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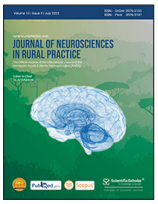

Letter to Editor

Bilateral simultaneous lower motor nerve facial palsy as presenting symptom of cryptococcal meningitis in a non-immunocompromised patient

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Dear Editor

The average annual incidence rate of facial nerve paralysis is 23–25 patients/100,000 population.[1] Simultaneous bilateral facial palsy (involvement of the opposite side within 30 days of the onset of one side) occurs in <1%.[1] A review from various centers revealed that 0.6–0.8% of cases are bilateral among patients with facial palsy.[2-5]

Bilateral facial nerve palsy is caused by infections: Neuroborreliosis, human immunodeficiency virus (HIV), syphilis, leprosy, infectious mononucleosis, trichinosis, poliomyelitis, mycoplasma, herpes virus, varicella-zoster virus, diphtheria, tuberculous meningitis, and otitis.[1] Other causes include cerebral venous sinus thrombosis, sarcoidosis, Guillain-Barre syndrome, and osteopetrosis.[6,7]

Cryptococcal infection presents as meningitis with severe headache and raised intracranial pressure. Bilateral sixth nerve palsy is common, but bilateral simultaneous seventh nerve palsy has not been reported.

A 35-year-old male presented to our emergency services, with a history of intermittent fever for 5 days, holocranial headache, inability to close his eyes, and slurring of speech for 3 days. History of altered taste sensation was present. On examination, his vital signs and general physical examination were normal. Fundus was normal; visual acuity was 6/6 in both eyes, extraocular movements were full, and bilateral peripheral facial paralysis with a Grade III (House–Brackmann facial paralysis scale) weakness [Figure 1] was noted. He also had impaired taste sensation, hyperacusis, and Bell's phenomenon in both eyes. Patient had no signs of meningeal irritation. Complete blood count, liver and kidney function tests, serum electrolytes, chest radiography, and computed tomography (CT) scan of the brain showed no abnormality. His CT thorax was normal [Figure 2], magnetic resonance imaging (MRI) brain plain, and contrast showed bilateral facial nerve enhancement and normal parenchyma [Figure 2]. The CSF analysis revealed normal pressure (170 mm CSF), cell count – 57/µl: All lymphocytes, protein 52.70 mg/dl (15–45 mg/dl), the glucose of 56 mg/dl (plasma glucose 101 mg/dl), acid-fast stain, Gram stain, and Venereal Disease Research Laboratory test were negative. Serum angiotensin-converting enzyme levels were 22.9 u/l (12–68), HIV antibody test by enzyme-linked immunosorbent assay (ELISA) was negative, and CD4 counts were 771 cells/dl. CSF cytospin showed degenerated cells, CrAg by latex agglutination test was positive, and India ink test was negative.

Intravenous (IV) amphotericin B 0.7 mg/kg/day was started with flucytosine 100 mg/kg/day and oral fluconazole 400 mg daily. Amphotericin was continued for 2 weeks and stopped. Oral fluconazole was continued (400 mg/day). The CSF culture yielded no growth at the end of 2 weeks. After 3 months, CSF was repeated, and CrAg and India ink were negative. Facial weakness improved; partially, headache subsided completely. He is currently on fluconazole (400 mg/day) and is on regular follow-up.

Our patient presented with bilateral simultaneous facial diplegia with acute-onset headache. He was initially suspected of having acute raised intracranial tension (ICT) syndrome with facial nerve palsy, and a search was made for various etiologies. His MRI brain showed gadolinium contrast-enhancing bilateral facial nerves. The CSF analysis showed lymphocytic pleocytosis with mildly elevated protein and positive CrAg by latex agglutination test and normal opening pressure (170 mm CSF). His HIV antibody testing by ELISA was negative and CD4 count was 771 cells/dl. He

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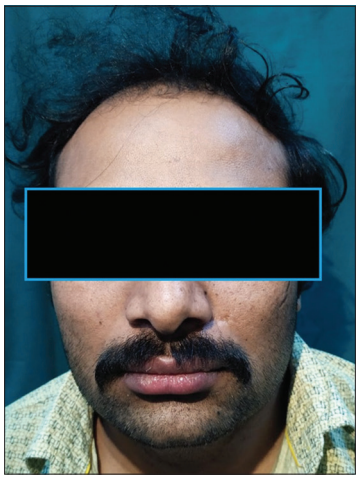

Figure 1: The patient was asked to show his teeth. He was unable to do.

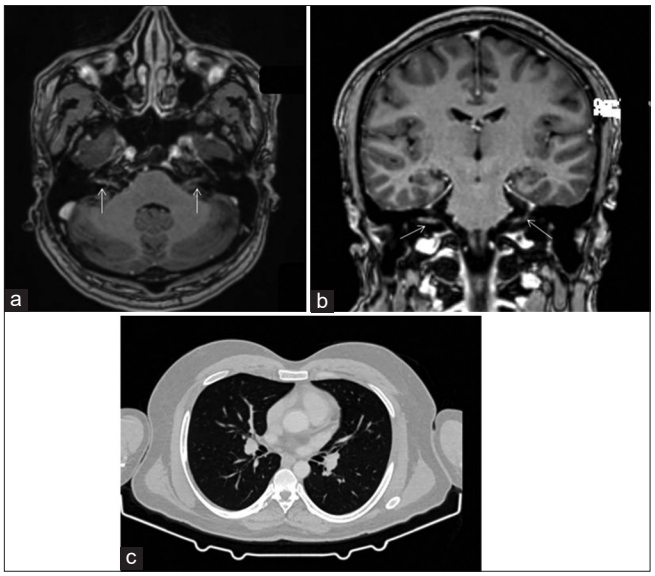

Figure 2: Magnetic resonance imaging, T1 post-gadolinium contrast axial (a) and coronal (b) shows bilateral facial nerve enhancement (white arrows). Computed tomography of thorax is normal without lymphadenopathy.

was finally diagnosed with cryptococcal meningitis with bilateral facial palsy due to the direct involvement of facial nerves by fungus.

Cryptococcus neoformans is saprophytic encapsulated yeast with extensive distribution in soil contaminated mostly from pigeons.[6] There are three serotypes pathogenic to humans: *Cryptococcus neoformans grubii*, *Cryptococcus neoformans gattii*, and *Cryptococcus neoformans neoformans*.[7] Infection is acquired by inhalation of the organism and is asymptomatic or limited to the lungs. Hematogenous dissemination, especially to the meninges, leads to fatal outcomes in immunocompromised patients.[6]

Cranial nerve palsies are seen in about 25%, most commonly the abducens nerve. The involvement of multiple cranial nerves is very unusual.[8] Cranial neuropathies (II, VII, VIII, IX, X, and XII) occur in isolated cases secondary to basal arachnoiditis.[9] Cryptococci are thought to physically block the passage of CSF across the arachnoid villi and subarachnoid spaces, leading to high ICT. Gradually, it leads to compression of the cranial nerves causing neuropathies.[9] Sixth cranial nerve palsy is very common in the setting of raised intracranial pressure as a false localizing sign, and it is well reported in cryptococcal meningitis.[10] The direct fungal invasion can cause cranial nerve injury without raised intracranial pressure.[10] Our patient had a bilateral facial weakness with normal CSF pressure (170 mm of H20). MRI showed enhancement of facial nerves. This suggests direct fungal invasion of cranial nerves rather than raised intracranial pressure as CSF opening pressure was normal.[11]

The CSF analysis usually reveals a lymphocytic pleocytosis with raised protein and low sugar levels. The diagnosis of cryptococcal meningitis can be established with India ink stain in more than 50% of the cases of cryptococcal meningitis in HIV-negative cases and more than 90% of patients with acquired immune deficiency syndrome.[12] The CSF sample should also be evaluated for cryptococcal antigen assay that is positive in almost all cases except very early in the disease or in those with very high titers (prozone effect) and in certain patients with cryptococcomas. The methods used for antigen detection are latex agglutination test and enzyme immunoassay. Both tests are more than 90% sensitive and specific. Cryptococcal antigen titers usually decrease with treatment, but it can remain at low titers for long periods even after adequate therapy. A positive fungal culture is the gold standard for diagnosing cryptococcal infection, and CSF samples show fungal growth in almost all cases.[13] In our patient, the India ink test and fungal culture were negative, and CrAg was positive. After 3 months, all were negative.

The duration of treatment for cryptococcal infection is based on the host's immunity and anatomic sites of involvement. For immunocompetent individuals with cryptococcal meningitis, the standard therapy consists of amphotericin B 0.7–1.0 mg/kg/day and 5-flucytosine 100 mg/kg/day for 6–10 weeks. An alternative to this regimen is amphotericin B 0.7–1.0 mg/kg/day plus 5-flucytosine 100 mg/kg/day for 2 weeks, followed by fluconazole 400 mg/day for a minimum of 10 weeks. Fluconazole "consolidation" therapy may be continued for as long as 6–12 months, depending on the patient's clinical status. Our patient is immunocompetent. He was treated with amphotericin band flucytosine for 2 weeks and is continued on fluconazole at 400 mg/day.[14]

Evaluation of a patient with bilateral facial paralysis depends on the history and examination. Workup should include

complete blood count, fluorescent treponemal antibody test, HIV, fasting glucose, erythrocyte sedimentation rate, antibodies for Lyme disease, and antinuclear antibody measurement. Lumbar puncture and contrast-enhanced magnetic resonance imaging are helpful.

Cryptococcal meningitis in the non-immunocompromised patient has never been reported to be associated with bilateral facial palsy to the best of our knowledge. Evaluation of a patient presenting with headache and bilateral facial palsy must include MRI and CSF studies to rule out neuroinfections. Early diagnosis and treatment of cryptococcal meningitis improve the outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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