International Journal of Infectious Diseases 15 (2011) e147–e150

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Acute optic neuritis following infection with chikungunya virus in southern rural India

Nice Rose [a], T.M. Anoop [b,*], Anil P. John [b], P.K. Jabbar [b], K.C. George [b]

[a] Department of Ophthalmology, Kottayam Medical College, Kerala, South India
[b] Department of Medicine, Kottayam Medical College, Kerala 686008, South India

ARTICLE INFO

Article history:
Received 1 April 2010
Received in revised form 11 October 2010
Accepted 14 October 2010

Corresponding Editor: Jane Zuckerman, London, UK

Keywords:
Chikungunya
Acute optic neuritis

SUMMARY

Objectives: To define acute optic neuritis following infection with chikungunya virus (CHIKV) and to determine the efficacy of treatment with corticosteroids of acute optic neuritis.
Methods: This was an observational study involving 10 patients, who were confirmed cases of infection with CHIKV with acute optic neuritis in one or both eyes. A complete ophthalmic examination was performed in all cases. All 10 patients were treated with intravenous methylprednisolone for 3 days, followed by oral prednisolone for 2 weeks, thereafter reducing the dose of prednisolone over 1 month.
Results: Of the 10 patients in the study, seven were male and three female. Seven patients had unilateral optic neuritis and three patients had bilateral optic neuritis. Initial visual acuity in the affected eyes ranged from perception of light to visual acuity of 6/6. After treatment, nine out of 10 patients improved to visual acuity of 6/12 or better. Color vision became normal in eight patients in our study. After treatment, a relative afferent pupillary defect persisted in four patients and six patients had normal pupils. A statistically significant improvement in vision was found after treatment ($p \leq 0.001$). Visual field (HFA FF 120) examination showed various types of defect. Visual fields returned to normal in four patients, while the remaining six patients had persistent diffuse visual field defects.
Conclusions: CHIKV infection may cause acute-onset of visual loss due to acute optic neuritis. Prompt recovery of vision may follow steroid therapy. Physicians should be aware of the possibility of acute optic neuritis following CHIKV infection so that a preventable cause of vision loss can be treated effectively.

1. Introduction

Chikungunya is an acute febrile syndrome characterized by high-grade fever with chills, myalgia, headache, photophobia, skin rash, and severe disabling arthritis.[1] Chikungunya fever is most often a self-limiting febrile illness,[1] however recent outbreaks appear to have been more severe than previous outbreaks, with more systemic manifestations and even death.[2,3] Ocular abnormalities described in these recent outbreaks are optic neuritis, papillitis, neuroretinitis, panuveitis, non-granulomatous anterior uveitis, and retinitis.[4–7]

Here we present an observational study of acute optic neuritis following chikungunya virus (CHIKV) infection during a short epidemic, over the period from July 12 to August 21, 2007 in the state of Kerala, southern rural India.

2. Methods

This was an observational study involving 10 patients who were confirmed cases of infection with CHIKV with acute optic neuritis in one or both eyes. The study was conducted in the Department of Ophthalmology and Internal Medicine, Kottayam Medical College, Kerala, following the viral fever epidemic, during a 6-week period from July 12 to August 21, 2007.

A routine hemogram, including total count, differential count, erythrocyte sedimentation rate, platelet count, and peripheral blood smear was done. Anti-nuclear antibody, blood culture, Widal test, Mantoux test, IgM leptospiral antibody, IgM dengue antibody, test for syphilis, and retroviral antibody tests were also performed.

A complete ophthalmic examination, including best-corrected visual acuity (BCVA; Snellen chart), color vision (Ishihara pseudoisochromatic color vision plates), pupillary reaction (RAPD, relative afferent pupillary defect), and visual field (Humphrey field analyzer), as well as intraocular pressure by applanation tonometry, indirect ophthalmoscopy of the dilated fundus, slit lamp biomicroscopy of the anterior and posterior segments, and visual evoked potentials were performed in all cases. RAPD was graded as

* Corresponding author. Tel.: +91 9447134973.
E-mail address: dranooptm@yahoo.co.in (T.M. Anoop).

1201-9712/$36.00 – see front matter © 2010 International Society for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.ijid.2010.10.004

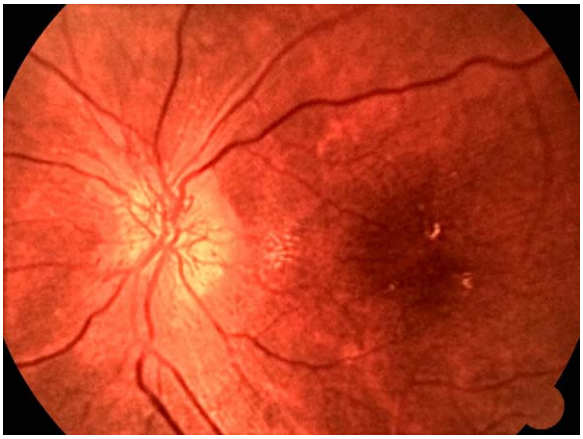

Figure 1. Fundus photograph of a 42-year-old woman with acute optic neuritis following chikungunya fever, showing disc edema.

grade 1+ to grade 4+. Grade 1+ is a weak initial pupillary constriction followed by greater redilation; grade 2+ is an initial pupillary stall followed by greater redilation; grade 3+ is an immediate pupillary dilation; and grade 4+ is no reaction to light (amaurotic pupil). Fundus photograph of a 42-year-old woman with acute optic neuritis following chikungunya fever, showing disc edema is shown in Figure 1.

All patients were diagnosed to have a CHIKV infection based on typical clinical presentation of acute fever with severe disabling arthralgia and a positive IgM CHIKV serological test, and negative test results for dengue, typhoid, malaria, and tuberculosis. A screening magnetic resonance imaging (MRI) was also performed in all patients to rule out any form of demyelination.

All 10 patients were treated with intravenous methylprednisolone 1 g/day for 3 days, followed by a daily dose of 1 mg/kg body weight of oral prednisolone for 2 weeks, thereafter reducing the dose of prednisolone over 1 month. Blood pressure, body weight, blood sugar, serum electrolytes, and electrocardiography were recorded before starting therapy. None of our patients had risk factors like hypertension or diabetes mellitus or a previous history of visual loss. The patients were treated as inpatients during the period of intravenous therapy and were discharged over the next 3 days. Patients were followed up at 2, 3, and 4 weeks.

Visual function (color vision, visual field, and BCVA) was compared before and after intravenous methylprednisolone therapy. Informed consent was obtained from all study patients.

3. Results

Demographic and ocular features of the 10 patients with optic neuritis associated with CHIKV infection are described in Table 1. Of the 10 patients in the study, seven were male and 3 female. All patients in the study were in the age group 22–45 years. All 10 patients in the study series presented with sudden onset decrease in vision or blurring of vision, which deteriorated over the next few days. All 10 patients had a history of fever, joint pain, and skin rash 1–6 weeks prior to the onset of defective vision. Among the 10 patients, three had defective vision and pain on ocular movements in both eyes and seven had complaints only in one eye. None of these patients had demyelination in the screening MRI.

Seven patients had unilateral optic neuritis and three had bilateral optic neuritis. The types of optic neuritis in the study population were: unilateral papillitis (four patients), bilateral papillitis (three patients), retrobulbar neuritis (one patient), perineuritis (one patient), and neuroretinitis (one patient).

4. Visual acuity profile of eyes with acute optic neuritis following chikungunya

Initial visual acuity in abnormal eyes in our study ranged from perception of light (PL) to visual acuity of 6/6 (Table 1).

After treatment, nine out of 10 patients improved to visual acuity of 6/12 or better (Table 2). One patient who had an initial

Table 1
Demographic and ocular features of 10 patients with optic neuritis associated with chikungunya virus infection

Patient number, age/gender	Ocular symptoms	Ocular features	Visual field defect	IgM CHIKV Ab test	VEP	Type of optic neuritis	Laterality	Pre-treatment VA	Visual outcome (post-treatment VA)
1, 42/F	Defective vision	Disk edema, RAPD	Paracentral scotoma	Positive	115	Papillitis	Right eye	PL+*/6/6	6/6/6/6
2, 45/M	Defective vision	Disc edema, B/L pupillary sluggish reaction	Central scotoma both eyes	Positive	110	Papillitis	Both eyes	6/12*/6/6*	6/6/6/6
3, 24/M	Defective vision	Disc edema, disc hemorrhage, B/L pupillary sluggish reaction	Diffuse (severe) both eyes	Positive	110	Papillitis	Both eyes	CF2m*/CF3m*	6/12/6/12
4, 35/M	Defective vision	Disc edema, B/L pupillary sluggish reaction	Diffuse (severe) both eyes	Positive	130	Papillitis	Both eyes	6/36*/6/36*	6/6/6/6
5, 44/M	Defective vision	Disc edema, RAPD	Centrocecal scotoma	Positive	118	Papillitis	Right eye	6/36*/6/18	6/18/6/18
6, 38/M	Defective vision	Disc edema, disc hemorrhage, RAPD	Diffuse (severe)	Positive	110	Neuroretinitis	Left eye	6/6/CF1/2m*	6/6/6/6
7, 42/F	Defective vision	Disc edema, RAPD	Diffuse (mild)	Positive	118	Perineuritis	Right eye	6/6*/6/6	6/6/6/6
8, 31/F	Defective vision	Disc edema, RAPD	Diffuse (severe)	Positive	110	Retrobulbar neuritis	Right eye	6/60*/6/6	6/6/6/6
9, 22/M	Defective vision	Disc edema, RAPD	Diffuse (severe)	Positive	110	Papillitis	Left eye	6/6/6/36*	6/6/6/6
10, 35/M	Defective vision	Disc edema, RAPD	Peripheral constriction	Positive	110	Papillitis	Right eye	6/60*/6/6	6/6/6/6

B/L, bilateral; CF, counting finger; CHIKV Ab, chikungunya virus antibody; PL, perception of light; RAPD, relative afferent pupillary defect; VA, visual acuity; VEP, visual evoked potential (mean P100 latency, ms).

Table 2
Comparison of pre-treatment and post-treatment visual acuity outcome of patients with chikungunya infection-related acute optic neuritis

Visual acuity	Pre-treatment	Post-treatment
≥6/12	2	9
6/18–6/36	3	1
6/60–CF1m	2	0
CF1m–PL+	3	0
Total number of patients	10	10

CF, counting finger; PL, perception of light.

visual acuity of 6/36 improved to visual acuity of 6/18, and that same patient had early cataractous changes in both eyes; BCVA in the normal eye was 6/18.

5. Color vision outcome

After treatment, color vision became normal in eight patients. Color vision abnormality persisted in two patients.

6. Pupillary reaction

Before treatment, all 10 patients had pupillary abnormalities – seven had RAPD and three had bilateral optic neuritis with sluggish reaction of the pupil. After treatment, RAPD persisted in four patients, and six patients had normal pupils. A statistically significant improvement in vision was noticed after treatment ($p \leq 0.001$).

7. Visual field defects

Visual field (HFA FF 120) examination showed various types of defect, including central, centrocecal, and paracentral scotoma and peripheral constriction. Visual field returned to normal in four patients, while the remaining six patients had persistent diffuse visual field defects.

8. Discussion

Chikungunya virus infection has recently been reported to cause varied ocular manifestations, like non-granulomatous anterior uveitis, episcleritis, panuveitis, granulomatous anterior uveitis, optic neuritis, sixth nerve palsy, retrobulbar neuritis, retinitis with vitritis, neuroretinitis, keratitis, central retinal artery occlusion, choroiditis, exudative retinal detachment, and secondary glaucoma.[4–9] The types of optic neuritis in our study population were unilateral papillitis, bilateral papillitis, retrobulbar neuritis, perineuritis, and neuroretinitis. Patients with optic neuritis generally present with pain on eye movement associated with unilateral visual loss, visual field defects, and changes in color perception. The visual loss is progressive and may occur rapidly over several hours or more slowly over days.

The exact mechanism of optic nerve involvement following chikungunya fever is unknown.[5] The possible causes may be direct viral involvement and a delayed immune response after a viral infection. Several characteristics such as delay in onset, partial recovery of disc changes, bilateral involvement in a few patients, and good response to corticosteroid therapy indicate the possibility of an autoimmune mechanism in the pathogenesis of the disease.[5] The onset of visual symptoms a few weeks after chikungunya fever in our patients favors the hypothesis that the ocular lesions could be an immune-mediated process rather than a direct viral infection. The prompt response to steroids also favors an immune-mediated cause.

In our study, after treatment with intravenous methylprednisolone, 12 out of 13 eyes improved to 6/12. One patient had an initial visual acuity of 6/36, which improved to 6/18, and that same patient had early cataractous changes in both eyes. The overall prognosis in terms of visual acuity, color vision, and visual field was good.

Corticosteroid therapy in the form of 3 days of intravenous methylprednisolone, followed by oral prednisolone in a tapering dose, could assist in the rapid recovery of visual function in patients with acute presentation of optic neuritis. In one clinical series, clinical response to intravenous pulsed dexamethasone led to rapid recovery of vision and visual function outcome in Indian patients with acute optic neuritis.[10]

Simultaneous onset of systemic and ocular disease suggests direct viral involvement. In contrast to the study by Mittal et al., all 10 patients in our study had defective vision 1–6 weeks after the onset of systemic disease and none had simultaneous systemic and ocular involvement. Mittal et al. described the mechanism of optic nerve involvement following CHIKV infection as being direct viral involvement in 36% and late optic nerve involvement, suggesting a delayed immune response (post-viral infection) in 64%.[5] Corticosteroid therapy may lead to rapid recovery of visual function in patients with acute presentation of optic neuritis, but has no role when treatment is initiated at a late stage of the disease.[5] Mittal et al. described three patients in whom treatment was initiated 1 month after the onset of visual symptoms for whom there was no visual improvement. This suggests that corticosteroid therapy has no role when treatment is initiated at a late stage of the disease. In our study, all 10 patients presenting with vision loss after 1–6 weeks of systemic disease were immediately started on corticosteroid therapy following the documentation of acute optic neuritis. Since we have no data to suggest the role of corticosteroids in patients with delayed presentation (after 6 weeks) of optic neuritis following CHIKV infection in our study, more clinical studies are needed to document the role of corticosteroids in late cases (after 6 weeks) of CHIKV-related optic neuritis.

In conclusion, even though chikungunya infection is a self-limiting illness, CHIKV infection may cause acute-onset visual loss due to acute optic neuritis. Prompt recovery of vision may follow steroid therapy. Physicians should be aware of the possibility of acute optic neuritis following CHIKV infection so that a preventable cause of vision loss can be treated effectively.

Funding

No funding or financial support was received from any company or party.

Ethical approval

This study was approved by the hospital ethics committee, Kottayam Medical College.

Conflict of interest

No conflict of interest to declare.

References

1. Ravi V. Re-emergence of chikungunya virus in India. *Indian J Med Microbiol* 2006;**24**:83–4.
2. Bandyopadhyay B, Bandyopadhyay D, Bhattacharya R, De R, Saha B, Mukherjee H, et al. Death due to chikungunya. *Trop Doct* 2009;**39**:187–8.
3. Mavalankar D, Shastri P, Bandyopadhyay T, Parmar J, Ramani KV. Increased mortality rate associated with chikungunya epidemic, Ahmedabad. *India Emerg Infect Dis* 2008;**14**:412–5.
4. Lalitha P, Rathinam S, Banushree K, Maheshkumar S, Vijayakumar R, Sathe P. Ocular involvement associated with an epidemic outbreak of chikungunya virus infection. *Am J Ophthalmol* 2007;**144**:552–6.

5. Mittal A, Mittal S, Bharati MJ, Ramakrishnan R, Saravanan S, Sathe PS. Optic neuritis associated with chikungunya virus infection in South India. *Arch Ophthalmol* 2007;**125**:1381–6.
6. Chanana B, Azad RV, Nair S. Bilateral macular choroiditis following chikungunya virus infection. *Eye* 2007;**21**:1020–1.
7. Mahendradas P, Ranganna SK, Shetty R, Balu R, Narayana KM, Babu RB, et al. Ocular manifestations associated with chikungunya. *Ophthalmology* 2008;**115**: 287–91.
8. Mahesh G, Giridhar A, Shedbele A, Kumar R, Saikumar SJ. A case of bilateral presumed chikungunya neuroretinitis. *Indian J Ophthalmol* 2009;**57**: 148–50.
9. Murthy KR, Venkataraman N, Satish V, Babu K. Bilateral retinitis following chikungunya fever. *Indian J Ophthalmol* 2008;**56**:329–31.
10. Sethi HS, Menon V, Sharma P, Khokhar S, Tandon R. Visual outcome after intravenous dexamethasone therapy for idiopathic optic neuritis in an Indian population: a clinical case series. *Indian J Ophthalmol* 2006;**54**:177–83.