnosis of ON.

ON accounts for approximately 25% of acute demyelinating syndromes in children, with an annual incidence of 1-5 per 100,000 cases^(1,7). ON is a medical condition that is commonly observed as an isolated idiopathic form in children. However, it may also be associated with acute or subacute demyelinating syndromes of the central nervous system, such as acute disseminated encephalomyelitis (ADEM), myelin oligodendrocyte glycoprotein antibody associated disease (MOGAD), multiple sclerosis (MS) and neuromyelitis optica (NMO). It has been observed that some patients initially diagnosed with isolated ON may eventually receive the final diagnosis of MS^(8,9). However, there is not enough data available about pediatric ON in our country. Therefore, in this study, we have retrospectively evaluated pediatric patients with the diagnosis of acute ON. We examined the demographic characteristics, diagnoses, clinical findings, laboratory and imaging results, responses to treatment, and clinical follow-up of these patients to evaluate the clinical features of ON in pediatric patients and to emphasize the significance of follow-up and treatment.

MATERIALS and METHODS

A cohort study was conducted at the Pediatric Neurology Clinic of Manisa Celal Bayar University Faculty of Medicine. The study analyzed the data

of all patients aged between 3 to 18 years who were admitted to the pediatric neurology service with suspected acute or subacute ON between January 2015 and January 2021. The data were collected from electronic medical records available in a computerized database. The analysis only included cases that were diagnosed with ON by neuro-ophthalmologists. The cases were identified by the symptoms such as pain with eye movements and/or loss of vision lasting for a maximum of two weeks. Other diagnostic indicators included decreased color vision, abnormal visual field, relative afferent pupillary defect (RAPD), and optic disc swelling. ON affecting both eyes at the time of registration or developed within one month after admission was considered bilateral ON.

The study population consisted of patients who had received the diagnosis of ON and evaluated by a neuro-ophthalmologist. Participants with incomplete information regarding the diagnosis of ON, pathologies of the other eye that affected visual acuity, or any signs of a previously experienced ON were excluded from the study. The patient's demographic data, clinical characteristics, treatment history, and discharge diagnosis were recorded upon admission.

Any recurrent ON or new neurological conditions emerged during follow-up were documented. ON was interpreted as isolated ON or a condition associated with other demyelinating diseases. The diagnosis of idiopathic ON was made according to the current diagnostic methodologies used at the time of admission and during the follow-up period after excluding all other possible etiologies for ON.

ON that occurs at least four weeks after the initial event associated with or without the presence of oligoclonal band (OCB) in the cerebrospinal fluid (CSF) samples of patients with normal cranial magnetic resonance imaging (MRI) findings but experienced at least two novel episodes is termed as recurrent ON^(10,11). The diagnoses were made based on the current diagnostic criteria. MS-associated ON was defined according to the 2017 revision of the McDonald diagnostic criteria for MS⁽¹²⁾. The follow-up period was described as the time interval extending from the patients' admission date to their last visit or the time elapsed during data collection.

All patients underwent initial examination by an experienced ophthalmologist, with periodic follow-up appointments for patients under treatment. Furthermore, study participants underwent cranial and orbital MRI scans, which were evaluated for signs of ON,

location of the lesions and post-gadolinium contrast enhancement.

All patients received a comprehensive evaluation, including a complete blood count, serological analyses for the identification of infectious agents, and biochemical and immunological blood tests. In children who underwent lumbar puncture, biochemical and microbiological test results of CSF samples, the presence of OCB (if any) and calculated immunoglobulin G index were recorded. If Neuromyelitis Optica Spectrum Disorder (NMOSD) or MOGAD was suspected, AQP4 and anti-MOG levels were measured in peripheral blood serum during diagnostic process or follow-up.

This study was approved by the institutional Ethics Review Board of Manisa Celal Bayar University (approval number: 386, date: 23.01.2023).

Statistical Analysis

The study analysed both quantitative and categorical data. The quantitative data was analysed using IBM SPSS Statistics 20 software program and presented as mean ± standard deviation or median and range. Categorical data was presented as frequencies and percentages. The level of statistical significance was set at $p < 0.05$.

RESULTS

A total of 18 patients diagnosed with ON were examined. Of them, 55.6% were girls and 44.4% were boys. None of them had a family history of ON or any demyelinating diseases. The average age at the first onset of ON was 13.8 ± 2.3 (range 7-18) years. The follow-up period of the patients ranged from 7 days to 42 months. During the follow-up period, the patients received the diagnosis of isolated ON (n=10; 56%), MS (n=7; 39%), and ADEM (n=1; 5%) (Table 1).

The most common complaints in our patients at first admission were vision problems such as blurred vision, vision loss, and pain at eye movements. In addition, patients complained of numbness in the hand (n=1), and headache (n=5). In our study, ON was unilateral in 16 (83.7%) and bilateral in 2 (16.7%) patients (Table 2). The initial visual examination was conducted on all of the study patients, and 16 patients underwent visual acuity testing. The tests revealed visual acuity of less than 0.5 in 8 patients after correction. Additionally, visual field examinations were performed in 11 patients and in 10 of them the visual field was affected at baseline. Visual field examinations were maintained during follow-up period in only two patients. Their visual fields improved in the sixth

and twelfth months, respectively. However, 10 patients did not receive a follow-up visual field examination. Baseline visual field examinations of 11 out of 18 patients revealed the presence of an impaired color vision.

In the neurological examination of our patients, in addition to eye findings, the patients had dysmetria (n=5), sensory loss (n=1), limited vision, (n=1) and abnormal pupillary reflexes (n=1). Our study found that 11 out of 14 patients who underwent visual evoked potential tests had prolonged central motor conduction times. In addition, we performed orbital MRI and cranial MRI on 16 patients, out of which optic nerve involvement was detected in 9 (56.2%) patients) who underwent orbital MRI. Lesions were found in 50% (n=8) of patients who underwent cranial MRI. Spinal MRI detected demyelinating lesions in 7, and spinal cord lesions in 3 patients at presentation (Table 3). Analysis of the sera of 14 patients to diagnose NMOS or to detect anti-MOG, AQP4 and anti-MOG antibodies yielded negative results. Elevated OCB type 2 and type 3 proteins were observed in 4 out of 6 patients who underwent CSF examination.

In our study, we administered pulse methylprednisolone therapy to all patients as an attack treatment at daily doses of 20-30 mg/kg for 3-5 days. Oral steroid maintenance therapy was given to 8 patients for 4-6 weeks. While we achieved a complete clinical response in all patients, ON recurred, as expected, in 2 patients who were initially diagnosed with MS. During clinical follow-up, visual symptoms improved within three days to one month (average ten days). Among the patients who returned for their follow-up visits, complete recovery was detected in the third month in 10, and partial recovery in the sixth month in 3 patients. The remaining five patients with isolated ON did not come for control. When we reached them by phone, they had not reported any complaints.

DISCUSSION

Although pediatric ON typically causes reversible vision loss that usually occurs within hours to days,

Disease group	Number (%)
Patients with Isolated optic neuritis	10 (50)
Patients with MS	7 (39)
Patients with ADEM	1 (5)
Total	18 (100)

MS: Multiple sclerosis, ADEM: Acute disseminated encephalomyelitis

it can lead to development of severe vision loss in some patients^(1,13). A study conducted on the risk of MS development among patients with isolated ON observed that children with bilateral ON had a lower risk of developing MS⁽¹⁴⁾. Recurrent ON is commonly associated with autoimmune or demyelinating diseases such as MS or NMOSD⁽¹⁵⁾. ON is more common in women, with a female to male ratio of approximately 2:1 in postpubertal children, similar to adults. However, it is seen at equal incidence rates in prepubertal girls and boys⁽¹⁶⁻¹⁸⁾. Due to the small number of patients in our study, pre- or postpubertal periods could not be evaluated separately, and the male-female ratio was 10/8. The average age at onset of pediatric ON varies between 9 to 11 years of age in the literature^(19,20). Age range of our study population

varied between 7 and 18 years, with an average age of 13.8 years. Children under 10 years of age are more likely to develop infectious optic neuropathies or isolated ON, while those older than ten years are more likely to develop MS⁽²¹⁾. In adult patients, ON typically presents as retrobulbar neuritis, while papillitis is more frequently observed in children. In our study, 83.3% of the patients had retrobulbar neuritis, there were no abnormalities on fundoscopic examination at first admission, but color vision deficiency with/without RAPD was observed.

Pain with eye movement is a common symptom in pediatric cases, with reported prevalence rates ranging from 33% to 77%⁽²²⁾. Headache is also frequently reported. One study reported its prevalence as 53% in children⁽²³⁾ which may be due to children's difficulty in distinguishing between pain behind the eyes and a headache. In our study, all patients in our ON cohort had vision loss at their initial visit, while 61.1% of them reported pain with eye movement, consistent with previous research. According to the study by Wilejto et al.,⁽²³⁾ 58% of cases of ON were unilateral and 42% of them were bilateral. Another study reported that bilateral involvement was more common. However, we found that approximately 83% of our cases had unilateral ON⁽²⁴⁻²⁶⁾. Various studies reported that visual acuity of children with ON recovers better compared to adult patients⁽²⁴⁻²⁶⁾. All the patients initially experienced reduced vision. Eight (50%) out of 16 patients evaluated for visual acuity had severe visual acuity of less than 0.5. However, during the follow-up period, the visual acuity of all patients, including those with MS, improved either fully or almost completely. We can interpret this high recovery rate in association with the low recurrence rates detected in our cases with isolated ON, scarce number of attacks of ON experienced by our cases with MS and failure to diagnose NMOS or

Table 2. Sociodemographic and clinical characteristics of pediatric patients diagnosed with optic neuritis	
	n=18 (%)
Gender	
Female	10 (55.6)
Male	8 (44.4)
Age at onset (year)	13.8±2.35 (7-18)
Follow-up, months, mean ± SD (range)	11.2±12.12 (1-42)
Relative afferent pupillary defect	
Present	15 (83.3)
Absent	3 (16.7)
Painful eye movements	
Present	11 (61.1)
Absent	7 (38.9)
Unilateral/bilateral	15 (83.3)/3 (16.7)
Visual evoked potential	
Normal	3 (21.4)
Abnormal	11 (78.6)
Oligoclonal bands in cerebrospinal fluid samples	
Present	4 (57.1)
Absent	3 (42.9)
MOG IgG serum	
Positive	0 (0)
Negative	14 (100)
AQP4-IgG serum	
Positive	0 (0)
Negative	14 (100)
Relapse	
Yes	3 (37.5)
No	5 (62.5)

SD: Standard deviation, IgG: Immunoglobulin G, MOG: Myelin oligodendrocyte glycoprotein, AQP4: Aquaporin-4

Table 3. Presence of demyelinating lesions detected by various neuroimaging techniques in pediatric patients with optic neuritis	
Neuroimaging techniques	Number (%)
Orbital MRI	
Present	9 (56.3)
Absent	7 (43.8)
Cranial MRI	
Present	8 (50)
Absent	5 (31.3)
Spinal MRI	
Present	3 (20)
Absent	12 (80)

MRI: Magnetic resonance imaging

anti-MOG-related diseases. Studies have found that ON has been reported as the presenting symptom in 25% of MS patients^(27,28). Also, it has been observed that 13-50% of children who experienced their first attacks of ON are diagnosed with MS during follow-up^(21,29,30). Furthermore, it has been reported that 38% of patients who presented with isolated ON were diagnosed with MS⁽¹³⁾.

A multicentre study conducted in our country found that cranial MRI abnormalities increased the risk of development of MS in female patients with unilateral ON older than 10 years⁽³¹⁾. In our study, 5 of 7 MS patients received the diagnosis of MS during their first attack of ON. One patient was diagnosed with MS six months after the first attack of ON, and the other patient 14 months later. As a result, in our study, 38.9% of the patients who applied to the ON clinic received the final diagnosis of MS in compatible with the relevant literature data.

It has been reported that an OCB can be detected in neuroinflammatory conditions such as MS, paraneoplastic syndromes, NMO spectrum disorders, and infections such as herpesvirus encephalitis⁽³²⁾. We revealed the presence of OCB type 2 in CSF samples of 6 out of 7 patients diagnosed with MS. It is important to monitor patients presenting to ON clinic with manifestations of the first attack of ON, as MS may be observed during follow-up of these patients.

According to Chang and Pineles⁽¹³⁾ steroid treatment is usually effective in patients who develop MS, but it does not prevent its recurrence. For the treatment of acute ON, use of pulse steroids at daily doses of 20-30 mg/kg for 3-5 days is recommended, and oral steroids should be taken for 4-6 weeks as a maintenance therapy. All patients in our cohort received pulse methylprednisolone treatment to relieve their attacks, and 8 more patients received oral steroid maintenance therapy. In our series, all five MS patients experienced a complete response, and only two of them had a relapse during follow-up.

Study Limitations

This study has several important limitations. Firstly, the limited number of patients evaluated in a retrospectively designed study performed in a single centre prevents generalisation of our findings. However, the fact that our study was conducted at a single centre increased the availability of healthy and homogenous data. Furthermore, in several cases, visual field examinations were not conducted after discharge, which restricted our ability to provide comments on

this issue. Prospectively designed studies with a larger number of patients diagnosed with ON and longer follow-up periods will provide valuable information about the course of the disease and the final diagnosis.

CONCLUSION

It is crucial to consider ON as a possible diagnosis for pediatric patients who experience symptoms such as vision loss, pain with eye movements, and blurred vision. Medical professionals should closely monitor these patients. The initial appearance of ON can be an isolated event or a sign of a demyelinating disorder linked with MS, NMOS, or anti-MOG. It is crucial to understand that even if these disorders were not detected during the first diagnosis of ON, they could still be identified during follow-up.

Ethics

Ethics Committee Approval: This study was approved by the institutional Ethics Review Board of Manisa Celal Bayar University (approval number:386, date:23.01.2023).

Informed Consent: Retrospective study.

Author Contributions

Concept: S.A.O., M.P., Design: S.A.O., Ç.Ç.K., Data Collection or Processing: S.A.O., Analysis or Interpretation: S.A.O., Ç.Ç.K., A.K.A., M.P., Literature Search: S.A.O., H.K., Writing: S.A.O., Ç.Ç.K., H.K.

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