



Recurrent Painful Ophthalmoplegic Neuropathy: A Case Report with Five Episodes

Rekürren Ağrılı Oftalmoplejik Nöropati: Beş Atak Öyküsü Olan Bir Olgu

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Abstract

Here, we describe an extraordinary case of a 38-year-old male patient with five recurrent episodes of ophthalmoplegia preceded by unilateral migraine-like headaches. He reported recurrent episodes of third cranial nerve palsy preceded by a pulsating and throbbing headache with mild photophobia for 48 hours responsive to steroid therapy, and this was his fifth attack. The clinical symptoms resolved completely after steroid therapy. After a detailed differential diagnosis was made to exclude alternative diagnoses, the patient was finally diagnosed as having recurrent painful ophthalmoplegic neuropathy (RPON). Two-thirds of RPON cases are monophasic. The underlying pathophysiologic mechanisms of RPON are still unclear, however, different hypotheses such as ischemia, demyelination, inflammation, or compression of the nerve are suggested. It is important to be alert for RPON in cases of recurrent ophthalmoplegia and make a detailed differential diagnosis

Keywords: Recurrent ophthalmoplegia, migraine, diplopia, neuropathy

Öz

Bu yazıda öncesinde tek taraflı migren benzeri baş ağrısı ve bunu takip eden oftalmopleji atağı şeklinde toplam 5 atak öyküsü olan 38 yaşında bir erkek hastayı ilginç olması ve nadir görülmesi nedeniyle sunmak istedik. Hasta belli zaman aralıkları ile tekrarlayan, öncesinde zonklayıcı tipte hafif fotofobinin eşlik ettiği baş ağrısı ve ardından 48 saat sonra gelişen 3. kranyal sinir felci şeklinde, her atakta benzer semptomatoloji ile giden tekrarlayıcı ataklar nedeniyle başvurmuştu ve bu beşinci atağı idi. Ataklar steroid tedavisine yanıt veriyordu ve atak sonrası klinik bulgularda tam düzelme mevcuttu. Alternatif tanı olasılıklarının dışlanabilmesi için detaylı bir ayırıcı tanı protokolü uygulandıktan sonra hasta rekürren ağrılı oftalmoplejik nöropati (RPON) tanısı aldı. RPON olgularının 2/3'ünün monofazik olduğu bilinmektedir. Altta yatan patofizyolojik mekanizmalar halen net olmamakla beraber iskemi, demiyelinizasyon, inflamasyon ve sinir basısı olası mekanizmalar arasında yer almaktadır. Tekrarlayan oftalmopleji ile giden olgularda klinisyenlerin olası RPON açısından dikkatli olması ve detaylı bir ayırıcı tanı protokolü uygulanması gerekmektedir

Anahtar Kelimeler: Rekürren oftalmopleji, migren, diplopi, nöropati

Introduction

Recurrent painful ophthalmoplegic neuropathy (RPON), previously known as “ophthalmoplegic migraine” is a rare condition characterized by recurrent unilateral headache episodes followed by one or more ipsilateral cranial nerve palsies (1). According to the most recent edition of the International Classification of Headache Disorders (ICHD-3), exclusion of orbital, parasellar, and posterior fossa lesions and a minimum of two episodes are needed to fulfill the diagnostic criteria (2). The most common cranial nerve involved is the oculomotor nerve, followed by the abducens

and trochlear nerves (3). The etiology is still unknown, and the attacks usually start in early childhood, but adult-onset cases have also been reported in the literature (4). Generally, there is a full recovery after the episodes but, on rare occasions, sequel symptoms remain where an underlying organic etiology may be considered.

Here, we report a patient with recurrent episodes of unilateral migraine-like headaches followed by ipsilateral ptosis and diplopia, which occurred in similar time frames of the year (November and December). We present this case to draw attention to the similarities of migraine and RPON and to discuss the pathophysiology of this rare syndrome.

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Case Report

A 38-year-old, right-handed male patient presented with a left-sided headache, ipsilateral ptosis, and diplopia. The patient described four former episodes nine years ago, five years ago, two years ago, and a year previously, with identical symptomatology, and this was the fifth episode. A unilateral, left-sided pulsating and throbbing headache started two days prior to diplopia and ipsilateral ptosis. The headache was located at the left frontotemporal area with a moderate pain and a visual analog scale score of 5. The patient had mild photophobia and no phonophobia, but the pain was aggravated with routine physical activities. The headache gradually reached its peak in 30 minutes and lasted 48 hours, did not improve with sleep, and resolved without any use of medication just before the ophthalmoplegia with diplopia and ptosis began on the ipsilateral side. The attacks were stereotypical in symptomatology at each episode; headaches were always unilateral and on the left side. The ophthalmoplegia resolved completely within two weeks without any treatment.

A neurologic examination during the episode revealed a left-sided ptosis, and limitations of all eye movements except outward abduction of the left eye bulb. Direct and indirect pupillary reflexes were preserved in the right eye contrary to the left pupil. The pupillary sizes were 5.5 mm and 3 mm for the left and right eyes, respectively. The palpebral fissures were measured as 2 mm in the left eye and 9 mm in the right eye. The fundoscopic examination was unremarkable. Other systematic and neurologic examinations of the patient were normal. See Figure 1.

Routine hemogram tests, complete blood count with electrolytes, blood urea nitrogen, liver function tests, thyroid function tests, a Venereal Disease Research Laboratory test,

angiotensin converting enzyme test, sedimentation rates, and blood tests to investigate vasculitic diseases were all nonspecific. An enzyme-linked immunosorbent assay test was performed for the diagnosis of possible granulomatous diseases, but these results were normal. The patient did not give permission for cerebrospinal fluid (CSF) analysis in the last episode, but the results of CSF analysis of the fourth episode showed a protein level of 95 mg/dL, a glucose level of 64 mg/dL (same time blood glucose level of 96 mg/dL), a chloride level of 123 mg/dL, and a lactate dehydrogenase level of 35 mg/dL. There were no blood cells, a negative mycobacterium polymerase chain reaction test, and no proliferation in cell cultures. All laboratory results were accepted as normal.

The results of the neuroimaging examinations with a 1.5 Tesla cranial magnetic resonance imaging (MRI), orbital MRI, and cranial magnetic resonance angiography with gadolinium revealed no gadolinium enhancement, no signs of aneurysms or neoplasms, and were completely normal (Figure 2). In view of the clinical signs and symptoms, and with the exclusion of other differential diagnoses through neuroimaging methods, we accepted the patient as having RPON. The patient received no medication in his first episode (he did not present to a hospital in his first attack) and improved spontaneously. He received pulse-steroid therapy with 1 mg/kg intravenous methylprednisolone for seven days in his second and third episodes and improved within one week. In the last episode, we administered the same therapy as 1 mg/kg intravenous methylprednisolone for seven days, and near-complete recovery of the extra-ocular motor functions was observed at the follow-up examination three weeks later.

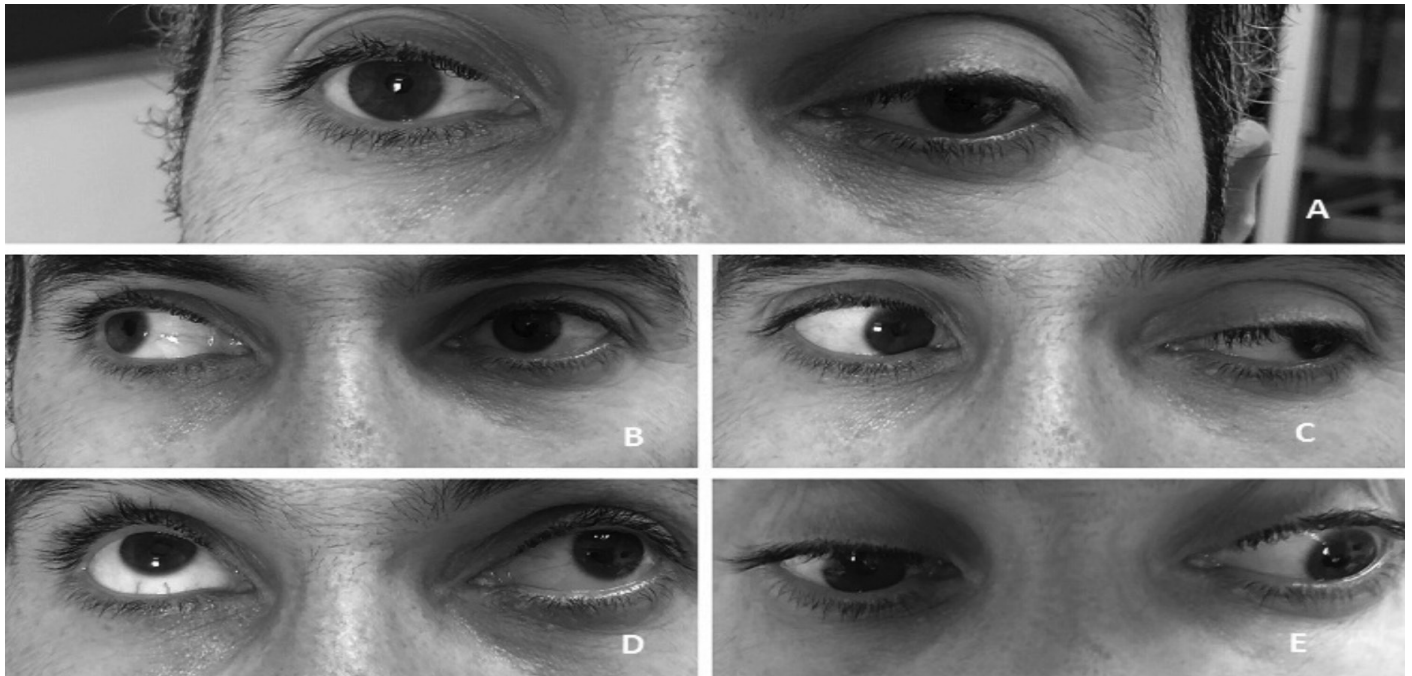


Figure 1. Images of eye showing left ptosis and third cranial nerve palsy. A. Neutral (primary) position B. C. D. E. Limitations of eye motions except abduction in the left eye on admission

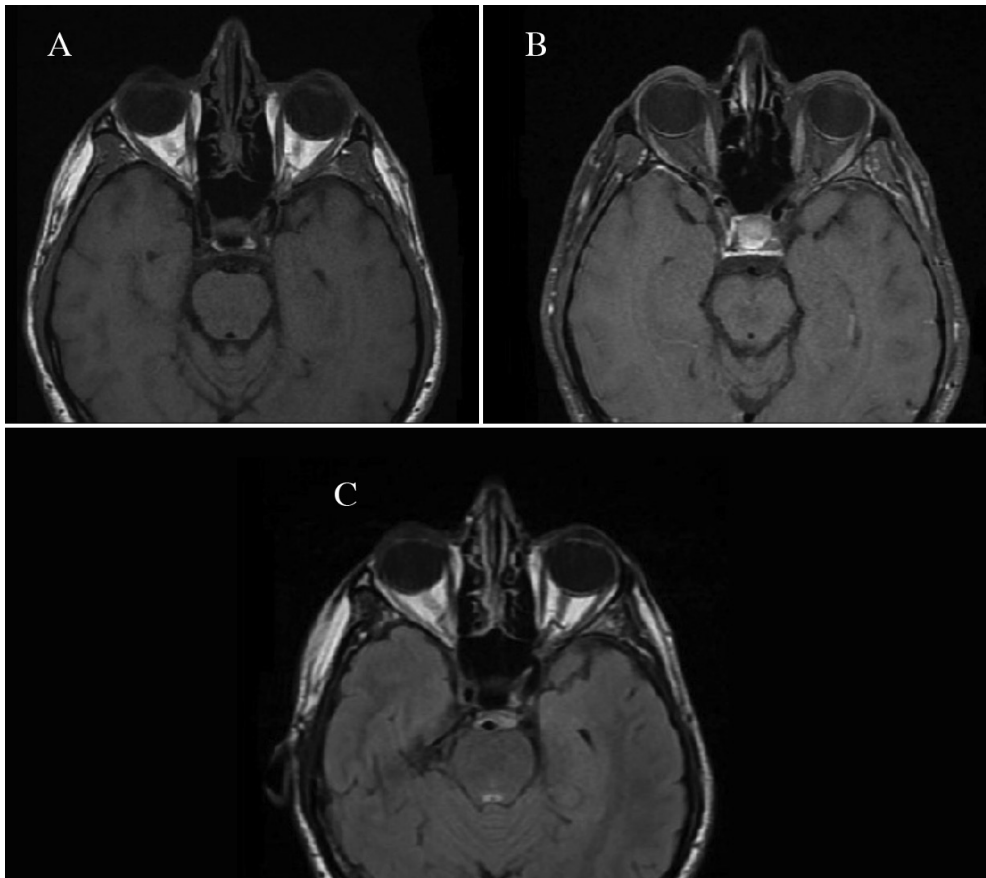


Figure 2. 1.5-T magnetic resonance imaging performed after the onset of ocular motor symptoms of recurrent painful ophthalmoplegic neuropathy. A, 3 mm-thin sliced T1-weighted imaging, B, 3 mm-thin sliced T1-weighted imaging (with gadolinium), C, T2-weighted imaging

Discussion

Here, we report a patient with five episodes of RPON with oculomotor nerve involvement. This is an extraordinary case given that two-thirds of RPON cases are a one-time episode only (5). Interestingly, each episode occurred in the same time frames (November and December) of the year.

RPON is a rare clinical condition with unilateral migraine-like headaches prior to the development of ophthalmoplegia. The prevalence of the disease is estimated to be 0.7 per million people worldwide (3). It is a diagnosis of exclusion after performing all diagnostic investigations and excluding other etiologies of ophthalmoplegia. RPON was first described in 1854 with its former name 'ophthalmoplegic migraine,' although this term has been rejected in the last version of ICHD-3 because of the different pathophysiologic backgrounds between migraines and painful ophthalmoplegia (1). The underlying mechanisms of RPON are still unclear. However, different hypotheses such as ischemia, demyelination, inflammation, and nerve compression have been suggested (5). The compression theory can be summarized as edema of the walls of the internal carotid artery leading to compression of the oculomotor nerve in the cavernous sinus (1). Another possible mechanism is that reduced blood flow in distant branches of the posterior cerebral and internal carotid artery may

result in ischemia of the oculomotor and abducens nerves and eventually ophthalmoplegia (5).

The inflammatory process is also blamed as another possible mechanism. The constant release of neuropeptides such as the calcitonin-gene related peptide from the fifth cranial nerve may trigger a neurogenic inflammatory response primarily of the oculomotor nerve and other cranial nerves, and result in headaches and ophthalmoplegia (1). This theory could explain the abnormal enhancement of the oculomotor nerve in T1-weighted MRI with gadolinium, especially at the root level, in some of the reported cases of RPON (5). However, in our case, there was no enhancement of the oculomotor nerve in cranial and orbital MRIs with gadolinium, and the neuroimaging studies were normal.

There are still arguments about the headache mechanisms in cases of RPON. The hypothesis of migraine as the primary cause of headache is not completely accepted because the duration of migraine is less than 72 hours, whereas the duration between the headache and ophthalmoplegia may exceed two weeks in some cases. A possible neuropathy of irritated trigeminal nerve fibers causing the headache is suggested to be a more acceptable explanation (1). In our case, the patient described unilateral migraine-like headaches, throbbing and pulsating in character, and aggravation with physical activity. There was mild photophobia and no phonophobia or aura was described. He had no family history of

migraine and no other previous migraine headache attacks before these episodes, but the duration of the headache was 48 hours, which may also be compatible with migraine-like headaches.

In conclusion, we reported a patient with five episodes of RPON with features of unilateral migraine-like headaches, responsive to steroid treatment, and almost complete resolution within three weeks. It is important to make a detailed differential diagnosis in cases of recurrent ophthalmoplegia. Further studies are needed to understand the natural course of RPON and to establish an effective therapy.

Ethics

Informed Consent: Informed consent is obtained from the patients.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.B.Ç., Concept: A.Ç.A., Design: A.Ç.A., U.E., Data Collection or Processing: A.B.Ç., N.Y., Analysis or Interpretation: A.Ç.A., U.E., Literature Search: A.Ç.A., N.Y., Writing: A.Ç.A., A.B.Ç.

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