Treatment of Movement Disorder Emergencies

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Abstract Movement disorder emergencies are defined as clinical scenarios where a movement disorder develops over hours to days, and in which morbidity and even mortality can result from failure to appropriately diagnose and manage the patient. The last decade has seen increasing recognition of various movement disorder emergencies, including acute parkinsonism, neuroleptic malignant syndrome, respiratory compromise in multiple system atrophy, dystonic storm, oculogyric crisis, and hemiballism, among others. This article will review the major movement disorder emergencies encountered in the hospital and office, emphasizing practical management and treatment.

Keywords Emergency · Parkinsonism · Neuroleptic malignant syndrome · Dystonic storm · Deep brain stimulation

Introduction

Movement disorders emergencies have received increasing attention in the last decade, with courses and lectures devoted to the topic at meetings of the American Academy of Neurology and International Movement Disorder Society. We define a movement disorder emergency as an event where patients develop a movement disorder over hours or several days, and in which morbidity and even mortality can result from failure to appropriately diagnose and manage the patient [1]. A complete review of this topic is beyond the scope of this article, and interested readers are referred to a recent text devoted to this topic [2]. The text that follows reviews 9 major movement disorder emergencies, focusing on practical

treatment and management. Because of the nature of this topic, most of the recommendations are based on class IV evidence, culled from a review of case reports. Major topics include acute or subacute parkinsonism, parkinsonism–hyperpyrexia in Parkinson’s disease, neuroleptic malignant syndrome, psychosis in Parkinson’s disease, respiratory compromise in multiple system atrophy, dystonic storm, tardive and neuroleptic-induced emergencies other than neuroleptic malignant syndrome, hemiballism, and Sydenham’s chorea.

Acute Parkinsonism

Most patients who develop acute parkinsonism do so because of exposure to dopamine receptor blocking agents, such as typical or atypical neuroleptic or anti-emetics. Acute parkinsonism is otherwise, fortunately, quite rare. Toxins that can trigger an acute parkinsonian state include 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, organophosphate pesticides, carbon monoxide, and methanol [3]. Parkinsonism may also follow viral infections, for example von Economo’s encephalitis [4], Japanese B encephalitis [5], Coxsackie B2 infection, West Nile infection, or human immunodeficiency virus infection. Chemotherapeutic agents or treatments for central nervous system malignancy may also trigger acute parkinsonism, either by causing direct injury to the basal ganglia (irradiation for bone marrow transplant [6]) or selective nigral toxicity (cytosine arabinoside [7], paclitaxel [8]). Other drugs that can also trigger acute parkinsonism include selective serotonin reuptake inhibitors, bupropion, lithium, valproate, cyclosporin, amiodarone, captopril, amlodipine, meperidine, and vincristine. Structural injury to the nigrostriatal pathway, from a tumor or in compression due to aqueductal stenosis, can also trigger an acute parkinsonian state [9].

Treatment of acute parkinsonism depends on identifying the proximate cause. Once this has been addressed, the next

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concern regards the need for symptomatic treatment. Both pre- (levodopa), and postsynaptic agents (dopamine agonists, amantadine) have been used with success. Patients who have severe impairment in mobility or in their ability to swallow are best treated initially with levodopa. Those who are suspected to have injury to postsynaptic structures should also be treated with dopamine agonists, as levodopa may not benefit such patients. Parenteral agents such as lisuride (not available in the USA) or apomorphine infusion may be required if swallowing is impaired. In patients with severe nigrostriatal denervation (such as rare patients with viral-mediated parkinsonism), there is a theoretical concern that treatment with high-dose levodopa could induce dyskinesias that might be long-lasting [10]. However, this concern is obviated by the need to treat patients who may be severely disabled. In practice, most patients with acute parkinsonism improve over months, and often the dose of levodopa can be reduced or, eventually, eliminated.

Parkinsonism–Hyperpyrexia in Parkinson’s Disease

The practice of admitting Parkinson patients to the hospital in order to withdraw them from levodopa (“levodopa holidays”) was abandoned following the report of a severe and potentially lethal syndrome mimicking neuroleptic malignant syndrome [11]. Over time, it became clear that patients with Parkinson’s disease can develop a syndrome of fever, rigidity, autonomic instability, elevated creatine kinase, and obtundation that is identical to neuroleptic malignant syndrome. Termed the parkinsonism–hyperpyrexia syndrome [12], it represents a reduced central dopaminergic state. This syndrome has been described in Parkinson’s disease patients who discontinue or reduce their Parkinson medications, but also in Parkinson patients as a premenstrual phenomena [13], in patients treated with deep brain stimulation where stimulators have been inadvertently turned off [14], and even in Parkinson patients who do not adjust their medications [15].

Treatment of the parkinsonism–hyperpyrexia syndrome in Parkinson’s disease depends first on prompt recognition. Affected patients must be managed in the intensive care unit, where metabolic derangements and fluid requirements can be closely monitored and addressed. If Parkinson medications have been reduced or discontinued, they should be promptly reinstituted. Although older literature reports on the use of bromocriptine to treat this syndrome, there is little rationale for using this agonist as opposed to the newer non-ergot agonists pramipexole or ropinirole. We routinely use levodopa in this setting, administering it by nasogastric tube if necessary. Dantrolene has also been used. The only double-blind, placebo-controlled study of this disorder suggested that 1 g daily of methylprednisolone shortened time to recovery [16].

Neuroleptic Malignant Syndrome

Neuroleptic malignant syndrome is one of the cardinal movement disorder emergencies. A high index of suspicion is critical to making the diagnosis, and the disorder should be considered in any patient encountered in hospital with parkinsonism and fever. Often these patients are identified by neurology consultants who are called to evaluate a patient in the emergency room or on the wards with fever and change in mental status. Recent diagnostic criteria have been published, and most patients have fever, rigidity, change in mental status, autonomic instability, and an elevated creatinine kinase [17]. All drugs with dopamine-blocking activity have been reported to induce the syndrome, and it can occur in individuals without any underlying psychiatric or neurologic disorder. Once encountered, patients are more likely to develop neuroleptic malignant syndrome again if re-exposed to triggering agents.

Affected patients must be managed in the intensive care unit, and the offending dopamine-blocking drug should be stopped immediately. Bromocriptine, levodopa, amantadine, rotigotine, dantrolene, lisuride [18], apomorphine [19], and non-ergot dopamine agonists have been reported as treatment options. Patients who do not respond to these agents may be rescued with electroconvulsive therapy [20].

Psychosis in Parkinson’s disease

Psychosis is perhaps the most common trigger for hospitalization of Parkinson patients. The spectrum of psychosis begins with visual illusions, misidentifications of actual visual stimuli. Over time, patients may develop frank hallucinations that are typically visual, often seeing unfamiliar people or animals. Further along the spectrum, patients may lose perspective that their hallucinations are not real. Fixed delusions are the most severe form of psychosis. Illusions or visual hallucinations with retained insight rarely are problematic, but the transition to loss of insight or fixed delusions can rapidly put patients at risk. Patients may respond to their visual hallucinations, may be threatened by them, and may react in ways that place their own safety or others’ at risk, leading to an emergency room visit and subsequent hospitalization. It is important to recognize that not all patients follow this stereotyped pattern, and patients can immediately develop psychosis or delusions without progressing through the other stages.

Vaughan and Goldman have proposed a useful practical algorithm for treating psychosis in Parkinson’s disease [21]. Precipitating factors such as systemic illness, metabolic derangements, infection (particularly urinary tract infection), or subdural hematoma from falls should be ruled out first. Anticholinergics, amantadine, monoamine oxidase-B inhibitors, catechol-O-methyltransferase inhibitors, and dopamine agonists should be discontinued. Most patients afflicted with

hallucinations without insight cannot tolerate such medications, and will function better when treated with levodopa as their sole dopaminergic stimulus. Hallucinations without insight or fixed delusions usually require the addition of either quetiapine or clozapine. Owing to the blood monitoring requirements of clozapine, quetiapine is usually used first. Typical neuroleptics and other atypical neuroleptics (risperidol, aripiprazole, ziprasidone) should be avoided, as these agents reliably worsen parkinsonism in Parkinson patients.

Abductor Paresis in Multiple System Atrophy

Patients with multiple system atrophy, a Parkinson-plus disorder that mimics Parkinson's disease, are at increased risk for respiratory compromise. In particular, patients with the autonomic variant of multiple system atrophy, otherwise known as Shy–Drager syndrome, may develop this life-threatening complication [22]. Symptoms typically begin at night, and the patient is usually unaware of the problem. The patient's bed partner may notice a change in their breathing pattern, often with episodes of breath-holding or new snoring. Over time, frank stridor develops, again typically at night, then spreads to occur during the day. Daytime stridor is an ominous complaint, with a high 1-year mortality. Patients may succumb to respiratory events or also to cardiac arrest. We have also encountered multiple system atrophy patients whose stridor occurred when their levodopa wore off. The mechanism of vocal cord dysfunction in Shy–Drager syndrome is complex, probably involving a combination of both selective paresis of the posterior crico-arytenoid muscles (the sole abductors of the vocal cords) and excess activation of the thyroarytenoid muscles that adduct the vocal cords [23–25].

Practical management of the airway in multiple system atrophy is complicated by the progressive nature of the illness. It is important to have an honest discussion early on with patients and their families about the risks and benefits of various approaches before a crisis precipitates intervention. Definitive airway protection requires a tracheostomy, but many patients are not interested in this option owing to the poor prognosis of the condition. Nasal continuous positive air pressure masks, botulinum toxin injection to the thyroarytenoids, and local laryngosurgery have also been tried. Unfortunately, even with a tracheostomy, patients may succumb to sudden death from cardiovascular events, likely due to pathologic involvement of autonomic centers in the brainstem [26–28].

Dystonic Storm

Dystonic storm refers to continuous unremitting generalized dystonic spasms. It is a terrifying entity for patients, and also

frightening for physicians managing such unstable patients. The syndrome typically occurs in patients who have an underlying diagnosis of dystonia, either in primary dystonia (e.g., DYT-1 dystonia) or secondary forms of dystonia (in children with cerebral palsy or pantothenate kinase-associated neurodegeneration). Fever, infection, or trauma may trigger dystonic storm, and once the condition begins, unremitting spasms can rapidly accelerate.

Patients with dystonic storm should be immediately admitted to the intensive care unit where fluid and electrolyte demands can be closely monitored. Rhabdomyolysis [29], airway compromise, and severe dehydration have been reported. A variety of medications has been tried as treatments for dystonic storm, including anticholinergics, baclofen, benzodiazepines, dopamine receptor blockers, and dopamine depletors [30]. In practice, these interventions are often unsuccessful, and sedation, airway protection, and paralysis may be necessary to terminate involuntary movements. Patients may need to be supported for days or even several weeks in the intensive care unit until sedation can be lifted. Prior to the widespread availability of deep brain stimulation, patients with medication-refractory dystonic storm often spent extended periods in intensive care units. Ablative lesioning surgery such as pallidotomy and baclofen pump insertion [31] were tried in several patients. Although anecdotal, bilateral deep brain stimulation of the globus pallidus interna is now considered the treatment of choice for severe medication-refractory dystonic storm [32]. Improvements in dystonia are typically achieved within hours to several days of initiating stimulation, as opposed to the days or weeks necessary for dystonia patients who are implanted non-emergently. Inadvertent interruption of stimulation in patients implanted for the treatment of storm can trigger a rapid recurrence of symptoms.

Tardive and Neuroleptic-induced Emergencies

Two unusual, but potentially dangerous, movement disorders can be induced by neuroleptics or dopamine receptor blocking agents—tardive respiratory phenomena and oculogyric crisis. Both conditions typically occur soon after initiation of neuroleptics. Male gender, rapid titration of dose, and use of high-potency agents probably increases the risk. Respiratory compromise from neuroleptics can be a frightening entity, with acute dystonia affecting the larynx or pharynx causing stridor and even acute airway closure [33]. Tardive respiratory dyskinesias can also be a life-threatening event. Oculogyric crisis was first described in patients with encephalitis lethargica, but is most commonly seen in the present day in patients exposed to neuroleptics. A wide variety of disturbances accompany the usual fixed, upward, and lateral posture of the eyes, including autonomic disturbances, a variety of movement disorders (dystonia, myoclonus), and obsessional thoughts [34].

Both acute dystonic reactions and oculogyric crises can be terminated within minutes by intravenous administration of anticholinergics or antihistamines. Diphenhydramine is usually available in resuscitation carts, and 25 or 50 mg given intravenously will usually terminate an event within 1 min. It is important to continue patients on oral anticholinergics for a period of time after the acute event, typically at least a week, in order to avoid a recurrence. The offending neuroleptic should obviously be discontinued, and further challenges with neuroleptics should be approached with great caution.

Hemiballism

Hemiballism–hemichorea is one of the most dramatic hyperkinetic movement disorder emergencies. Classically considered a localizing sign for a contralateral lesion in the subthalamic nucleus, most cases of hemiballism actually localize to lesions in the basal ganglia or contralateral hemisphere [35]. Although stroke is the most common cause, nonketotic hyperglycemia, toxoplasmosis, multiple sclerosis, and anticardiolipin syndrome can present with hemiballism [36]. Patients with severe hemiballism usually require hospitalization owing to the potential for exhaustion from excess movements or injury to the affected body regions.

A magnetic resonance image of the brain and routine laboratory studies usually indicate the cause. Once reversible etiologies have been excluded, antidopaminergic agents confer the most benefit. Typical neuroleptics such as haloperidol, perphenazine, pimozide, olanzapine, risperidone, and chlorpromazine have been used with success. Tetrabenazine offers the advantage of good tolerability and lack of risk of engendering tardive syndromes, although its titration is slower and it may not be readily available in hospitals [37]. Both typical neuroleptics and tetrabenazine can, however, induce parkinsonism on the unaffected side, particularly in the elderly population. Most patients improve with or without treatment, but for severe treatment-refractory patients, stereotactic procedures have been employed [38].

Sydenham's Chorea

Sydenham's chorea is a post-streptococcal movement disorder, associated with crossreactive antibasal ganglia antibodies. Patients classically develop chorea and mild hypotonia several weeks after a documented group A streptococcal infection. Most patients with Sydenham's chorea are ambulatory, and work-up and treatment can be coordinated in the outpatient arena. A small fraction of patients, however, may present with an ominous, severe hypotonic state with near quadriplegia. Swallowing impairment and aspiration risk may occur in this setting.

Two recent studies highlighted the role of immunomodulatory treatment in severe Sydenham's chorea. In 1 study of 10 patients, a dramatic and sustained improvement in weakness and hypotonia was achieved within 48 h of initiation of intravenous methylprednisolone followed by oral steroids [39]. A similar study of 20 patients of varying severity showed a marked reduction in requirement for neuroleptics in patients treated with intravenous immunoglobulin given over 2 days [40].

Summary

Movement disorder emergencies are an unusual group of neurologic disturbances where prompt diagnosis and management can make a huge difference in patient outcome. This review has focused on treatment of the most commonly seen emergencies. Further information is available in a text and several review articles devoted to this subject.

Required Author Forms Disclosure forms provided by the authors are available with the online version of this article.

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