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CASE REPORT

Leber Hereditary Optic Neuropathy Plus: A Case Report and Review of Literatures

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ABSTRACT

Background: Leber hereditary optic neuropathy (LHON) is an inherited visual loss and optic atrophy due to mitochondrial mutation. Most of these patients had not any other neurological signs and symptoms more than a visual loss. In a small group of the patients, other neurological manifestations may be occurs. This rare presentation of the disease was named " LHON plus syndromes." **Case Presentation:** A 15-year-old boy who was completely healthy until age 9, when he gradually developed painless visual loss in his right eye. After 3 months, similar symptoms occurred in his left eye. Within next 2 years, psychomotor regression happened, and at age 11, very intractable seizures were started. According to physical examination and past medical history, LHON plus syndrome was diagnosed for him. Management of seizure and other symptomatic treatments were started, and there was a weak response to drugs. **Conclusion:** Early diagnosis and ruling out treatable conditions are critical points in these patients.

INTRODUCTION

Leber hereditary optic neuropathy (LHON) is a maternally inherited loss of central vision with optic atrophy due to mitochondrial DNA (mtDNA) mutations. This syndrome is often found in male adolescents. In most of the patients, there are no other neurological manifestations (more than vision loss), and cerebral imaging is normal. However, some rare cases of LHON have been described with variable central nervous system (CNS) involvements. These cases called LHON plus syndrome (1). Overall, LHON is not a common condition, and LHON plus syndrome is very rare. Regarding current literature, there were only 7 similar cases to LHON plus syndrome with variable manifestations. Patients with LHON plus syndrome presented with vision loss and some other neurological manifestations such as dystonia, Parkinsonism, cerebellar ataxia, myoclonus, epilepsy, migraine, and mental retardation (2). There is no definite treatment for this condition, and symptomatic treatment is recommended in most of the patients. Herein we report a 15-year-old boy with LHON plus syndrome. To the best of our knowledge, this is the first report from Iran.

CASE PRESENTATION

The patient was a 15-year-old boy who referred to neurology ward from southern Iran (Bushehr Province). He was completely healthy until age 9 when gradually developed painless vision loss in his right eye. After three months, vision loss in his left eye was started. Funduscopy examination at the beginning of vision loss showed a hyperaemic optic nerve, telangectatic and tortuous peripapillary vessels. In our ward, his visual acuity was no light perception in both eyes. On slit-lamp examinations, the cornea, anterior chamber, and lens were normal. Severe optic atrophy, telangiectatic vessels, and retinitis pigmentosa were detected in the retina of both eyes (Figure 1). Neurological examinations were within normal ranges. Neuro imaging studies were normal. The patient was born full-term, with normal development until age 9. After visual loss in both eyes, the patient developed psychomotor regression, and in age 11 the patient was considered as mentally retarded. At age 11, very intractable seizures began. The patient had recurrent episodes of tonic-clonic seizures which were poorly controlled with several anti-convulsants. (sodium valproate, levetiracetam and lam-

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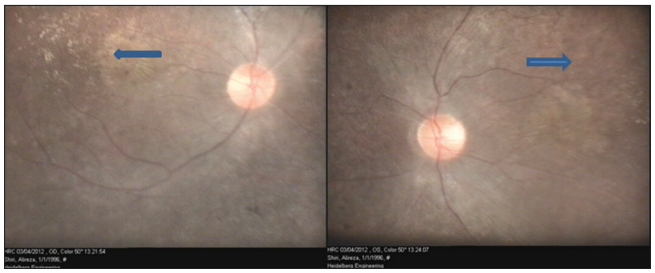

Figure 1. Funduscopy showed retinitis pigmentosa

otrigine were used with very weak response). Family history was not significant.

Routine laboratory investigations, such as complete blood count, liver, kidney, and thyroid function tests were within normal ranges. Ammonia and lactate levels, autoantibodies (i.e., anti ds DNA antibodies, antineutrophil cytoplasmic antibodies (ANCA) and neuro myelitis optica-IgG (NMO)), serology for an infectious cause such as Lyme disease, syphilis, herpes virus, and human immune deficiency virus (HIV) were all negative.

Visual evoked potential in both eyes was flat. Magnetic resonance imaging (MRI) of brain and orbit were normal. Electrocardiography (ECG) and echocardiography were normal. Electroencephalography showed nonspecific diffuse cerebral dysfunction. Multiple sclerosis (MS), ischemic optic neuropathies, other mitochondrial disorders or an overlap syndrome such as Harding's disease were in differential diagnosis which were ruled out during investigations. According to history and physical examination LHON plus syndrome was diagnosed for him. Other possible diagnoses included late-onset MS, ischemic optic neuropathies, a mitochondrial disorder or an overlap syndrome such as Harding's disease.

DISCUSSION

LHON is a maternally inherited disorder which is seen in male adolescents. This condition is characterized by the bilateral painless visual loss that typically progresses over weeks to months. Three different mtDNA mutations: G3460A, G11778A, and T14484C, in the ND1, ND4 and ND6 genes, (all encoding for complex I subunits of the mitochondrial respiratory chain) are associated with LHON phenotype (3). Several reports suggested different environmental causes such as smoking, alcohol abuse, exposure to some especial toxins, uncontrolled blood sugar (in diabetes), trauma to head; some of the medications (e.g., ethambutol and anti-retroviral therapy) are risk factors, which may exert an influence on LHON penetrance (4). LHON plus syndrome is an atypical form of the syndrome which includes variable CNS involvements.

In these patients, optic neuropathy is accompanied by other neurological manifestations such as various movement disorders, dystonia, tremor, parkinsonism, cerebellar ataxia, myoclonus, lesions of the basal ganglia, a Leigh-like syndrome, cerebellar atrophy, migraine, mental retardation, epilepsy, peripheral neuropathy, and some forms of skeletal deformities (1, 5).

There were few cases of LHON plus syndrome in literature, one of the first reports of presentation of LHON and the other neurological symptoms was in 1995 by Nikoskelainen EK (6). In this study, the authors introduce patients with LHON with some different movement disorders (dystonia and parkinsonism and MS-like presentations). In the latter case reports, ataxia (7) dystonia (8,9) and seizure (2) were reported as some other CNS manifestations of the disease.

Juvenile-onset encephalopathy, psychiatric disturbances, and regression as well as seen in our patient, are the other presentations that are very confusing for diagnosis (10). The overlap between LHON and MS-like symptoms (LHON-MS, Harding disease) is the other association and presentation of the disease (11).

Our patient was an adolescent with classic ophthalmologic features of LHON accompanied by refractory seizure, progressive cognitive deficit, and mental retardation. According to his past medical history, physical examinations and para clinical findings LHON plus syndrome was diagnosed. The management of these patients remains largely supportive and symptomatic (12).

CONCLUSION

LHON plus syndrome is a rare condition with no definite treatment. Early diagnosis and ruling out treatable conditions are very important points in these patients.

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AUTHORS CONTRIBUTION

All authors contributed equally in this study

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