Movement Disorder Emergencies

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INTRODUCTION

Movement disorders are neurologic disorders characterized by inadequate voluntary movements (hypokinetic) or presence of abnormal involuntary movements (hyperkinetic). Management of either type of movement disorders is mainly outpatient-based . Movement disorder emergencies are conditions evolving over hours to days , in which failure to diagnose and manage promptly can result in significant morbidity and mortality[1]. The emergent nature of these occasions is either inherent to the disease process itself, as in neuroleptic malignant syndrome (NMS), or is caused by excessive movements, as in dystonic storm. The management of movement disorder emergencies comprises three major components: supportive care, temporizing measures, and disease-specific therapy.

ACUTE PARKINSONISM

Acute Parkinsonism, developing over days to hours, is most commonly seen in exposure to dopamine blocking drugs. A host of toxins like MPTP (1-methyl-4-phenyl-1,2,3,6 tetrahydropyridine), organophosphates, carbon monoxide and methanol have been implicated in causing an acute parkinsonian state[2]. Patients are typically poor levodopa responders. Parkinsonism may follow viral infections affecting the substantia nigra. It can present as somnolent-ophthalmoplegic form, akinetic-mutic form and hyperkinetic form. Japanese B encephalitis, CMV, HIV and others have been incriminated as the principal offenders. CSF study showing lymphocytosis, elevated protein and oligoclonal bands help in diagnosis.Treatment is supportive alongwith empirical use of acyclovir. Response to dopa therapy is unsatisfactory.

Acute parkinsonism have been reported as a devastating complication of cancer chemotherapy with varied agents like CHOP(cyclophosphamide,doxorubicin, vincristine, prednisone), paclitaxel, antifungals like amphotercin B and others[3].

These patients usually show a favourable response to levodopa therapy. An extremely rare but potentially reversible cause of acute Parkinsonism is mechanical compression of the nigrostriatal pathway by an intracranial mass. Patients manifest symptoms of raised intracranial tension and tectal compromise. Response to levodopa and ventricular shunting have been documented.

NEUROLEPTIC MALIGNANT SYNDROME(NMS)

Among movement disorder emergencies, NMS is a potent cause of true medical emergency.. As its name implies, it usually presents as a potentially fatal, idiosyncratic reaction to neuroleptics. Although typical neuroleptics induce most cases of NMS[4], the syndrome has been reported with almost all antidopaminergic drugs (both dopamine depletors and dopamine receptor blockers [DRBs]. NMS is also reported in patients with Parkinson's disease after abrupt withdrawal of levodopa; in this setting it is better termed "parkinsonism-hyperpyrexia" syndrome The common denominator of these triggering events is a precipitous drop in dopaminergic transmission in the brain. HIV, severe dehydration and exposure to heat trigger NMS. The manifestations of NMS encompass autonomic instability (manifested by labile blood pressure, tachycardia, tachypnea, diaphoresis and incontinence of urine/faeces), altered mentation, and

motor abnormalities that include bradykinesia and rigidity. Laboratory work-up typically reveals increased creatine kinase(>200 to even >1000 IU/L), leukocytosis, and an increased iron level.

Whenever a diagnosis of NMS is considered, the offending neuroleptic should be discontinued, and the patient should be monitored closely in an intensive care unit setting. Vigorous hydration to prevent rhabdomyolysis, and external or internal cooling, should be implemented. Benzodiazepines, dopaminergic agents, and dantrolene are medications that have been used in NMS with benefit[5]. A three-tier approach has been proposed[5]. In mild cases of NMS, benzodiazepines alone usually can stabilize the condition. When the severity of NMS is moderate, with more significant hyperthermia or rigidity, dopaminergic medications such as bromocriptine, other agonists (pergolide, pramipexole, ropinirole), levodopa, and amantadine are a reasonable next step. As NMS reaches a full-blown, hypermetabolic state, addition of dantrolene may be beneficial. Methylprednisolone pulse therapy has been shown to shorten the duration of NMS due to abrupt withdrawal of dopaminergic medications in patients with Parkinson's disease Methylprednisolone pulse therapy did not seem to affect mortality, and its effect on neuroleptic-induced NMS is unclear. In cases of NMS refractory to medical treatment, electroconvulsive therapy has been used successfully.

MALIGNANT CATATONIA AND SEROTONIN SYNDROME

These syndromes share the same pathophysiology and clinical features with NMS, but they have different causes[6]. The inciting event in serotonin syndrome is a rapid increase in central serotonergic tone. Common triggers are selective serotonin uptake inhibitors, monoamine oxidase inhibitors, L-tryptophan, ergots, and triptans. The key differentiating features between NMS and serotonin syndrome are as follows-Table I.

Table 1. Differences between NMS and Seroronin Syndrome

SYNDROME	NMS
Onset rapid, within 24 hrs	Onset slower, within 7 days
Symptoms : agitation, diarrhea	Dysphagia, hypersalivation, incontinence
Presenting signs : dilated pupils, myoclonus, hyperreflexia	Bradykinesia, extrapyramidal rigidity, hyperthermia, rhabdomyolysis
23 deaths reported until 1999.	15-20% mortality

The preceding event in the rare entity malignant catatonia are stroke,encephalitis, Cushing's disease and Wernicke's encephalopathy. Psychiatric disturbance, intense agitation and catatonia followed by severe parkinsonlike state dominate the clinical picture. Treating serotonin syndrome requires discontinuation of offending serotoninergic medications, usually with the addition of cyproheptadine. Successful management of malignant catatonia also hinges on recognizing the underlying psychiatric disturbance and treating it.

ACUTE DRUG INDUCED DYSTONIAS

In addition to NMS, antidopaminergics can induce other hyperkinetic movements that may sometimes require emergent treatment[7]. Acute dystonia or akathisia occurs in susceptible individuals immediately after exposure to a dopamine depletor or DRB. Acute dystonia can manifest as generalized or focal dystonia, with a propensity for laryngeal dystonia and oculogyric crisis.The latter disease, also seen in encephalitis lethargica, produces a panoply of disturbances ranging from opisthotonus,intense rage,autonomic disturbances and extreme motor urge in addition to the ocular deviation commonly described.

Acute akathisia is characterized by subjective restless feelings accompanied by objective restless movements. Timely diagnosis of these disorders hinges on obtaining a complete medication history, including possible accidental exposure. Their courses are self-limited after the offending medications are discontinued. Anticholinergics are effective for both dystonia and akathisia Intravenous diphenhydramine aborts acute dystonia[8] in minutes. Intravenous benzodiazepines can be used as an alternative for acute dystonia. For acute akathisia, in addition to anticholinergics, vitamin B6, mianserin, propranolol, and mirtazapine have all been shown to be effective. Clonidine and cyproheptadine also have been reported effective for acute akathisia.

Tardive syndromes also follow antidopaminergic exposure. Common manifestations of tardive syndrome are classical tardive dyskinesia, tardive dystonia, and tardive akathisia. Different from acute dystonia and akathisia, tardive syndromes usually occur in a delayed fashion after at least 1 month of exposure However, if the causative medication is withdrawn abruptly, a unique, acute presentation of

tardive syndrome may surface, particularly in children, which is named "withdrawal-emergent" syndrome. Frequent choreic movements involve the trunk, limbs, neck, and rarely the face, in contrast to the stereotyped orobuccal movements in classical tardive dyskinesia. Resuming the causative medication is the most effective way to suppress withdrawal-emergent syndrome The medication can then be withdrawn gradually at a slower pace without detrimental consequences.

DYSTONIC STORM

Dystonia is a syndrome of sustained muscle contractions, frequently causing twisting and repetitive movements, or abnormal postures. A crisis of sudden, unremitting,continous severe worsening of dystonia can happen occasionally and has been called dystonic storm or status dystonicus[9]. It is mostly encountered in children and adolescents with primary or secondary dystonia. Common triggers of dystonic storm are changes in medications and concomitant illness. Paradoxical worsening during initiation of chelating treatment in Wilson's disease is another well-recognized trigger. In addition to incapacitating motor function and pain, dystonic storm can cause rhabdomyolysis and acute renal failure. Therefore, creatine kinase, electrolytes, and renal function need to be monitored closely during dystonic storm.

Weathering a dystonic storm inevitably requires substantial sedation, and sometimes medically induced coma. Once dystonia quiets down, a gradual switch from sedatives to more specific antidystonic agents should be planned as soon as possible, in order to minimize complications of prolonged sedation. Anticholinergics, baclofen, and antidopaminergics are most commonly used . Botulinum toxin injection, intrathecal baclofen, pallidotomy, and recently, deep brain stimulation have been used as last resorts if the dystonia remains refractory to medical treatment.

PSEUDO-DYSTONIC EMERGENCIES

Pseudo-dystonias, conditions that mimic dystonia, include four disorders that may present as emergencies:

Acute infectious torticollis: Rare but reported in eastern and northern China(10). Torticollis occurs as a sequel to infectious(viral) or inflammatory process of the head and neck, also called as Grisel's syndrome.

Neoplastic torticollis: Rare presentation of spinal cord tumours[11]. Chiropractic manipulation prior to diagnosis trigger respiratory arrest and quadriplegia .

Atlanto-axial rotatory subluxation: Uncommon but potentially devastating form of acute torticollis in children. Typical presentation with acute head tilt, contralateral neck rotation and mild neck flexion due to increased laxity of spinal ligaments and degree of freedom of C1-C2 vertebra[12].
Localized tetanus: Cephalic tetanus usually follows a facial injury. Trismus may be unilateral and accompanied by ipsilateral 7th nerve palsy and often mimics jaw dystonia.

AIRWAY OBSTRUCTION IN MOVEMENT DISORDER SYNDROMES

In movement disorders, airway obstruction can occur when the disease processes affect the coordination of the larynx, particularly the vocal cords. Two commonly encountered scenarios are abductor paralysis in multiple system atrophy[13] and adductor dystonia in certain dystonia syndromes.

Multiple system atrophy is a parkinsonism with various combinations of extrapyramidal, cerebellar, and autonomic deficits. Amidst the plethora of chronic symptoms of multiple system atrophy, an acute event of airway obstruction can emerge at any stage of the disease, more commonly in advanced patients. Symptoms of snoring, intermittent nocturnal inspiratory stridor, sleep apnea usually herald a full-blown episode of airway obstruction Daytime stridor is an ominous sign carrying a mean survival of 0.8 years. If an aggressive approach is wished, the patient should have a sleep study and fiberoptic laryngoscopy by an otolaryngologist experienced in the disorder. For low-grade abductor paralysis, a noninvasive device is considered first, such as a continuous positive airway pressure machine. High-grade abductor paralysis warrants a surgical intervention. Tracheostomy is the most reliable procedure to maintain a patent airway. Other less invasive options include arytenoidectomy, cord lateralization, and cordectomy.

Adductor dystonia of the vocal cords can occur in primary dystonia such as laryngeal adductor breathing dystonia and in secondary dystonia[13]. Primary spasmodic dysphonia, which can affect the adductor, is a task-specific condition only symptomatic during speech but not during breathing; therefore, airway obstruction is not a concern. Fiberoptic laryngoscopy is often required to confirm the presence of adductor dystonia. In a less urgent situation, botulinum toxin injection into adductor muscles of the vocal cords has been performed safely and successfully for adductor dystonia .The injection is performed sequentially, with an interval of 2

weeks, into each side of the vocal cords to prevent the risk of complete paralysis. In severe emergency, endotracheal intubation and laryngeal surgery are considerations.

BALLISM AND RELATED CHOREIFORM EMERGENCIES

Ballism is a proximal severe form of chorea, with irregular, large-amplitude, involuntary movements typically affecting the proximal portions of the extremities. Violent flinging of the shoulder and kicking of the leg are examples of ballism. Most ballism occurs unilaterally (hemiballism). It is extremely distressing and disruptive to patients, and can inflict injuries or interfere with care. The most common cause of hemiballism is acute stroke. Although hemiballism is classically localized to the contralateral subthalamic

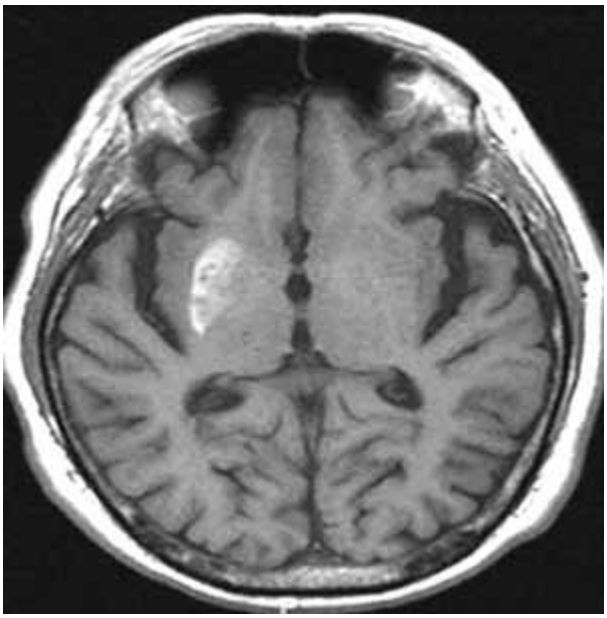

Fig.1: MRI Picture of Nonketotic Hyperglycemia

nucleus, strokes at other sites can also cause hemiballism. Nonketotic hyperglycemia is another cause of acute ballism increasingly recognized in the Asian population.It presents with the typical hemiballism-hemichorea syndrome coupled with MRI findings of T1 hyperintensities in the contralateral striatum (Fig.1). Other etiologies of acute or subacute ballism are infections, autoimmune diseases, tumors, and drugs.

Acute hemiballism generally evolves to less violent hemichorea or hemiathetosis in a few days. In these cases, only protective measures, such as bed padding and restraint, are needed. Symptomatic treatment is deferred, until ballism persists without a tendency to subside for several days. Antidopaminergics are the mainstay treatment for ballism[14].

A dopamine depletor should be considered before a DRB because of the risk of tardive syndrome. Between the two dopamine depletors tetrabenazine and reserpine, tetrabenazine is preferable because of its shorter half-life and fewer peripheral complications such as orthostasis and diarrhea. If a dopamine depletor is unavailable, ineffective, intolerable, or contraindicated, then a DRB such as a neuroleptic is considered. Because of the risk of tardive dyskinesia, neuroleptics should be used as short-term therapy, and the risk and rationale for their use needs to be explained to the patient. During the titration of an antidopaminergic medication, the possibility of iatrogenic NMS needs to be kept in mind.. Besides antidopaminergics, experience is limited with other medications used to treat ballism, such as valproate, amitriptyline, gabapentin, sertraline, and trihexyphenidyl[14] which may help by virtue of their GABAergic action.

Harbord[15] and several others have reported cases of severe ICU chorea in patients with acute febrile illness.EEG and other lab tests to rule out reversible causes of ICU chorea such as phenytoin intoxication and APLA.

TIC EMERGENCIES

Tic status patients present with the dual feature of A) continous tics that cannot be suppressed voluntarily for more than several seconds and B) present a personal risk to the patient. The goals of therapy are to provide symptomatic relief and to decrease morbidity. The treatment plan depends on the patient's previous response to anti-tic medication and discontinuation of tic precipitating drugs like methylphenidate. Low-potency anti-tic medications, such as clonidine and guanfacine, are unlikely to abort tic status alone, and more aggressive approaches are often required. For tics that are still responsive to benzodiazepines, a rapid titration of benzodiazepines often controls tic status effectively. For tics unresponsive to benzodiazepines, a dopamine depletor is a reasonable choice if it has not already been tried. The major contraindication of using a dopamine depletor is depression. Because patients with severe tics may already be depressed, they need to be evaluated carefully for possible depression before using a dopamine depletor. If a dopamine depletor is contraindicated or has failed in the past, a DRB such as a neuroleptic may be the only remaining option for tic status.

Botulinum toxin injection also is useful to treat motor tics

at amenable sites (eg, blinking tics and cervical tics[16]. When phonic tics are a major part of the tic crisis and are refractory to medications, they are called malignant phonic tics as seen occasionally in Tourette's syndrome. Botulinum toxin injection, performed unilaterally in one vocal cord, has been used successfully and safely to treat malignant phonic tics.

A special subset of acute dramatic tics can be seen in children with PANDAS (Paediatric Autoimmune Neuropsychiatric Disorders associated with Streptococcus). These patients present at 6 or 7 years age with acute dramatic tics and obsessive-compulsive disorders following Group A beta-haemolytic streptococci infection. Rapid identification and prompt treatment with plasmapheresis or IVIG prove to be lifesaving[17].

SELF MUTILATING MOVEMENTS

Self-mutilations can occur in psychiatric disorders as well as in hyperkinetic movement disorders. In hyperkinetic movement disorders, self-mutilations are movements that are involuntary and inflict injuries as the consequence. The distinction between psychogenic self-mutilating behaviors and hyperkinetic self-mutilating movements is not always straightforward. Common examples of self-mutilating movements are tongue-biting dystonia, self-injurious tics, and self-mutilations in Lesch-Nyhan syndrome. The treatment of tics is as discussed previously.

Tongue-biting dystonia usually results from a combination of tongue-protrusion dystonia and jaw-closing dystonia. A similar condition, lip-biting dystonia, sometimes accompanies tongue-biting dystonia. Tongue-biting dystonia can occur in primary or secondary dystonia, and it is a distinctive feature of neuroacanthocytosis and pantothenate kinase-associated neurodegeneration. In treating tongue-biting dystonia, safety measures such as protective mouth guards, tube feeding, and airway support need to be applied first. In addition to antidystonic medications, botulinum toxin injection has been successfully used to treat tongue-biting dystonia. The toxin is injected into the tongue-protruding muscle (genioglossus) and into the jaw-closing muscles (masseter and temporalis)[18].

NONEPILEPTIC MYOCLONIC EMERGENCIES

Most myoclonic emergencies are epileptic myoclonic seizures, and their management is beyond the scope of movement disorder emergencies. However, nonepileptic myoclonic emergencies do occur. Distinguishing between epileptic and nonepileptic myoclonus requires electroencephalography. Most nonepileptic myoclonic emergencies occur in settings of toxic-metabolic states or acute destructive encephalopathy. The distribution of myoclonus in such conditions is multifocal or generalized, echoing the diffuse nature of the underlying etiologies. Management of these conditions should focus on the underlying cause, and symptomatic treatment for myoclonus is usually not indicated. However, there are situations in which symptomatic treatment is needed (eg, when myoclonus interferes with care, interrupts voluntary movements, or causes discomfort). Benzodiazepines are very effective antimyoclonic medications, although their use may be limited by unwanted sedation[19]. Among anticonvulsants, valproate and levetiracetam are notably antimyoclonic and are less sedating than benzodiazepines . However, valproate and levetiracetam are mostly effective for cortical myoclonus. They are less effective for myoclonus of subcortical origin, which sometimes coexists with cortical myoclonus. Sodium oxybate, a GABA-ergic medication, has been found to be effective for myoclonus of both cortical and subcortical origins.

Nonepileptic myoclonic emergencies can also occur in patients with hyperekplexia, an exaggerated startle syndrome[20]. In hyperekplexia, the startle response is sustained and exaggerated by auditory, tactile(nose tapping), or visual stimuli. Hyperekplexia may be hereditary or acquired. Hereditary hyperekplexia is usually caused by mutations in the glycine receptor gene, and symptoms begin in infancy or early childhood. Acquired hyperekplexia has been reported after diffuse cerebral insult or associated with a brainstem lesion. Urgent management of hyperekplexia is necessary when tonic spasms lead to apnea or drop attacks. Hereditary hyperekplexia responds dramatically to benzodiazepines like clonazepam. The experience in treating acquired hyperekplexia is limited.

CONCLUSION

Movement disorders, though known mostly for its beguilingly indolent and non-emergent course, can often challenge the clinician with a wide array of perplexing and potentially life threatening situations. Precise knowledge of the pathophysiological and clinical spectrum can aid in differentiating the myriad of movement disorder emergencies. Rapid diagnosis and rational treatment with the best effective drugs can reverse this potentially devastating condition.

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