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Ocular Manifestations of Chikungunya Fever

Manifestações oculares na febre Chikungunya

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Abstract

Chikungunya fever is a world public health problem with the potential to generate epidemics of high morbidity, since a high number of patients may present prolonged joint sequelae and ophthalmological alterations. Ophthalmologic manifestations may be present in the acute phase of the disease or begin after several weeks of the onset of the disease. In the world literature is described from more common and easy to treat changes such as conjunctivitis to more complex changes and that can occur with severe visual sequelae such as retinitis and optic neuritis.

Keywords: *Chikungunya fever; Chikungunya virus; Eye infections, viral; Arbovirus infections*

Resumo

A febre Chikungunya é um problema de saúde pública mundial, com potencial para gerar epidemias de alta morbidade, visto que elevado número de pacientes pode apresentar sequelas articulares prolongadas e alterações oftalmológicas. As manifestações oftalmológicas podem estar presentes na fase aguda da doença ou ter início após várias semanas da instalação do quadro. Na literatura mundial é descrito desde alterações mais comuns e de fácil tratamento como conjuntivites até alterações mais complexas e que podem cursar com sequelas visuais graves como a retinite e neurite óptica.

Descritores: Febre de Chikungunya; Vírus Chikungunya; Infecções oculares virais; Infecções por arbovírus

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Introduction

Chikungunya fever, caused by the virus of the same name, is a disease manifesting with joint involvement, and is potentially debilitating due to the intensity and chronicity of the pain. [1] Transmission occurs through the bite of the female mosquitoes Aedes Aegypti and Aedes Albopictus infected with the Chikungunyavirus, characterizing an arbovirus. [2]

It was first identified in 1952 in an epidemic in Makonde Plateau, southern Tanzania, and its name means in its original language "the one who bends", a reference to the antalgic posture of the infected patient. [3]

In Brazil, the first native case was confirmed in Oiapoque-AP (on September 13, 2014), and seven days afterwards new cases were confirmed in Feira de Santana-BA. [4]

In Brazil, 185,854 probable cases of Chikungunya fever were recorded in 2017, and in 2018 there were 85,221 probable cases with 65,480 (76.8%) confirmed according to data from Sistema de Notificação e Agravos de Notificação (SINAN). [5]

In 2019, until the twelfth epidemiological week between 12/30/2019 and 3/23/2019, there were 15,352 probable cases of Chikungunya fever in the country, with an incidence of 7.4 cases/100,000 inhabitants. The Southeast region had the highest number of probable cases of Chikungunya (66.5%) compared to the total of the country. Among the Federative units, Rio de Janeiro stands out for the highest incidence rate with 47.7 cases/100,000 inhabitants. Laboratory findings confirmed 2 deaths from Chikungunya fever, and 10 deaths were confirmed during the same period in 2018. [5]

The Ministry of Health recommends the notification of any suspected case to the epidemiological surveillance service within seven days (Annex of Ordinance No. 204/2016), while suspected deaths are immediately reported (up to 24 hours). Suspected cases are defined as sudden onset fever and arthralgia, or severe acute onset arthritis that is not explained by other conditions or which has an epidemiological link with a confirmed case.[2]

Laboratory diagnosis is performed through serological tests. During the acute phase of infection, high titers of the virus are present in the blood, allowing viral RNA to be searched by the Polymerase Chain Reaction (PCR) technique between the first and fifth day.[2,6] Serological tests allow the detection of specific antibodies (M-IgM type immunoglobulins) from the second day after onset of symptoms, whereas in the second week after infection, G-type immunoglobulin (IgG) is already detected. [2,7]

Clinical manifestations

Virus-infected patients present the acute phase with high fever (greater than 39 ºC), severe arthralgia, myalgia, and maculopapular rash.[8]

The onset of symptoms is abrupt and occurs after an incubation period of three days. The resolution of fever and skin rash usually occurs within a few days.[9] About 15% of individuals are asymptomatic.[8]

Most patients have joint pain and edema that are typically symmetrical and can affect any joint.[8] The complaint of arthralgia begins after the first week of onset of symptoms, and may last up to three years. [10]

In severe cases, encephalitis, myocarditis, hepatitis and multiple organ failure may occur. Neurological involvement leads to seizures, mental disorders, flaccid paralysis and even death. [11,12]

Ocularocular manifestations

Ophthalmic alterations resulting from Chikungunya fever are described in a few studies. In a retrospective study carried out in India, the onset of development of ocular manifestations varied from 4 to 12 weeks (average of six) of acute disease. [13]

In the presence of these manifestations, Chikungunya fever is ranked as atypical form, considered the most severe one. Ocular alterations possibly occur due to the immune response associated with the hypersensitivity reaction. This response is initiated by antibodies against viral antigens that are also responsible for joint involvement in systemic disease. [14]

Occurrence of ocular manifestations may be associated with the direct effect of the virus (when followed by systemic manifestations), immunological response (on late manifestations)[15], or drug toxicity. [2] The exact mechanisms of ocular involvement in Chikungunya fever are not yet fully elucidated.

In the cornea, epithelial and endothelial cells are the virus's preferred targets, while fibroblasts are affected in the scleral connective tissue, smooth muscle stroma of the ciliary body and iris.[16,17]

Cases of conjunctivitis, along with hyperemia and ocular discomfort, similar to other viral conjunctivitis have been identified.[18] The most commonly found alteration was bilateral anterior uveitis often associated with increased intraocular pressure.[13,19]

Regarding the symptoms reported during the acute period of infection, the study by Esporcatte et al. noted that 4 patients (12.50%) reported conjunctivitis, and 19 retroorbital pain (59.38%).[20] In a retrospective study of 139 Chikungunya positive serology patients carried out in a general emergency in Puerto Rico in 2014, conjunctivitis was described in 27 patients (19.40%), and we observed 13 patients (9.40%) with symptoms associated with anterior uveitis described as unilateral conjunctival hyperemia, ciliary injection, and pupil irregularity. However, a non-specialist doctor diagnosed it without the aid of a slit lamp. [21] Literature reported that photophobia, conjunctival hyperemia, and retroorbital pain are frequent findings in the acute phase of the disease, and may present without other ophthalmic alterations. [22]

In the retrospective study by Mahendradas et al., five patients had iridocyclitis in the acute phase of the infection with no alterations in gonioscopy examination nor fundoscopy.[13] Lalitha et al. described 11 cases of patients with anterior uveitis (10 non-granulomatous and one granulomatous) diagnosed within three months of the acute phase of infection.[23]

Regarding the increase in intraocular pressure, the study by Esporcatte et al.showed one patient with increased intraocular pressure associated with increased optic disc excavation (ranging from 08-30 mmHg). [20] In the study by Mittal et al., 5 patients were diagnosed with increased intraocular pressure (36.8±10.3 mmHg) induced by uveitis.[24] Another study described 5 patients with intraocular inflammation with increased intraocular pressure ranging from 27-42 mmHg. It was controlled three weeks after specific treatment of the inflammatory process.[13]

Regarding visual acuity, ithe chronic phase of the disease (12.72 ± 7.70 months) showed the variation with the best correction between 20/20 and 20/60.[20] In a retrospective study carried out in India in 2007 of a series of 37 cases up to three months after diagnosis of the disease, the visual acuity found ranged from 20/20 to light perception in 1 patient. [23] In the study by Mittal et al. visual acuity with the best correction

ranged from 20/40 in 11 eyes (61.10%) to worse than 20/200 in 2 eyes (11.10%).[15] In another retrospective study with 9 patients, the best corrected visual acuity ranged from 20/20 to 20/20,000 (equivalent to 60 cm hand movement).[13, 25]

In the work of Esporcatte et al., dry eye diagnosis was reported in 20 patients (62.00%) through tear function tests. In these, alterations were found in 9 individuals only in the rupture time of the tear film (45.00%); in 11 individuals, both in rupture time of the tear film and the Schirmer test (55.00%). Four patients had alterations in the green lissamine test (12.50%). No statistical significance was found between dry eye and the patient age. [20]

Lalitha et al. observed 3 patients with keratitis, but with a similar dendritic pattern to that caused by herpes virus, who underwent the recommended treatment for herpetic keratitis with acyclovir to obtain improvement of the condition.[23]

Posterior segment involvement may manifest with retinitis,[13, 18, 23] choroiditis,[23] neuroretinitis[26, 27] and optic neuritis.[24] Retinitis may present with vitreitis, hemorrhage, and retinal edema with retinal vasculature involvement, which may resemble herpesvirus infection.[13] Most retinitis patients have visual acuity recovery within 10-12 weeks. After the infection, only mobilization of the retinal pigment epithelium is evident on fundoscopy. In a few cases, macular ischemia and optic disc alterations may occur allong with permanent reduction in visual acuity.[28]

Acute visual loss may occur in cases of optic neuritis secondary to infection by the Chikungunyavirus, and visual recovery is treated with systemic corticosteroid therapy. In the study by Mittal et al., 36% of patients with optic neuritis had concomitant ocular systemic manifestations suggesting direct involvement of the virus. [24]

Lalitha et al. diagnosed 3 patients with retrobulbar optic neuritis with afferent pupillary defect, although fundoscopy had no changes. Optic neuritis was diagnosed in older patients.[23]

Treatment

There is yet no specific treatment nor vaccine to prevent infection. Current treatment includes symptomatic drugs such as oral anti-inflammatory drugs and hydroxychloroquine (antimalarial drug).[29]

Ocular manifestations are treated according to the structure affected. In case of conjunctivitis, the treatment is symptomatic with the use of eye lubricants and cold dressings. For the treatment of uveitis, topical and/or systemic corticosteroids may be used, and if intraocular pressure increases the use of hypotensive eye drops may be associated. Oral corticosteroids are used in posterior pole alterations (retinitis and optic neuritis), and in the most severe cases with involvement of the optic disc, hospitalization and intravenous corticosteroid therapy are required. [19]

Final Thoughts

There have been reports in the world literature of ocular manifestations caused by the Chikungunyavirus starting both in the acute phase and after several weeks of infection. It is known to occur from the most common and easily treated alterations such as conjunctivitis to the most complex ones, and which can develop with severe visual sequelae such as retinitis and optic neuritis. [28] Therefore, as long as there are endemics caused by this virus, it must be included as a differential diagnosis of eye disorders.

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