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When time is of the essence: Managing care in emergency situations in Parkinson's disease

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ABSTRACT

A movement disorder emergency is an acute or sub-acutely evolving neurological illness predominated by a primary movement disorder. Although Parkinson's disease (PD) is a chronic, progressive disorder, patients may present with a variety of acute symptoms. Timely diagnosis and management is crucial to reduce mortality and morbidity. The underlying causes of an emergency in PD may be attributable to either disease related emergencies which occur as a direct consequence of the disease pathophysiology or secondary to anti-parkinsonian medications, such as Parkinsonism-hyperpyrexia syndrome, acute psychosis, etc. Indirect disease related emergencies, are those which not directly associated with the disease but occur secondary to deficits produced by the disease, e.g. falls and pneumonia. Emergencies in patients with PD may also be related to deep brain stimulation or systemic illnesses which are unrelated to PD. Complications may also occur during the surgical management of patients with PD owing to the effects of the disease on cardiovascular and respiratory functions or interactions of PD medication with anesthetic agents. Additionally, although motor complications are expected to form a majority of ER admissions in PD, several studies have reported indirect or non-PD related complications as the predominant primary reason for emergency admissions. The present article aims to review emergencies encountered in patients with PD with focus on the identification and management of these emergencies.

1. Introduction

A movement disorder emergency is a neurological disorder, in which the clinical presentation is dominated by a primary movement disorder. The disorder may evolve acutely or sub-acutely, and failure to promptly diagnose and manage the patient may lead to significant morbidity and rarely mortality [1]. Although Parkinson's disease (PD) is predominantly a chronic, slowly progressive movement disorder, patients may present to the emergency room (ER) with a wide spectrum of acute symptoms. Up to 16–45% of patients with PD visit an ER once a year, and they visit the ER more frequently in comparison to a matched reference group [2].

The reasons for ER visits in PD may be categorized as (Fig. 1):

1. Direct disease related emergencies: These occur as a direct consequence of disease pathophysiology or secondary to anti-parkinsonian medications, e.g. Parkinsonism-hyperpyrexia syndrome, severe levodopa induced dyskinesia, acute psychosis, etc.
2. Indirect disease related emergencies: Emergencies not directly associated with the disease rather occur secondary to deficits produced by the disease, e.g. falls and aspiration pneumonia.
3. Deep brain stimulation (DBS) related emergencies: These may be related to surgical procedures, hardware malfunction or stimulation induced.
4. Unrelated emergencies: Non-PD related systemic complications.
5. Emergencies arising in special situations: Surgical management in PD.

Although motor complications are expected to form a majority of ER admissions in PD, indirect or non-PD related complications are the most important reasons for emergency admissions [3–10]. The present article aims to review emergencies encountered in patients with PD with a focus on the identification and management of these emergencies.

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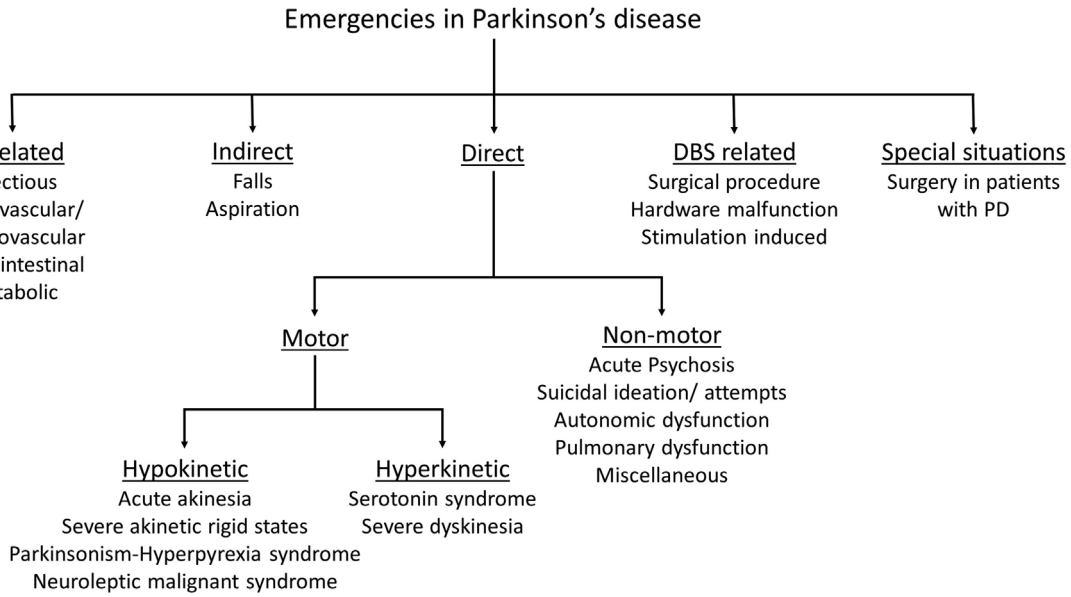

Fig. 1. The spectrum of emergencies which may be observed in patients with Parkinson's disease.

2. Direct disease related emergencies

Direct disease related emergencies occur as a direct consequence of either the pathophysiology of PD or secondary to anti-parkinsonian medications. These emergencies may manifest as either motor or non-motor symptoms.

2.1. Motor

2.1.1. Hypokinetic

2.1.1.1. Severe akinetic rigid states. Motor fluctuations are common in advanced PD. They may be observed in up to 40% of patients, 4–6 years after the onset of disease onset, and a 10% increase in frequency is observed with every additional year [11]. Although usually benign, motor fluctuations especially OFF state fluctuations may present as an emergency. OFF periods may become prolonged, unpredictable and unresponsive to medications. Patients may have significant worsening of rigidity, bradykinesia, postural instability and freezing. Psychiatric features of panic, anxiety and depression may also worsen. Additionally, autonomic dysfunction may be observed in the form of diaphoresis, tachycardia and variability in blood pressure [12,13]. Such sudden fluctuations may be precipitated by changes in the existing antiparkinsonian regimen, addition of a new drug (particularly dopamine receptor blockers), concurrent infections, metabolic derangement, and subdural hematoma if the worsening is preceded by a fall [14]. Patients should be thoroughly investigated and medication history should be carefully analyzed to find a probable cause for the worsening.

Super-OFF is a rare complication observed in patients with advanced PD. The super-OFF state may be significantly worse in comparison to an untreated state or after drug withdrawal for longer periods of time. This may occur either at the beginning or towards the end of a levodopa-induced full ON, and symptoms may last from minutes to over an hour [15]. The pathophysiology of these episodes is unclear and low plasma levodopa and striatal dopamine concentrations may produce a negative feedback via presynaptic auto receptors or predominantly inhibitory postsynaptic receptors [16]. Clozapine has been reported to significantly reduce the severity of the super OFF phenomenon [16].

2.1.1.2. Acute akinesia. Acute akinesia (AA) or akinetic crisis is a life-threatening complication of PD, with an annual incidence of 0.3% and death rate of 15% [17,18]. Patients with AA present with symptoms bearing a strong resemblance to neuroleptic malignant syndrome (NMS). There is an acute worsening of symptoms, the patient may be almost completely akinetic, and this may be associated with dysphagia, dysautonomia, hyperthermia, and/or increased levels of serum muscle enzymes [17]. AA can be triggered by multiple factors such as sudden alterations in treatment regimen, stoppage of medication, trauma, infections or gastrointestinal tract diseases.

The mechanism of AA is unclear, with unknown risk factors which are unrelated to the stage of disease or medication dosage. Severe loss of striatal dopamine transporter function has been reported in two patients with AA [19]. The key features which aid in differentiating AA from NMS or parkinsonism-hyperpyrexia syndrome (PHS) are the duration of the crisis which is long and may last several weeks, and complete unresponsiveness to anti-parkinsonian emergency medication such as subcutaneous apomorphine or nasogastric levodopa [17]. Additionally, this refractory unresponsiveness to levodopa and apomorphine is independent of the precipitating event.

2.1.1.3. Parkinsonism-hyperpyrexia syndrome. Parkinsonism-hyperpyrexia syndrome (PHS) is a potentially fatal albeit rare complication observed in patients with PD. PHS is clinically similar to NMS and may be indistinguishable from NMS with the exception of pre-existing parkinsonism. In 1981, a syndrome similar to NMS was reported in a patient who had no exposure to neuroleptics but had discontinued large doses of anti-parkinsonian drugs [20]. There was considerable variability in nomenclature for this syndrome until the term PHS was coined to describe a syndrome similar to NMS in the absence of exposure to neuroleptic drugs [21]. PHS may also occur in atypical parkinsonism [18,22].

The most common precipitating factor for PHS is sudden withdrawal of anti-parkinsonian medication, especially levodopa. The 'levodopa holiday' was a commonly employed rapid reduction and withdrawal of dopaminergic drugs, in an attempt to 'reset' the dopaminergic system [23]. These drug holidays were prevalent in the 1980's despite the risks of complications such as PHS, and although this is no longer in practice, there are other situations which may trigger PHS. The patient or caregiver may suddenly stop one or more drugs [24], medication may be changed or stopped due to another systemic illness (surgical or medical) [25], aggressive reduction in medication

following DBS, or hardware problems related to DBS [26,27]. Additional precipitants include neuroleptic medication, dehydration, excessively hot weather, systemic infections, abnormal intestinal drug absorption and the pre-menstrual state [25,28,29].

The clinical features of PHS are very similar to NMS and follow a relatively fixed timeline. Onset usually occurs between 18 hours and 7 days after change in medication. The initial symptom is severe rigidity with or without tremor, which rapidly progresses to an immobile state [25]. Over the next 72–96 h, patients become hyperpyrexic with alterations in mental status ranging from agitation and confusion to stupor. Autonomic signs such as tachypnea, tachycardia, variable blood pressure, diaphoresis, pallor and urinary incontinence may occur. Leukocytosis (up to 26,000/mm^3) and elevated creatinine kinase (CK) (260–50,000units/L) will be observed. Respiratory distress requiring mechanical ventilation, mutism, seizures and myoclonus may also occur [30].

Despite the similarities between PHS and NMS, there are a few subtle but important differences do exist. In comparison to NMS, patients with PHS have a longer latency prior to onset of symptoms (94 h vs 49 h), PHS has a lower elevation of CK and leukocytes, and a shorter duration of hospitalization in comparison to NMS [31].

PHS is a life-threatening condition and requires rapid detection and reintroduction of anti-parkinsonian medication (Fig. 2). History should be clarified to ascertain the precipitating factor: predominantly drug withdrawal, neuroleptic drugs, or absence of stimulation in patients with DBS. The pre-morbid dose of levodopa should be re-introduced via nasogastric tube, orally or via intravenous infusion (50–100 mg infused over 3 h) and should be repeated 4 times a day [25,32]. Dopamine agonists (DA) primarily bromocriptine can be given orally or via nasogastric tube. Other DAs like oral ropinirole (1–2 mg 3 times/day) or pramipexole (0.18–0.36 mg 3 times/day), transdermal rotigotine (2–4 mg/24 h), or subcutaneous apomorphine (1–2 mg/hour) may also be used [25]. Supportive measures such as rehydration, antipyretics, and cooling blankets should be used. Dantrolene sodium (10 mg/kg/day in 3–4 divided doses) may also be given if rigidity is severe and unresponsive to other drugs [32]. Metabolic parameters should be checked and complications such as infections, respiratory distress requiring mechanical ventilation and acute renal failure should be adequately managed [32]. Methylprednisolone (1 g intravenous/day for 3 days) in addition to levodopa, bromocriptine and dantrolene sodium has been shown to be efficacious in a placebo-controlled trial [33].

2.1.1.4. Neuroleptic malignant syndrome. NMS was first identified in the 1960s during the early trials of haloperidol [34]. NMS is frequently observed as a movement disorder emergency with an estimated incidence of 0.2% [35]. As mentioned in the previous section, PHS is the terminology employed for the symptom complex of NMS when observed in a patient with PD. It is essential to be aware of these terminologies being used interchangeably when describing a patient of PD who presents with hyperthermia, muscle rigidity, altered mental status, CK elevation, and autonomic dysfunction, with a background of dopamine agonist withdrawal [36,37]. Detailed discussion regarding NMS is beyond the purview of this article.

2.1.2. Hyperkinetic

2.1.2.1. Serotonin syndrome. This is a rare but potentially fatal emergency produced due to hyperstimulation of 5-hydroxytryptamine receptors. In patients with PD, this hyperserotonergic state may be induced by a combination of therapeutic doses of monoamine oxidase inhibitors (MAOI), and selective serotonin reuptake inhibitors (SSRIs) [38,39]. Depression is relatively common in PD, and SSRIs are commonly used. Hence, patients with PD may be at a higher risk of developing serotonin syndrome (SS).

Although several symptoms of SS overlap with PHS, there are a few features pathognomonic of SS (Table 1) [12,39,40]. Typically, the onset of symptoms in SS is within 24 h. Myoclonus, hyperreflexia, diarrhea and mydriasis are characteristic signs of SS. The biochemical profile of SS is similar to PHS [39]. SS may be diagnosed on the basis of the Hunter Serotonin Toxicity Criteria [41]. This includes the use of a serotonergic agent in addition to any of the following: (1) myoclonus, agitation or diaphoresis, (2) tremor and hyperreflexia, (3) hypertonia, (4) hyperpyrexia. Additionally, other causes such as infections, intoxication, hormonal or metabolic abnormalities, and drug withdrawal

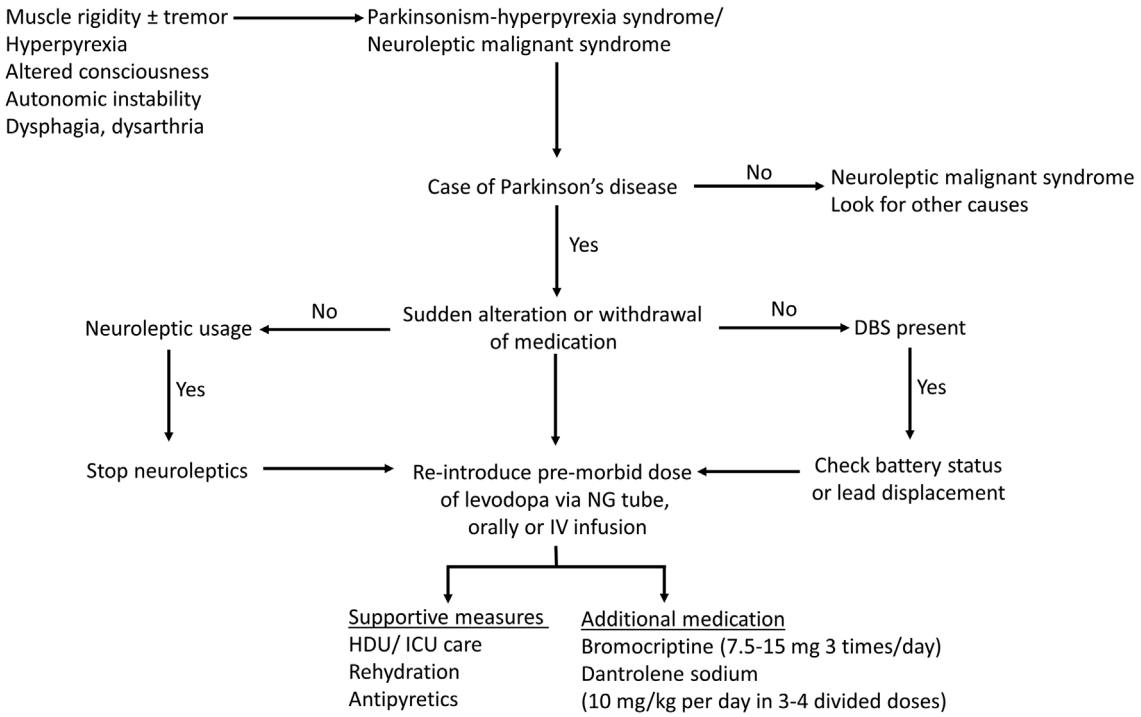

Fig. 2. Approach and management of Parkinsonism-hyperpyrexia syndrome. DBS: Deep brain stimulation; HDU: High dependency unit; ICU: Intensive care unit.

Table 1
Comparison of features of Parkinsonism-hyperpyrexia syndrome and serotonin syndrome.

	Parkinsonism-hyperpyrexia syndrome	Serotonin syndrome
Trigger	Levodopa withdrawal, DBS related problems, neuroleptics	SSRIs, MAOIs, SNRIs TAs
Onset	Hours to days	< 12 h
Course	Prolonged	Resolves rapidly
Clinical features		
Hyperpyrexia	+ + (> 90%)	+ (50%)
Hypertonia	+ + (> 90%)	+ (50%)
Hyperreflexia	- (Hyporeflexia)	+ (50%)
Altered sensorium	+ + (> 90%)	+ (50%)
Autonomic Dysfunction	+ + (> 90%)	+ (50–90%)
Tremor	±	+ +
Myoclonus	–	+ + (50%)
Mydriasis	–	+ +
Diarrhea	–	+ +
Laboratory abnormalities		
Elevated CK	+ + (> 90%)	+ (< 20%)
Leukocytosis	+ + (> 90%)	+ (< 15%)
Elevated hepatic transaminase level	+ + (> 75%)	+ (< 10%)

+ +: Key features of the syndrome which are crucial for diagnosis and are observed in the vast majority of patients; +: Symptoms may occur in a small group of patients and are not mandatory for diagnosis; ± : May or may not be present; -: Absent.
CK: Creatinine kinase; DBS: Deep brain stimulation; MAOI: Monoamine oxidase inhibitors; SNRI: Serotonin–norepinephrine reuptake inhibitors; SSRI: Selective serotonin reuptake inhibitor; TA: Tricyclic antidepressants.

must be ruled out.

Discontinuation of serotonergic medication, and adequate supportive care – antipyretics, rehydration, sedation, airway management, and muscle relaxants form the mainstay of treatment of SS [39]. Although chlorpromazine has been reported to be useful in SS, it should be avoided in patients with PD due to its adverse impact on the management of PD [39]. Dopaminergic drugs should be avoided as they may produce an exaggerated hemodynamic response and exacerbate SS [42].

2.1.2.2. Severe dyskinesia. Levodopa induced dyskinesia may be commonly observed in varying degrees of severity in up to 50% of patients with PD treated for over 5 years with levodopa [43]. Usually these dyskinesias are benign and may be managed on an outpatient basis. However, they may become severe and life-threatening as they may lead to rhabdomyolysis, dehydration and respiratory distress [12,39]. Factors which may precipitate a sudden, severe increase in dyskinesias include addition of long acting DAs, catechol-o-methyl transferase (COMT) inhibitors, DBS stimulation and infections [12].

Dyskinesia-hyperpyrexia syndrome (DHS) is composed of severe dyskinesias which lead to exhaustion, rhabdomyolysis, hyperpyrexia, and confusion [44]. It is similar to PHS, except that patients have dyskinesia instead of rigidity. A dyskinetic storm resembles DHS, and this term is frequently used in the context of stimulation-related motor complications in DBS [45]. Generalized dyskinesia may lead to respiratory distress if the respiratory muscles are involved [46–48].

Treatment of DHS and dyskinetic storm involves adjustment of dopaminergic medication, benzodiazepines, modification of DBS stimulation parameters, treatment of concurrent infections and supportive care. Amantadine hydrochloride or DBS may be considered for long term management [39].

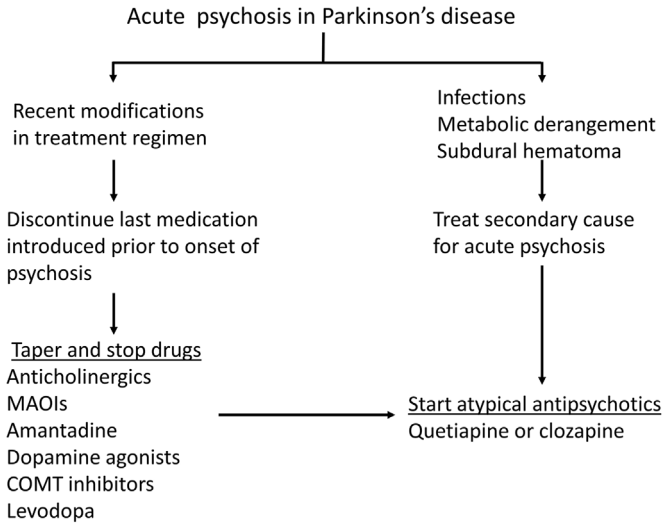

Fig. 3. Approach and management of acute psychosis in Parkinson's disease. COMT: catechol-o-methyl transferase inhibitors; MAOI: Monoamine oxidase inhibitors.

2.2. Non-motor

2.2.1. Acute psychosis

Psychosis is observed in around 40% of patients with PD [39], it is a common reason for inpatient admission and a strong predictor of nursing home placement [49]. The occurrence of psychosis is higher in PD with dementia, observed in 45–64% of patients [50,51]. The pathophysiology of psychosis in PD includes a complex interplay of exogenous and endogenous factors. Recent changes in medication, and other metabolic or neurological causes should be investigated in acute psychosis [52,53] (Fig. 3). A key component of treatment of acute psychosis in PD is reviewing PD medications. The last medication started prior to the onset of psychosis should be excluded first. Other drugs should be excluded in the following order – anticholinergics, MAOIs, amantadine, DAs, COMT inhibitors, and levodopa [52,54]. Atypical neuroleptics, specifically quetiapine or clozapine should be introduced [53]. Owing to the risk of agranulocytosis with clozapine, and the need for constant monitoring of leukocyte counts, quetiapine is preferred for long term management.

2.2.2. Suicidal ideation or attempts

Suicidal ideation and attempts have been reported to be 2–10 times more common in patients with PD in comparison to the general population [55]. This can be observed in patients of PD with and without DBS. It is more prevalent in patients with a history of impulse control disorders (ICD), compulsive medication use, depression or apathy and occasionally in the unmarried patients [45,56]. Patients who present with either suicidal ideations or attempts should be evaluated in collaboration with a psychiatrist. The premorbid state should be assessed to ascertain pre-existing depression or other psychiatric disorders, such as psychosis or ICD behaviors [57]. If a patient is depressed, antidepressants may be started and in severe cases electroconvulsive therapy may be necessary [58]. In patients who develop such symptoms following DBS, it is imperative to ascertain whether the patient had preoperative depression or if there is a state of impulsiveness, disinhibition or depression following DBS [59]. In patients where these symptoms may be stimulation induced, the lead position should be checked, and voltage and frequency should be checked. Vigilant and thorough pre- and post-operative screening and assessment for depression and suicidal ideations are critical preventive measures.

2.2.3. Autonomic dysfunction

Dysautonomia is a disabling complication of PD and orthostatic hypotension, and bowel and bladder problems are commonly observed [60]. Patients with orthostatic hypotension may present with an episode of syncope which may occur either when treatment with dopaminergic drugs has been initiated, or in cases of advanced PD. In the first situation the medication may be initially stopped and then increased very gradually to the optimal dosage. In patients with advanced PD, long term measures such as compression stockings, increased salt and water intake, gradual change of posture and drugs like fludrocortisone, midodrine, droxidopa or pyridostigmine should be employed [13,61]. The presence of significant dysautonomia, in early PD is a red flag and multiple system atrophy should be ruled out.

Constipation is observed in around 50–80% of patients with PD [62]. In extreme circumstances it may lead to fecal impaction and bowel obstruction [13]. Several cases of sigmoid volvulus have also been reported in PD [63]. Patients with PD who present with a distended abdomen, absent bowel sounds, abdominal pain or tenderness should be promptly evaluated.

2.2.4. Pulmonary dysfunction

Patients with PD have respiratory disturbances ranging from minimal subclinical dyspnea to acute hypoxia [64,65]. Pulmonary dysfunction in PD may be peripheral, central or mixed. The dysfunction may also be dependent on levodopa i.e. OFF state, ON state or secondary to dyskinesia.

1. Peripheral pulmonary dysfunction: This may be either a restrictive, obstructive or mixed pattern. Upper airway obstruction has been observed in up to 33% of patients with PD. Patients with PD can develop laryngeal spasms and they may present in the emergency room with wheezing or stridor [65–68]. The responsiveness of obstructive respiratory dysfunction to levodopa is debatable. Levodopa responsive restrictive respiratory dysfunction which presents as exertional dyspnea has also been reported in PD [64,69].
2. Central pulmonary dysfunction: Dyspnea observed in PD may be secondary to abnormalities in the central control of ventilation, patients tend to have an impaired perception of dyspnea and may have episodes of sleep apnea [65].
3. Pulmonary dysfunction associated with levodopa: Rarely patients present with severe laryngeal stridor due to OFF state dystonia [68]. As discussed earlier, severe dyskinesias may also produce respiratory distress [46–48]. Patients have also been known to develop fluctuations in respiratory functions which are similar to motor fluctuations [47].

2.2.5. Miscellaneous

2.2.5.1. Dysphagia. Manifestations of dysphagia ranging from drooling to serious complications like aspiration pneumonia and malnutrition [39] has been reported in patients with PD. This usually goes unnoticed until it leads to severe complications. Furthermore, dysphagia may lead to difficulties in consumption of PD medication. Patients should be regularly evaluated for these complaints and alterations in diet, feeding habits, and tube feeding may help avoid complications. A percutaneous gastro-jejunostomy should be considered as a long-term option in patients with severe dysphagia. Additionally, alternate forms of drug delivery such as transdermal patches, infusion pumps, or nasogastric delivery of medication should be provided to ensure adequate treatment.

2.2.5.2. Sensory. Sensory complaints in patients with PD include pain in the absence of dystonia, akathisias and restless leg syndrome [13]. Although seemingly insignificant they may occasionally be severe enough for a patient to seek an emergency consultation. Five types of pain have been described in patients with PD – dystonic, central neuropathic, musculoskeletal, radicular-neuropathic and pain-associated restlessness [70]. In some situations, this pain tends to fluctuate with motor fluctuations and can be levodopa responsive.

2.2.5.3. Complications of levodopa gel infusion. A few reports have described the occurrence of symptoms akin to Guillain-Barre syndrome or polyneuropathy following treatment with parenteral levodopa gel infusion [71]. Mixed patterns of neuropathy, either axonal and demyelinating or purely axonal forms have been reported [72]. A case of severe encephalopathy with confusional state, axonal neuropathy with severe flaccid tetraparesis has also been described in conjunction with levodopa gel infusion therapy [73]. Although the exact pathophysiology is uncertain and reports are sparse, it is critical to be aware of the possibility of such a situation.

3. DBS related emergencies (Fig. 4)

DBS has been commonly utilized for management of the motor manifestations of PD, and there are several emergencies which may arise secondary to DBS. These may be related to the surgical procedure, hardware or stimulation [45]. The discussion of emergencies which arise due to the surgical procedure and hardware are beyond the scope of this review, and the possible complications have been summarized in

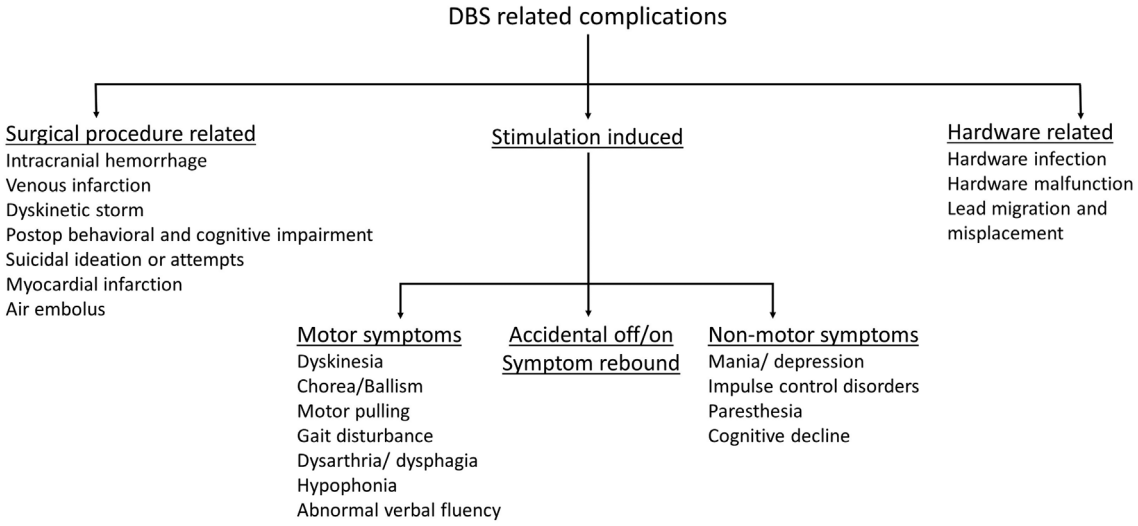

Fig. 4. Deep brain stimulation related complications.

Table 2
Management of stimulation related complications in patients with Parkinson's Disease who had undergone Deep Brain Stimulation.

Complication	Management
Motor	
Dyskinesia	Reduce dopaminergic medication. Program gradually. Propofol may be given in severe cases. Try a dorsal contact.
Chorea/ballism	Reduce dopaminergic medication. Program gradually. Try a dorsal contact.
Motor pulling	Reduce pulse width or voltage. Bipolar stimulation with alternate lead contacts may be tried. Check lead location, replacement may be necessary.
Gait disturbance	Try low frequency (60 Hz) with higher pulse width or voltage.
Dysarthria/dysphagia	Change stimulation to bipolar or decrease pulse width, voltage or frequency. Check lead location and try another contact. Speech therapy.
Hypophonia	Change stimulation to bipolar or decrease pulse width, voltage or frequency. Try another contact. Speech therapy.
Abnormal verbal fluency	Try a dorsal contact DBS lead. Change stimulation bipolar or decrease pulse width, voltage or frequency.
Non-motor	
Anxiety	Increase frequency and dosage of dopaminergic drugs and consider a dorsal DBS contact. Supportive psychiatry care.
Mania	Behavioral therapy, adjust medication and stimulation. Stop dopamine agonists and start quetiapine. Consider dorsal DBS contact and/or reduce pulse width, voltage and frequency.
Impulse control disorder	Discontinue dopaminergic agonist, add quetiapine. Consider dorsal DBS contact and/or reduce pulse width, voltage and frequency.
Severe depression	Behavioral therapy, counselling, medication adjustment, and/or stimulation adjustment. Check lead location. Supportive psychiatry care.
Paresthesia	Reduce voltage or pulse width and try bipolar stimulation or another contact.
Cognitive decline	May be related to disease progression, surgery or stimulation. Check lead location and consider a dorsal contact.

Fig. 4.

3.1. Stimulation related motor symptoms

These are commonly observed complications which are highly responsive to reprogramming of voltage, frequency and pulse width. These include chorea, dyskinesia, gait disturbance, motor pulling, dysarthria, hypophonia and abnormal verbal fluency [45]. Management approach for these complications is listed in Table 2 [45].

3.2. Stimulation induced non-motor symptoms

Paresthesia, behavioral and cognitive issues may emerge when stimulation spreads to surrounding, limbic and associative regions [45]. Depression and mania are serious stimulation-related issues and often require admission, medication adjustments and reprogramming. Management approach for these complications is listed in Table 2 [45]. Suicidal ideation or attempts are serious stimulation induced complications, management of which has been discussed in an earlier section. A transient decline in cognition or change in behavior may be observed in patients following DBS surgery. However, this impairment may persist in patients who had significant pre-operative cognitive dysfunction. In case of persistence of cognitive impairment in a previously normal patient, a thorough diagnostic workup should be conducted to rule out underlying or exacerbating contributory conditions.

3.3. Accidental off/on and symptom rebound

A DBS device may unpredictably turn on/off and this may be due to potential environmental triggers such as store security devices or magnetized ice freezers [74]. If patients have more than one IPG device, they should be placed a minimum of 6 inches apart to prevent cross-communication and unintended reset of the devices to default stimulation settings [45].

Severe rebound of symptoms may occur following battery failure and these rebounds are more dramatic in patients with good response to DBS [45]. Management is associated with checking device status, and if off, resuming stimulation is adequate. If the device is on, battery status, impedance, current drain should be evaluated.

4. Indirect disease related emergencies

4.1. Falls

Falls are commonly observed in PD, and around 2/3rd of patients fall each year [4]. These usually occur secondary to postural instability, orthostatic hypotension and more frequently in the OFF state [39]. These increase mortality and morbidity, and increase the risk of fractures, specifically in the neck of femur [75]. Falls also reduce patient mobility and lead to increased dependence. Physical therapy and assistive devices are necessary preventive measures.

4.2. Aspiration pneumonia

This is an important emergency which occurs secondary to dysphagia in patients with PD. It is one of the most prevalent causes of emergency admission in patients with PD [2,9,76]. Early recognition of dysphagia is necessary to reduce the probability of developing aspiration pneumonia.

5. Unrelated emergencies

The most common reasons for ER visits in PD are unrelated to the pathophysiology of PD [2]. The prevalence of non-PD related systemic abnormalities is as follows: Infectious disease:21–32%, cerebrovascular or cardiovascular disorders:8–11%, and metabolic abnormalities:2–6% [5,7,12]. It is crucial to ensure continuous and adequate dopaminergic medication while the patient is under treatment for these systemic complications. Sudden withdrawal may lead to PHS.

6. Special situations: surgery in patients with PD

PD pathophysiology plays a significant role in the peri-, intra- and post-operative management of patients with PD. Additional peri-operative workup and anesthetic considerations are necessary to avoid complications which may occur owing to the impact of PD on the respiratory and cardiovascular systems [77]. Several significant side effects of common PD medication influence anesthetic management (Table 3) [77–79]. A detailed discussion is beyond the purview of this review and in summary the basic considerations are:

1. *Perioperative:* Dysphagia, pulmonary dysfunction, and cardiovascular complications including orthostatic hypotension and ventricular arrythmia may occur in patients with PD. Thorough perioperative evaluation is necessary to avoid complications.
2. *Intraoperative:* Patients with PD may develop severe dyskinesias in response to propofol. During long surgical procedures, the regular dosing of PD medication should be administered via nasogastric tube to avoid post-operative distress.

Table 3
Side effects of medications commonly used in Parkinson's disease which may influence anesthetic management.

MAOIs (Selegiline, rasagiline)	Primarily serotonin toxicity when administered with opiates, SSRIs, TCAs, cocaine, and antibiotics such as ciprofloxacin and fluconazole.
Antidepressants	TCAs worsen orthostatic hypotension, and SSRIs prolong the QT interval.
Domperidone	Prolongation of QT interval and increased risk of sudden cardiac death.
Quetiapine	Prolongation of QT interval

MAOIs: Monoamine oxidase inhibitors; SSRI: Selective serotonin reuptake inhibitors; TCA: Tricyclic antidepressants.

Propofol, halothane, fentanyl, morphine and alfentanil should be avoided in patients with PD [77].

3. *Postoperative:* PD medication at pre-operative dosage should be re-instituted as soon as possible. Opioid analgesics should be avoided, and serotonin toxicity may occur if serotonergic agents are administered in concurrence with MAOIs.

7. Conclusions

Adequate knowledge pertaining to the diagnosis and management of emergencies in patients with PD is critical to reduce mortality and morbidity. Acute complications are frequently secondary to changes in drug regimen and should always be investigated. Additionally, co-morbid conditions or intercurrent illnesses may lead to significant distress and the possibility of these conditions should also be explored.

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