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ORIGINAL ARTICLE

Movement disorders in emergency settings: a prospective study

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Abstract

Introduction Acute movement disorders (MD) are etiologically heterogeneous entities. Since studies on the relative frequency of different MD and their underlying diseases are limited, we performed a prospective study to investigate the spectrum of various MD and their causes in patients presenting with acute MD in an emergency room (ER) setting.

Objective To describe the spectrum and outcomes of acute MD in a prospective cohort and to guide its management.

Methods We investigated acute MD in 96 consecutive patients admitted to ERs between 2013 and 2017. Time of disease onset, type of MD according to published criteria, diagnostic workup, and outcome were collected.

Results 73.9% of patients had hyperkinetic MD. Tremor was the most common symptom (19.8%), followed by myoclonus (17.7%), dystonia (15.6%), and chorea (11.4%). Other hyperkinetic MD (9.4%) included were gait disorders (imbalance due to involuntary movement), dyskinesia, akathisia, hemiballism, and oculogyric crisis. Hypokinetic MD included acute parkinsonism (15.6%), off-state (4%), akinesia (3%), and rigidity (3%). Co-occurrence of more than one MD was seen in 19.7% of patients. Time delay to medical consultation was between < 24 h and 28 days. Five etiological groups were recognized: drug-induced (29.2%), functional (19.8%), neurodegenerative diseases (15.6%), structural brain damage (11.5%), others (24.0%, metabolic, inflammatory, infective, undetermined). Outcome was better for neurodegenerative diseases and for drug-induced MD. Functional movement disorders (FMD) showed less favorable outcome.

Conclusions Acute MD is a distinct cause of ER admission, and a variety of treatable diseases may be the underlying cause of this symptom. Uncertain course is more probable in FMD and in structural brain lesions.

Keywords Movement disorders · Emergency · Drug-induced · Functional · Neurodegenerative

Introduction

Although movement disorders (MD) are commonly viewed as chronic diseases that are followed and treated in ambulatory care settings, a growing number of patients with MD present with acute, severe syndromes, or complications of their underlying neurological problems. Many patients admitted to the ER with acute-onset MD are assessed by medical professionals who are usually not trained in the diagnosis and management of these conditions due to a lack of specialized consultants. Consequent misdiagnosis and mistreatment of the conditions underlying MD could have serious consequences. While some guidelines are available for recognition and management of urgency in MD, they are still heterogeneous and puzzling entities and pose a diagnostic challenge for most clinicians [1]. An acute MD is defined as any neurologic disorder evolving acutely or subacutely over hours or days in which MD was the only or the dominant feature of the illness and required emergent evaluation and treatment [2]. Occurrence of an acute MD points to underlying systemic, neurologic, or sometimes functional processes. Often, it may be an adverse effect of a drug and is also illustrative of certain neurological disease in which delayed diagnosis can lead to significant distress for the patients with consequences on their quality of life. Recently, interest has been growing in the recognition and management of acute-onset MD in adults, as is evident from publication of several reviews in the last few

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years [1, 3–5]. Nevertheless, studies on the relative frequency of different MD (as a clinical phenomenon) and their underlying diseases are lacking, especially for acute MD in adult practice. In the present study, we aimed to prospectively record consecutive patients presenting to the emergency department with acute MD. We investigated the nature and spectrum of various MD in patients presenting acutely, along with the relative frequency of the conditions underlying the MD and outcomes in individual patients.

Materials and methods

Ninety-six subjects, aged 15 years or older, with acute MD referred from two ERs to a Neurology Unit were included in the study, according to strategic sampling to cover both rural and urban districts with a drainage population of approximately 170,000. Anonymous data were collected prospectively from June 2013 to May 2017, in accordance with local privacy laws. For the purposes of this study, patients were seen by three neurologists expert in MD diagnosis and treatment. Each neurologist completed a data form, which included information on past and present medical history, physical examinations, laboratory tests, and radiological imaging studies. Diagnosis in the ERs, decision to admit the patient or not, and the ward where each patient was admitted were also recorded. MD were defined according to clinical criteria as described on the website of the Movement Disorders Society (https://www.movementdisorders.org/MDS/About.htm). An acute MD was defined as any neurologic disorder evolving acutely or subacutely over hours or days (maximum 28 days) in which MD, considered disabling for the patient, was the only or the dominant feature of the illness and required emergent evaluation and treatment [2]. In cases with a mixed MD, only the predominant one was counted for classification. Some diagnoses were made retrospectively based on biochemical analysis and neuroimaging findings. Individuals were defined as having a life-threatening MD if they were admitted to the intensive care unit as a consequence of their MD, or if the MD was symptomatic of a life-threatening neurological illness. Participants were followed up as part of routine clinical care during a time window of 3 years. Outcome was stratified as follows: good outcome refers to complete recovery or partial recovery with return to previous levels of activity; unfavorable course refers to partial recovery without return to previous levels of activity, unchanged, or death.

Statistical analysis

A Fisher's exact test was used to test the differences in proportions for categorical variables. Two-sided P values less than 0.05 were considered statistically significant.

Results

During the time window of the present study, 131,537 patients were admitted to the emergency room. A total of 6690 neurological examinations were requested by ER physicians. Ninety-six individuals (0.073% of total patients admitted, 1.4% of neurological examination requested) with acute MD were prospectively included in the present study. Patient characteristics are summarized in Table 1. There was a balanced gender distribution (45.8% male, 54.2% female) and the mean age at presentation was 52.88 years (± 21.76, range 15–87 years). Hyperkinetic MD accounted for the majority of the cases, occurring in 73.9% of patients ($n = 71$). Tremor was the most common MD seen in 19.8% subjects ($n = 19$), followed by myoclonus in 17.7% ($n = 17$), dystonia in 15.6% ($n = 15$), and chorea in 11.4% ($n = 11$); other hyperkinetic MD were seen in 9.4% ($n = 9$) and were gait disorders (imbalance due to involuntary movement, $n = 3$), dyskinesia ($n = 2$), akathisia ($n = 2$), hemiballism ($n = 1$), and oculogyric crisis ($n = 1$). Acute-onset parkinsonism was the most represented hypokinetic MD ($n = 15$; 15.6%), followed by off-state ($n = 4$), akinesia ($n = 3$), and rigidity ($n = 3$). Acute-onset parkinsonism was referred to previously healthy patients (or without history of neurodegenerative disease) admitted in ER for a movement disorder. Akinesia, rigidity, and off-state were referred to patients with acute worsening of a known neurodegenerative disease. Mixed MD, with co-occurrence of more than 1 kind of MD, was seen in 19 patients. The mean duration from the onset of MD to the neurological consultation was

Table 1 Patient characteristics

Patient number	96
Mean age (± SD, range)	52.88 (± 21.76, 15–87)
Sex (% males)	45.8
Time of symptoms onset (%)	
≤ 24 h	25 (26.0)
≤ 7 days	35 (36.5)
> 7 days	36 (37.5)
Type of movement disorder (%)[a]	
Hyperkinetic	71 (74.0)
Hypokinetic	25 (26.0)
Mixed	19 (19.8)
Cause of movement disorder (%)	
Drug-induced	28 (29.2)
Psychogenic	19 (19.8)
Neurodegenerative disease	15 (15.6)
Brain lesion	11 (11.5)
Others[b]	23 (24.0)

[a] Movement disorders were defined according to clinical criteria as described on website of the Movement Disorders Society

[b] Metabolic ($n = 8$), disimmune/inflammatory ($n = 7$), infective ($n = 6$), undetermined ($n = 2$)

8.48 days. We classified the etiologies underlying the acute MD into five groups: drug-induced 29.2% ($n = 28$), functional 19.8% ($n = 19$), neurodegenerative diseases 15.6% ($n = 15$), vascular/structural 11.5% ($n = 11$), others 24.0% (metabolic $n = 8$, disimmune/inflammatory $n = 7$, infective $n = 6$, undetermined $n = 2$). Diagnostic workup included brain magnetic resonance imaging in 42.7% of patients ($n = 41$), electroencephalography in 20.8% ($n = 20$), electromyography in 10.4% ($n = 10$), and lumbar puncture in 9.3% ($n = 9$). Hospitalization was required for 34% of patients ($n = 33$), and 4.2% ($n = 4$) of them were admitted to the intensive care unit. Hospital admission is significantly related to the presence of structural brain damage (10/11, $p = 0.0001$), and hospital discharge to home was related to the diagnosis of functional movement disorder (FMD, $n = 17/19$, $p = 0.015$). After discharge, the average length of follow-up was 8.4 months ($n = 88$; 8 patients dropped out). During follow-up (or at discharge for patients who dropped out), 49.0% of patients ($n = 47$) had complete recovery, 34.4% ($n = 33$) had partial recovery, 12.5% ($n = 12$) were unchanged, and 4.2% ($n = 4$) of patients died (brain glioma, tetanus, prions, dementia following severe sepsis). Outcomes for the different conditions underlying the MD are summarized in Table 2.

Discussion

This study highlights that acute MD represent an important clinical entity in emergency settings despite the fact that literature on the frequency of various acute MD and their underlying etiologies in adulthood is lacking. Some studies have been performed on acute MD in pediatric practice [6–8] but literature on their recognition and management in adults is limited to case reports or reviews and mainly focuses on drug-induced MD [9]. To our knowledge, this prospective study is the largest reported study to date in the setting of acute MD. Considering the number of patients admitted in ER in our setting in the period considered, the percentage of acute MD is quite low (0.073%); nevertheless, they are crucial in neurological practice considering their diagnostic difficulties and the importance of a rapid therapeutical approach.

In terms of gender, our sample represents a fairly equal distribution, with the exception of the FMD group where females represented 73.6% of subjects, as reported in outpatient care settings [10].

From a phenomenological point of view, all types of common MD were seen. Tremor and myoclonus were the most common acute MD in our patients; parkinsonism, dystonia, and chorea followed closely behind. Only two cases of FMD presented tics associated with tremor. Indeed, it is often difficult to define the absolute onset of tic disorders, and acute dramatic presentations "Tourette storm" are very uncommon [3–5]. The observations in our study, concerning relative frequency of various acute MD and etiology, were slightly different from those reported in pediatric studies [6–8].

In this study, near one third of patients had drug-induced MD and this represents the most common etiology with tremor, dystonia, myoclonus, and parkinsonism. The most common cause of drug-induced MD was neuropsychiatric medications in 57% of patients, followed by gastrointestinal medications in 10% of patients. These results confirmed that MD should be considered not only and not always as a chronic disease [11, 12]. An accurate history of medication in these cases is crucial for fast and accurate diagnosis. One patient with neuroleptic malignant syndrome, due to abrupt dose escalation of lithium and risperidone, required intensive care management and had incomplete recovery with subtle head and left hand tremor. In the diagnostic process of the acute drug-induced MD, we excluded other medical causes and considered a temporal relation to the initiation of the drug, a dose–response relationship, and a lack of pre-existing abnormal movement. Most of the drugs causing MD are either neuroleptic agents that interfere with dopamine neurotransmission or central nervous system stimulants, which enhance dopaminergic mechanisms [13, 14]. Conversely, MD is an unusual adverse effect of other drugs and there is often no obvious explanation of its occurrence [12].

FMD represent the second most significant percentage of acute MD (19.8%) in this cohort. Neurologists are often urgently requested to evaluate a patient in the ER who later receives a final diagnosis of FMD. Since almost all MD cases seen by neurologists may have a functional equivalent, a differential diagnosis is sometimes difficult [5, 10]. Therefore, two subjects of this group, one with parkinsonism and the

Table 2 Outcomes according to the conditions underlying the movement disorder

	Good outcome	Unfavorable course[a]
Clinical groups (%)		
Functional	9 (13.2)	10 (35)*
Drugs	21 (30.9)	7 (25)
Neurodegenerative disease	14 (20.6)	1 (4)**
Structural anomalies	7 (10.3)	4 (14)
Others	17 (25.0)	6 (21)
Total	68 (100.0)	28 (100.0)
Time of onset		
< 24 h	20 (29.4)	6 (21.4)
≤ 7 days	27 (39.7)	7 (25.0)
> 7 days	21 (30.9)	15 (53.6)
Total	68 (100.0)	28 (100.0)

[a] Good outcome corresponds to complete or partial recovery with return to previous activity levels; unfavorable course corresponds to partial recovery without return to previous activity levels, unchanged, or death

*$p = 0.0219$;**$p = 0.059$ (NS)

other with cervical dystonia, needed admission to exclude organic causes. Tremor, dystonia, and myoclonus were the most commonly described FMD in our study, confirming the proportion described in outpatient adult settings and in MD emergencies in childhood [6, 10]. Interestingly, only 5 out of 19 subjects with FMD had comorbid psychiatric diagnoses and 42% of all FMD patients experienced maximum severity of the symptom within a week of MD onset. The diagnosis of FMD may be challenging given the lack of accurate and reliable tests and requires the presence of a number of characteristics: fast progression to maximum severity, incongruous signs, distractibility, variability, selective or inconsistent disability, and entrainment with tremor [15]. FMD may not be benign, and most patients experienced difficulty returning to previous activity levels and with relapses during follow-up. We also observed 10 patients (10.4%) presented with hypokinetic MD directly related to their neurodegenerative morbidity (parkinsonian patients with worsening motor features as disabling "off," severe akinesia, "off" state dystonia); moreover, in 15.6% of our patients presented in ER with acute hypokinetic MD, acute-onset parkinsonism was not related to a previous diagnosis of neurodegenerative disease. Half of this group were associated with or triggered by concurrent medical conditions, such as infections or adverse effects associated with medications. Two subjects with Parkinson's disease had deep brain stimulation (DBS)-related emergencies. After many years of DBS for the treatment of Parkinson's disease, it has now been recognized that a range of postoperative urgent situations and emergencies may occur [16]. The problems that patients with Parkinson's disease encounter when acutely admitted to a hospital are known to be numerous and serious. These situations have been inventoried through a systematic review of literature on reasons for emergency care in PD patients [21]. Between 16 and 45% of PD patients visit an emergency ward once a year and more frequently than their matched reference group [22, 23]. The remaining 5.2% of patients included cases of Huntington's disease, frontotemporal dementia, multisystem atrophy, atypical parkinsonism, and DYT1.

A notable portion of our patients presented with acute MD as the presenting sign of a general medical condition [24]. Metabolic, cerebrovascular, and neoplastic diseases contributed to the majority of the cases. Unlike in the pediatric studies, we had a clear underrepresentation of inflammatory/autoimmune etiologies; chorea was the acute MD in one patient with NMDA receptor encephalitis and in two patients with rheumatic chorea. Two patients with a final diagnosis of multiple sclerosis had, as a first symptom, respectively, dystonia (right arm) and tremor (left leg); one case of acute disseminated encephalomyelitis revealed subacute parkinsonism as the clinical presentation. We also encountered a pregnant woman with an unstable propriospinal myoclonus. A primary infective cause was seen in 6.2% of patients and, even if one of the less numerous categories of the study, three of these patients were admitted to the intensive care unit; one patient, who presented with parkinsonism and mild mental confusion, had subsequent virological confirmation of HZV encephalitis; we later diagnosed tetanus in two patients presenting with spontaneous and stimulus-induced rigidity. Since these involuntary muscle spasms resulted in abnormal postures, we included them in our cohort, drawing attention to the importance of certain "cannot miss" diagnoses in the context of acute MD. In one case, a patient with a history of HIV infection showed a clinical picture of acute parkinsonism related to brain involvement. Another case presented with recent limb myoclonus in the context of cognitive impairment and mild ataxia, with conclusive diagnosis of prion disease. We also reported a patient with torticollis associated with a retropharyngeal abscess.

Finally, two patients showed respectively mixed arm tremors and mild myoclonus of the lower extremities but, despite extensive investigations, they did not receive a final diagnosis.

Acute MD often occur in the context of medical illness, either as the presenting sign of the illness or as a related feature of the underlying disease process. Early recognition of an underlying medical cause for MD is essential as the treatment and prognosis differ significantly depending on the underlying pathophysiology [16–20].

Acute MD can be associated with considerable morbidity and mortality, largely because of the serious nature of the underlying disorder [19]. In some cases, the MD per se may be very disabling and potentially fatal, causing debilitation, rhabdomyolysis, acute renal shutdown, and other systemic metabolic alterations requiring admission to intensive care units [2–4]. As many as 33 patients in our cohort were admitted and 4 had life-threatening illnesses requiring intensive care management (a patient with Huntington's disease had specific disorders related to swallowing).

An examination of the different etiologies reported in our study and described in the literature shows that the majority of the conditions underlying acute MD are potentially treatable with a good outcome (b, c, d). In our series, many cases are iatrogenic and drug-related MD. It is especially important to recognize this because the disorder will often clear completely with medication adjustment. Elderly patients are particularly at risk as they frequently use multiple medications and have less physiologic reserve [25]. The majority of tremors that are diagnosed as medication-induced are due to enhanced physiological tremor, but clinicians should be aware that a patient may have an underlying essential tremor or PD that is unmasked when treated with an exacerbating agent [26]. As we noted, medication-induced tremor was not fully resolved in four patients observed for an average time of 6 months. Additionally, a neurodegenerative disease might underlie parkinsonism in a minority of patients exposed to antipsychotics

[27]. FMD are an increasingly emerging and cryptic diagnosis: they can be easily mistaken for organic diseases for which treatment cannot be delayed, emphasizing that the timely, accurate diagnosis of FMD is of crucial importance especially in emergency situations [28, 29]. Although rare, parkinsonism or other MD may present as a stroke mimic with erroneous activation of a stroke code [30].

Our study confirms that, in this time of highly sophisticated laboratory and imaging diagnostic tools, the diagnosis of many MD is still largely made in the clinical setting where pattern recognition is crucial. Nevertheless, brain magnetic resonance imaging, neurophysiologic exams, and lumbar puncture may be required in certain cases.

Patients with MD nearly always present as outpatients but this may include acute manifestations, often in an emergency room setting, where there are a lot of differential diagnosis to consider and the possibility of underrecognizing the disorders. Once adverse drug effects and functional neurological symptoms have been considered, it is crucial to investigate some causes in which delayed diagnosis in less emergent situations can lead to slowly evolving and often irreversible neurological damage with fatal results.

Data has been acquired according to modern ethical standards and has been approved by the legally appropriated ethical committee.

Authors' contributions DC, BM, MT—study concept and design
DC, AC, AL, GM, SM—data collection
DC, BM—statistical analysis
DC, BM—analysis and interpretation
DC, MA, AC, BM—critical revision of the manuscript for important intellectual content
DC—study supervision

Compliance with ethical standards

Data has been acquired according to modern ethical standards and has been approved by the legally appropriated ethical committee.

Conflict of interest The authors declare that they have no conflict of interest.

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