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Mini Review

Pediatric Dyskinesias: Need for a Careful Approach of Inclusive Exclusions

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Abstract

Movement disorders in children need fast and elaborate evaluation to not to miss any of the rare, variegated and usually eponymous diagnoses, ranging from basal ganglia lesions proper, DRD2 genetic disorders, Lance-Adams syndrome, traipsing focal dystonias in facial muscle groups - similar to the Edgar alien (of MIB, the film), and the neck and truncal (opisthotonus to Pisa) dystonias, to myoclonic seizures. Amelioration of the distress improves the quality of life of the children and caregivers. Dyskinesias as side effects of antipsychotics and psychogenic presentations are more common than organic causes. Ambiguous responses from the child pose us difficulty in differentiating from stereotypical movements, more so if accompanied by intellectual difficulty. An inclusive approach to the diagnosis of pediatric dyskinesias, starting from ruling out the commoner causes like infections, inflammation (central or musculoskeletal), toxins and electrolyte imbalance. History of fever, behavioral disturbances especially self-mutilation, drug intake, family history of genetic disorders, previous intensive care admissions, comorbid psychiatric conditions including mood disorders and OCD, intellectual disability, and interpersonal conflicts form important cues in clinching the primary diagnosis. A probable high incidence of suicidal ideation in dyskinesia syndromes is a worrisome observation. Early diagnosis and treatment of dyskinesia should improve functional capacity and self-esteem. Emphasis on routine genetic screening, neuro-imaging studies, EEG, assessment of suicidal risk, and managing to minimize the patient's physical and psychological disabilities with appropriate drugs beginning at the earliest, monitoring, support and psychosocial rehabilitation, ensures a favourable outcome.

Keywords: *Pediatric Dyskinesias; Movement Disorders; DRD2 Genetic Disorders; Lance-Adams Syndrome*

Movement disorders in children are usually distressing for the caregivers as well. Frustrated children become irritable, may cry incessantly, disrupt caregiver's routine, and may become completely dependent for personal care, grooming and having food, among others. Education, play, social interaction and interests dwindle with increasing symptoms, resulting in a gross effect on their quality of life.

These disorders may have a myriad differential diagnoses starting from lesions localized in basal ganglia to congenital and metabolic disorders. However, dyskinesias as side effects of antipsychotics and psychogenic (conversion or dissociative neurological disorders) presentations are more common than organic causes. Ambiguous responses from the child pose us difficulty in differentiating between myoclonus, myoclonic seizures, tics, and others, more so if accompanied by intellectual difficulty.

An inclusive approach to the diagnosis of pediatric dyskinesias

Acute presentation obviously mandates infections, inflammation (central or musculoskeletal), toxins and electrolyte imbalance. After ruling out them, we are confronted with the unending list of peculiar differential diagnoses varying from a fancy eponym of Lance-Adams

syndrome, traipsing focal dystonias in the face - similar to the Edgar alien (of MIB, the film), head and neck, and truncal (opisthotonus to Pisa) dystonias:

1. **Drug history:** Extrapyramidal side effects due to the antiemetic metoclopramide, the prokinetic levosulpiride, antipsychotics (given for the behavioral disturbances of autism spectrum disorders, and schizophrenia), may present as dystonia (opisthotonus, head and neck dystonia), acute or tardive dyskinesia. The latter should not be disregarded merely because of the age group being younger. Even tardive dyskinesias are acute at the first instance, with only the antipsychotic drug history suggesting the tardiness in the diagnostic term.

2. **History of febrile illness:** Children with chorea following a history of fever, joint pain and palpitations implicate post-streptococcal Sydenham's chorea. A similar history with features of obsessive compulsive disorder point to the now controversial PANDAS. Choreiform movements with headache, irritability and fatigue following viral febrile illness point to hyperkinetic form of basal ganglia encephalitides like encephalitis lethargica (Von Economo's syndrome). Another probably post-infection or autoimmune cause is the Westphal-Leyden syndrome presenting with chorea alongside acute ataxia, proximal muscle rigidity and vertigo.

3. **Genetic dyskinesias:** We should also consider the genetically determined dystonia-plus syndromes like Dopa-responsive dystonia (DRD) - a mostly pediatric-onset, neurometabolic disorder with cognitive deficits, and myoclonus-dystonia syndrome - characterized by lightning jerks during writing. Then there are the mutations in the genes of DRD2 and DRD4, dopamine receptor D2 and D4 types respectively. Benign hereditary chorea of early childhood (with dysarthria, tremors, hypotonia, intellectual disability) and childhood onset neuroacanthocytosis syndromes (with orolingual dyskinesia, chorea, dystonia, tics) may also be considered for genetic evaluation.

4. **Action myoclonus:** (AM) with a recent history of asphyxia - as in perinatal asphyxia, suffocation or attempted hanging, or following cardiac resuscitation, may point to Lance-Adam's syndrome (LAS) [1]. AM may be predominant in upper limb and orolabial muscles, with minimal cerebellar ataxia [2]. Chronic posthypoxic myoclonus in LAS is a rare complication after hypoxic brain injury and successful resuscitation, with AM starting days to weeks after the event and persisting thereafter [3,4]. Though EEG is inconclusive [5-7], PET scan may show a mild bilateral decrease of glucose metabolism in the frontal lobes, VL thalamus and brainstem [8]. Around one in 3 documented LAS patients show history of suicide attempts [9,10]. Reduced 5-HIAA in CSF was found in LAS [2,5,11]. Along with zonisamide, valproate, levetiracetam and piracetam, clonazepam [2,5,10] and fluoxetine [12,15] (both increasing 5-HIAA in CSF) were also effective in many cases [15].

5. **Comorbid mood disorders:** Those sad, withdrawn and with a history of recurrent suicidal attempts apart from dyskinesias, may have cingulo-striatal lesions [13,14,16].

6. **Comorbid obsessions:** Young adolescents with dyskinesias and hypersexual obsessions or paraphilia may denote lesions in the striatum and basal forebrain. Evidence of tics with predominant compulsions and obscene verbal perseveration may point to Tourette's syndrome [17].

7. **Developmental delay with dyskinesia:** Spasticity and dyskinesia with global developmental delay beckons the differentials of cerebral palsy or (if with an infancy or later onset) intracerebral hemorrhage predominantly from vascular malformations.

   Others with developmental delay, should prompt ruling out of genetic disorders including inborn errors of metabolism, wherein the dyskinesias or roving dystonia's may have a typical onset by 7 - 8 years of age. Mineral deposits in the lenticular nuclei in MRI, may implicate Wilson's disease, pantothenate kinase-associated neurodegeneration or other hemochromatosis, or hypercalcemic states.

Autism-like stereotypical movements with intellectual disability, alongside proportionate short stature, excessive lordosis, kyphosis and other features like incurved fifth fingers and excessive body hair, self-mutilation suggest the possibility of Cornelia de Lange syndrome.

Fringe differentials of a Childhood disintegrative disorder and Rett's syndrome may be suspected with history of stereotypical hand movements mimicking dyskinesias, along with language and communication deficits, biting and other self-injurious behavior.

8. **Autosarcophagy:** (Self-cannibalism) [18] has been documented in autism spectrum disorders, Lesch-Nyhan syndrome and other metabolic disorders (with stereotypes), and somatic sensory deficits (psychogenic dyskinesias). Lesch-Nyhan syndrome is characterized by dystonia, chorea or hemiballismus, increased uric acid levels, difficulty in mobility, male exclusiveness and HPRT1 gene mutations.

9. **Dyskinesia as a dissociative (conversion) symptom:** This occurs in persons with chronic hedonistic droughts, foraging for psychological support, in a background of inexpressible distress, cramping personal frailties and incapacitations, perceived ongoing declension of conscience, guilt or situational tight corners. It serves as a channel of phonetizing the cryptic signs of distress from pestering psychological conflicts. Scales like Monday-Jankovic criteria [19] are useful to delineate psychogenic myoclonus, in addition to Fahn and Williams criteria. Yawning and pandiculation may be considered as physiological dyskinesias, with respect to physical and neuropsychological relaxation.

10. **A mandatory consideration:** Ruling out malingering and factitious disorder [20] would be prudent especially when anamnesis suggests similar spuriously unexplainable neurological complaints, with a background of perceived unfulfilled and continuous need for care, insightful attention seeking, and gains like waivers from school work and domestic duties, monetary grants and compensations, and more attention from family and friends.

11. **An imposter in seizures:** The fontal lobe partial seizures of motor cortex, should be ruled out if the abnormal movements are predominantly nocturnal, and involve truncal muscles. Focal changes in the EEG would clinch the diagnosis. Motor automatisms of temporal lobe epilepsy can be ruled out by the presence of awareness to the surroundings and clear consciousness during the movements.

12. **Myoclonic jerks:** Like juvenile myoclonic epilepsy and Ramsay Hunt syndrome may be excluded by the nocturnal (and dawn) jerks, and shingles along with facial and/or cerebellospinal signs, respectively. Benign myoclonus of early infancy, myoclonic-astatic epilepsy are close differentials. Lennox Gastaut syndrome with intellectual or learning disability, followed by recurrent seizures of multiple types, drop attacks, and a specific (slow spike-and-wave) pattern in EEG, usually remain refractory to antiepileptic drugs. Interictal localized myoclonus seen in epilepsia partialis continua (Kozelnikov's syndrome) is usually accompanied by brief psychosis and sometimes fugue state.

13. **Infantile spasms:** (West syndrome) along with intellectual disability and hypsarrhythmia, are a typical expression of a deranged brain - in prenatal disorders including tuberous sclerosis, congenital infections, Down syndrome, hydrocephalus, migrational disorders like schizencephaly and Sturge-Weber syndrome, perinatal disorders including hypoxic-ischemic encephalopathy, trauma and intracranial hemorrhages, and postnatal disorders including pyridoxine dependency syndromes, inborn errors of metabolism such as phenylketonuria, maple syrup urine disease, lysosomal disorders, meningitis, encephalitis.

Management

Appropriate blood and urine investigations may rule out inborn errors of metabolism. Imaging studies like MRI brain can elaborate on congenital neuronal anomalies and strokes. Karyotyping and targeted PCR studies may reveal specific genetic disorders including inborn errors of metabolism and Rett's syndrome.

Dyskinesias improve with minimal dosage of antipsychotics preferably with an anticholinergic cover; while baclofen and lorazepam are considered for dystonias, drug-induced dystonia may require anticholinergics; myoclonus improve with clonazepam [5,11] and sodium valproate, while stereotypical movements, tics, compulsive and self-mutilating behaviour may improve with SSRIs and other serotonergics. Relaxation therapy and caudate/striatum-targeted invasive procedures have been theorised to help.

Psychological stress secondary to the pediatric dyskinesias can increase the frequency and severity of the attacks [21]. About one third of the patients have varying degrees of anxiety and depression [22]. Depression secondary to a severe, disabling and persisting dyskinesia, poor coping, hopelessness, poor peer relations (associated with cognitive deficits), and perceived social isolation, increase the risk of suicidal phenomena [13,14,22]. Documented low 5-HIAA in CSF and 5HT in brainstem and midbrain have been found in suicidally inclined adolescents with chronic movement disorders [16].

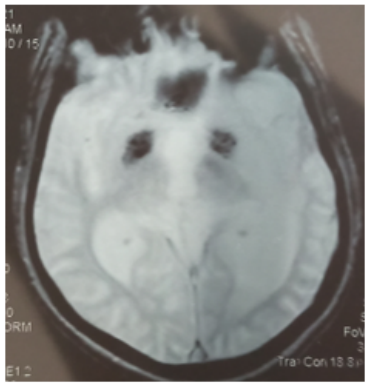

Figure 1a: *MRI brain plain, axial T2, showing neurodegeneration with brain iron accumulation.*

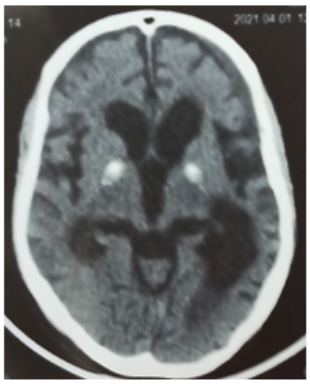

Figure 1b: *CT brain plain showing neurodegeneration with brain iron accumulation.*

Conclusion

A probable high incidence of suicidal ideation in dyskinesia syndromes is a worrisome observation. Early [9] diagnosis and treatment of dyskinesia should improve functional capacity and self-esteem. Emphasis on routine genetic screening, neuro-imaging studies, EEG, assessment of suicidal risk, and managing to minimize the patient's physical and psychological disabilities with appropriate drugs beginning at the earliest [13,14], monitoring, support and psychosocial rehabilitation, ensures a favourable outcome.

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