

## Case Report

### Combination therapy in hemiballismus-hemichorea syndromes – a report of two cases

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#### Abstract:

Hemiballismus-hemichorea is an uncommon disorder. In the past, patients developing hemiballismus and hemichorea were considered to have poor prognosis with high morbidity and even mortality at times. While majority of patients of hemiballismus go into spontaneous remission, some severe cases require prolonged treatment. We here describe two such cases of which one presented to us with post stroke hemiballismus, unresponsive to monotherapy and the other was an HIV positive patient with unresponsive hemichorea secondary to CNS toxoplasmosis. Both these patients responded well when combination therapy was instituted and had normal recovery.

**Keywords:** hemiballismus-hemichorea; tetrabenzine; haloperidol; valproate; combination therapy

DOI: <http://dx.doi.org/10.3329/bjms.v13i4.17536>

Bangladesh Journal of Medical Science Vol. 13 No. 04 October '14. Page: 484-487

#### Introduction:

Movement disorders like hemiballismus or hemichorea are one of the most dramatic disorders in neurology. It is a rare disorder and most clinicians see only a handful of cases in their career. Both these disorders share common etiologies, prognosis and treatment, often co-existing in the same patient. It has been shown that this disorder can be caused by infarcts or haemorrhages in a variety of locations both inside and outside the basal ganglia. Treatment protocol is not standardized as the condition is uncommon. Antidopaminergic therapy is the mainstay of treatment, with surgical procedures reserved for unresponsive cases. We report two cases of refractory hemiballismus-hemichorea which responded well to combination pharmacotherapy.

#### Case 1:

A 78 year old, right handed gentleman, known case of diabetes mellitus, hypertension, ischemic heart disease on regular treatment for the same, presented to us with involuntary violent jerky movements of left arm and left leg since 3 days, movements being absent during sleep. The movements were preceded by an episode of giddiness and headache the previ-

ous night. On admission, patient was conscious, well oriented. On examination of the motor system, tone was normal in all limbs; power was 4/5 in left upper and lower limbs and 5/5 in the right upper and lower limbs (MRC grade), deep tendon reflexes were all normal and symmetrical while the left plantar response was extensor. Cranial nerve examination was normal. The patient had uncontrollable, poorly patterned, violent, flinging movement of left upper and lower limbs (proximal group of muscles more involved than the distal group) which were occurring several times a minute and causing impairment of any purposeful activity with the involved limbs. The sensory system was normal and there were no cerebellar signs. CT scan of the brain was done revealing right basal ganglia bleed. (*Figure 1*)

A diagnosis of **post stroke hemiballismus** was made. The patient was put on Tab Haloperidol 0.5 mg thrice daily but he developed acute dystonic reaction. He was switched over to Tab. Tetrabenzine 25 mg thrice daily which showed no improvement even after 5 days. We therefore added Sodium Valproate 500 mg three times daily with which the symptoms completely disappeared after 6 days. On

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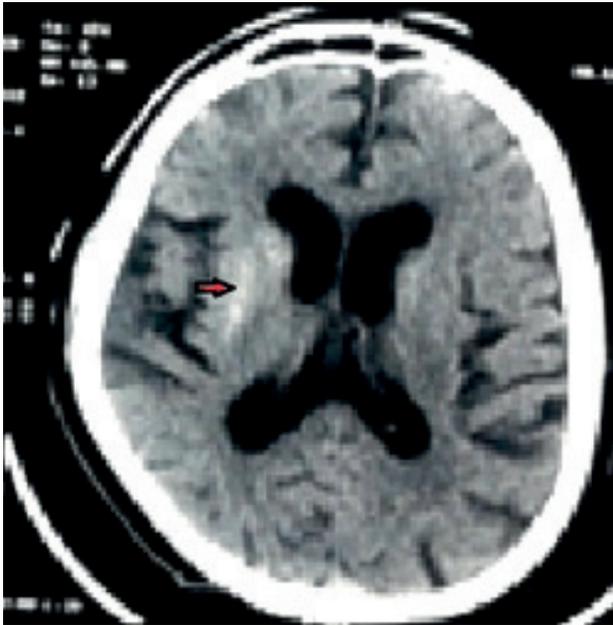


Figure 1 : NCCT Brain showing right basal ganglia bleed

follow up visit after a month, tetrabenzine and later valproate were tapered and eventually stopped. Patient was found to be normal on three month follow up.

**Case 2:**

A 36 year old gentleman presented to our hospital with abnormal, involuntary movements of left sided of the body since 4 days, gradually increasing in range and intensity. He was a diagnosed case of pulmonary Koch's since last three months, on anti tubercular treatment. Patient was also a known case of HIV and on anti retroviral drugs (CD4 count - 120). On examination, the patient had mild weakness with power of 4/5 (MRC grade) in left upper and lower limbs with non-repetitive, irregular, involuntary, semipurposful movements of left upper and lower limbs. MRI brain showed lesions in basal ganglia (involving caudate nucleus and globus pallidus), thalamus, and right cerebellum. (Figure 2)

With the differential diagnosis of toxoplasmosis and tuberculosis in mind, CSF examination was done which showed: proteins-83mg/dl, WBC-10/hpf, sugar-50mg/dl and normal ADA levels. Serum toxoplasma IgM antibody analysis was done and found to be positive. The diagnosis of **toxoplasmosis** was made and patient was put on sulfadiazine-pyrimethamine combination. In view of the severe choreiform movements patient was initially started on tab haloperidol 0.5 mg thrice daily, dose of which was gradually increased to 2 mg thrice daily over 7 days but resulted in no improvement. While

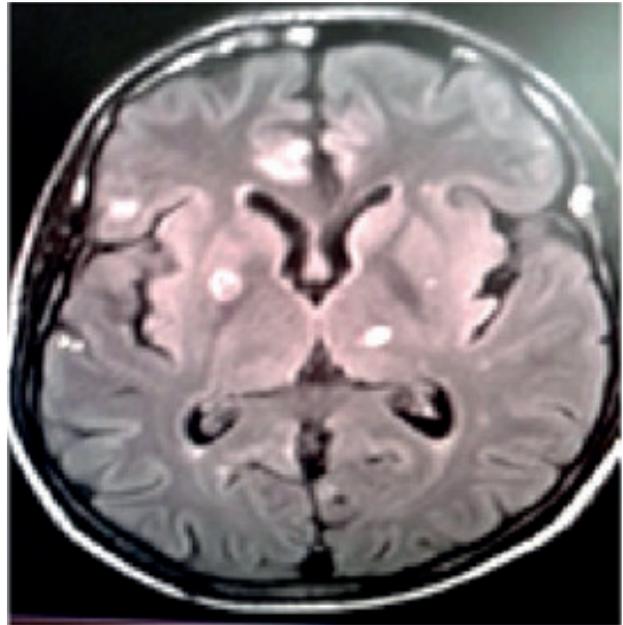


Figure 2 : MRI Brain showing multiple disseminated lesions of toxoplasmosis

in hospital, patient developed 2 episodes of generalised seizure which were controlled by intravenous lorazepam. In view of seizures and non-responsive chorea, Tab. Valproate 500 mg thrice daily was added to the treatment regimen. A combination of haloperidol and valproate was continued for next 10 days and the intensity of movements decreased by 50%. Later Tab Tetrabenzine 25 mg thrice daily was added to the treatment with which the movements reduced by 90%. Patient was discharged on treatment with combination of haloperidol, valproate and tetrabenzine alongwith anti retroviral and anti-tubercular treatment. On one month follow up, the choreiform movements had completely stopped and patient was asymptomatic neurologically. The follow up MRI with contrast was performed which showed marked resolution of lesions. Valproate had to be discontinued later and dose of Haloperidol had to be reduced as the patient developed hepatitis. The drugs were eventually stopped and patient was normal on 2 month follow up.

**Discussion:**

Hemiballismus is a rare movement disorder characterised by violent, involuntary movements restricted to one side of the body predominantly affecting proximal muscles. Hemichorea refers to movements that are similar in character but lower in amplitude, affecting both distal and proximal limbs. These two entities share common etiologies, prognosis, treatment and often co-exist in the same patient. It was traditionally thought that hemiballismus arises from

injury to the subthalamic nucleus, and hemichorea from lesions in caudate within the basal ganglia. Recent studies however show that damage to other areas of the brain can also be responsible for causing these disorders.<sup>1</sup> Stroke is by far the most common cause of hemiballismus-hemichorea. Hemiballismus as a result of stroke occurs in only about 0.45 cases per hundred thousand stroke victims.<sup>2</sup> Non structural causes like nonketotic hyperglycemia is the second most common reported cause of hemiballismus with more than 60 cases reported till now. Movement disorders appear when blood glucose levels get too high and then subside once glucose levels return to normal.<sup>3,4</sup> Traumatic Brain Injury<sup>5</sup>, Amyotrophic Lateral Sclerosis (causing neuronal loss and gliosis involving subthalamic nucleus and other areas of the brain)<sup>6</sup>, neoplasms in the basal ganglia<sup>4</sup> can also result in hemiballismus. Tuberculomas can also damage parts of the basal ganglia, sometimes resulting in hemiballismus. Demyelinating plaques attack the myelin sheaths on neurons leading to disorganized signal and can also cause the chaotic movements. Patients with HIV often have complications that arise along with AIDS. Hypoglycemia due to pentamidine use in patients with AIDS has been known to cause hemiballismus. In some patients, hemiballismus has been the only visible symptom to alert the physician that the patients may have AIDS. It is typically a result of a secondary infection that occurs due to the compromised immune system and the most common infection causing hemiballismus is cerebral toxoplasmosis as was seen in our patient. Most of the lesions that result from this infection are found in the basal ganglia. As long as the diagnosis is not missed, this type of hemiballismus can be treated just as well as in patients without HIV. When treating hemiballismus or hemichorea, it is first important to treat these correctable underlying conditions. In some patients, it may be self-limiting and not even need treatment.<sup>4</sup> Due to rarity of the disorder, the treatment protocols are not standardized and are based on random

case reports. No studies have been conducted on a large sample size so as to standardize the therapy. The drugs that have been found to be effective are dopamine blockers like perphenazine, pimozide, haloperidol, and chlorpromazine which are the standard choices for treatment. Also positive results have been obtained with atypical neuroleptics such as risperidone, olanzapine and clozapine and with other presynaptic dopamine depleters such as reserpine. Anticonvulsants like topiramate, valproate, clonazepam have been used with success. In addition, there have been reports of effective treatments with trihexyphenidyl and amitriptyline.<sup>7,8</sup> Intrathecal baclofen<sup>5</sup> has been used to treat hemiballismus in one case report. Botulinum injection is also a treatment option in trials. Patients using tetrabenzene have been found to have a dramatic response in hemiballismus. However, lowering the dosage leads to a return of symptoms. This drug works by depleting dopamine with a minimal risk for extrapyramidal side effects.<sup>8</sup> For refractory cases however, toxicity with higher doses is a major issue. Functional neurosurgery can be done in patients with severe hemiballismus that has not responded to treatment. Lesioning of the globus pallidus or deep brain stimulation of the globus pallidus have been tried. Combination therapy, as used in our case can help avoid these invasive procedures in non-responsive cases.

### **Conclusion:**

The view that hemiballismus is a disorder carrying a grave prognosis is incorrect. The treatment protocol however, is not standardized due to rarity of this condition and lack of large scale trials. Toxicity with higher doses of a single drug can be a major concern with monotherapy. Tetrabenzene should be preferred over haloperidol as the first line of treatment due to low risk of extrapyramidal side effects. Combination therapy can help avoid invasive procedures in non-responsive cases, and hence should be considered for refractory cases. However, further studies need to be conducted to strengthen our findings.

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