Dystonia

P. ADJEI 2013

Introduction

- Syndrome of sustained muscle contraction- Repetitive movements or postures

- Due to co-contraction of antagonistic muscles

Types of Dystonia

- Focal dystonia → one body part
- Segmental dystonia → two or more body adjacent body part

Classification of Dystonia

Primary Dystonia

- Primary Dystonia (childhood onset generalized primary dystonia)
- Sporadic Dystonia (Adult onset primary focal dystonia)
- Dopa responsive Dystonia
- Heredodegenerative dystonia
  - Wilsons disease(AR)
  - Huntington's disease(AD)
  - SCAs(AD)
  - Lubag (X linked dystonia parkinsonism)
  - Rapid Onset dystonia parkinsonism
  - NBIA(PKAN) (AR)
  - Neuroacanthosis
- Degenerative syndromes
  - MSA
  - PSP
  - CBD

Secondary Dystonia

- Perinatal trauma/hypoxia
- Stroke
- Focal brain lesions(Putamen)
- Drug induce dystonia's
  - Acute Drug induced dystonia
  - Tardive Dystonia
  - Tardive dyskinesia

Evaluation

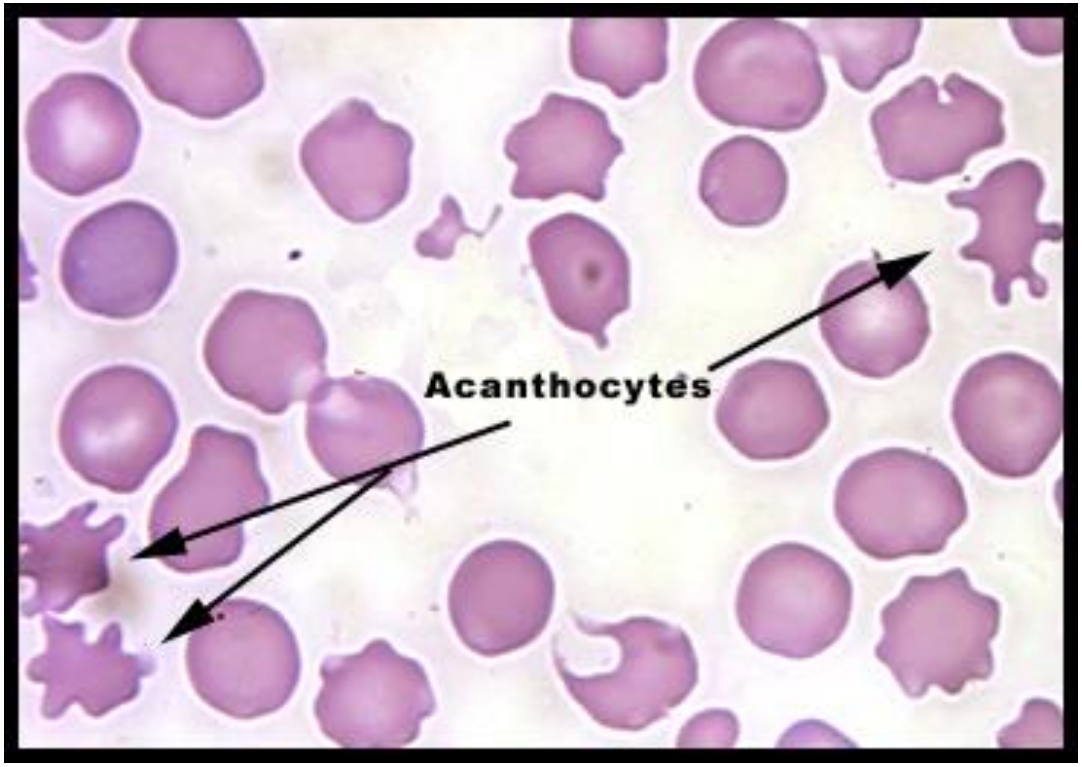
- Adequate history
  - Age at onset
  - Course of illness
  - History of psychiatric illness
  - Neuroleptic drug use
- Physical examination
  - Focus and identify the abnormal movement i.e. pattern recognition- challenging even to experienced neurologist

Investigations

- Exclude Wilson's disease
  - Serum Cu
  - 24hr urinary copper
  - Slit lamp examination for KF rings
- Check DYT1 gene <25years
- Other genetic tests
    - HD
    - SCAs
- MRI of Brian
- Fresh blood film for acanthocytes

Acanthocytes

An abnormal red blood cell that has thorny projections of protoplasm



Clinical manifestations of Adult onset focal and Segmental Dystonia

- Blepharospasms / Hemifacial Spasms
- Oromandibular dystonia
- Lingual dystonia
- Meige syndrome(Blepharospasms + oromandibular dystonias)
- Cervical Dystonia
- Spasmodic dysphonia
- Task specific dystonias(writers cramps)

PRIMARY DYSTONIA(Oppenheim's Dystonia)

DYT1 gene

Affects 1/3000

Ashkenazi Jews

AD with low penetrance

- Childhood onset
- Starts from the foot and has a variable spread to segmental or generalized
- craniocervical usually spared
- Action induced dystonia

- DNA testing is available- usefulness in prenatal or presymptomatic diagnosis

- Treatment
  - Trial of dopamine in absence of DNA
  - High dose anticholinergic
    - Baclofen
  - Benzodiazepines
  - Dopa depleting drugs

Dopa- responsive dystonia(DRD)- Segawa's disease

- AD with incomplete penetrance
- Mutations in GTP hydroxylase gene(DYT 5)
- AR forms exist where the mutations are found in Tyrosine Hydroxylase gene

- Girls> Boys
- Lower limb onset – action induced generalized dystonia
- ***Diurnal variation of symptoms- Almost normal in the morning and deteriorate throughout day***
- Mild parkinsonism
- Para paresis in some presentation
- Some cases similar to CP

- L-DOPA up to 275 mg tid
  - No Dopa dose fluctuations

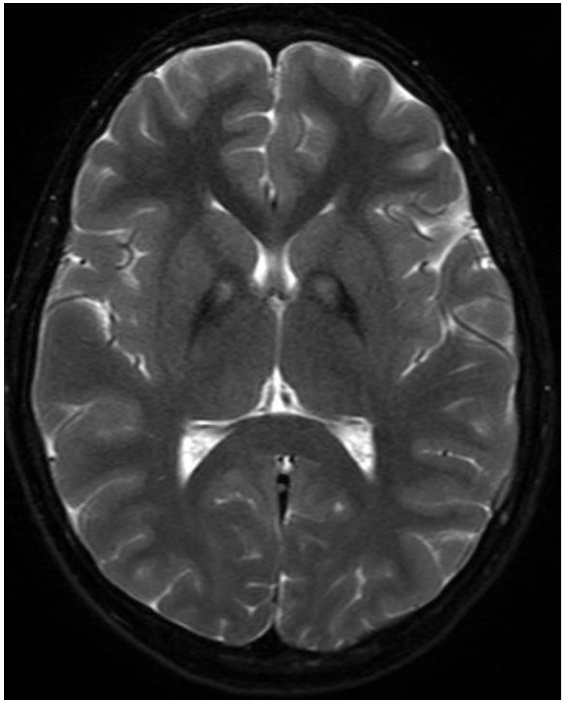
Pantothenate kinase- associated neurodegeneration(PKAN)

Neurodegeneration with Brian Iron accumulation

Formerly **Halloverdin Spatz** syndrome

- Dystonia
- Optic atrophy
- Dementia
- Retinitis pigmentosa
- Parkinsonism
- Death

- AR condition/ childhood onset
- Atypical forms occur in adulthood but no EOT sign on MRI
- PANK2 gene mutations- pantothenate kinase an important enzyme in Vit B5(pantothenate) phosphorylation)
- HARP(Hypobetalipoprotienemia, acanthocytosis, retinitis pigmentosa and pallidal degeneration) syndrome linked to PANK2 gene mutations



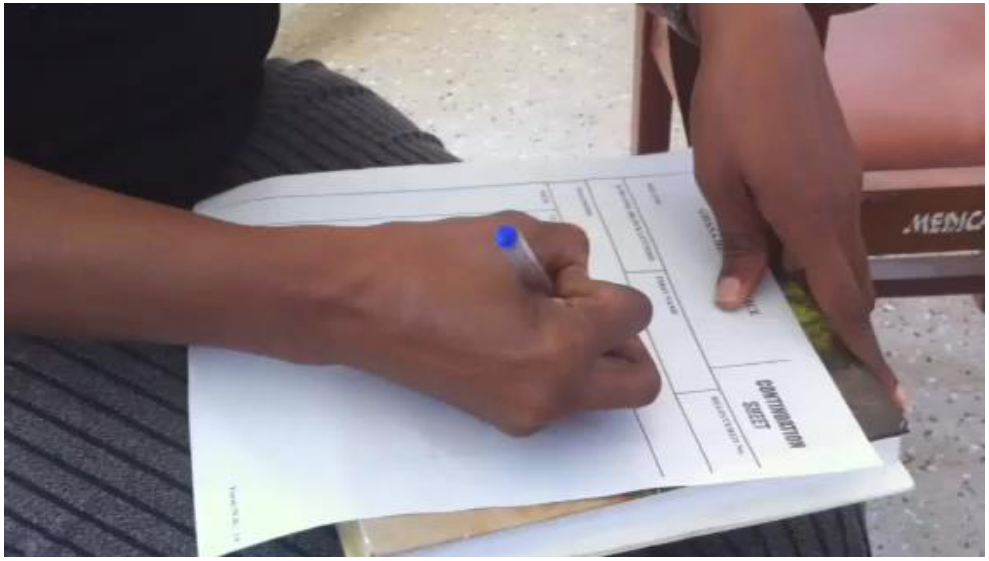
Eye of Tiger sign

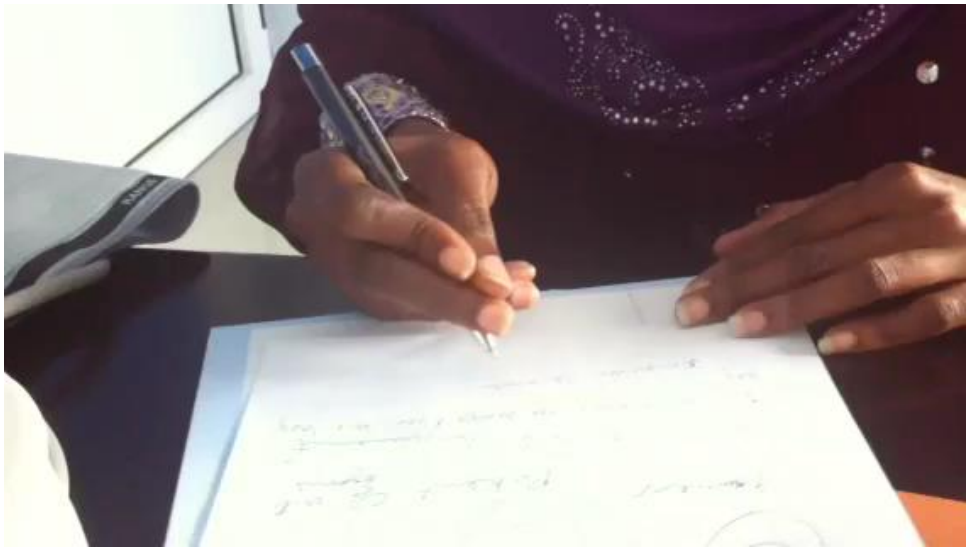
Adult Onset focal and Segmental Dystonia

Task Specific Dystonia

Writers Cramps 1

Flexion Type

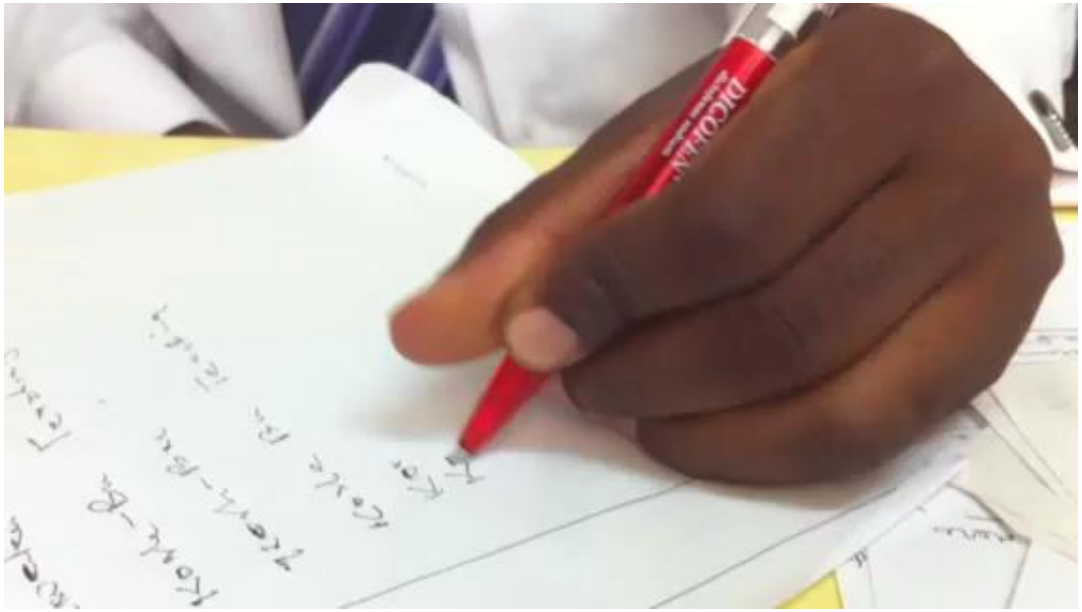




Task specific Dystonia

Writer's cramps 2

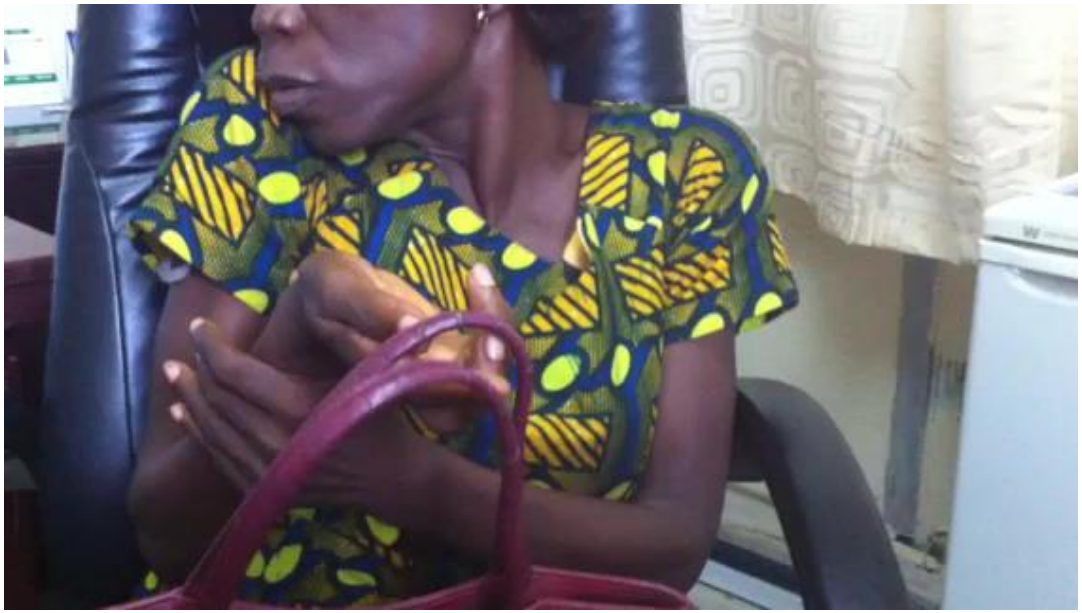
Extension Type



Sporadic Dystonia

Adult onset

Cervical Dystonia



Sporadic Dystonia

Adult onset 2

Meigs Syndrome

Sporadic Dystonia

Adult onset 3

Hemifacial Spasms

Acute Drug Induced Dystonia

Metoclopramide

Occurs 1-3 days of use of drugs

Abnormal postures, neck dystonia, tongue or jaw postures

Treat with IV/IM Cogentin 2mg or Benadryl 50mg

Tardive Dystonia

- Truncal dystonia is most typical form
- Focal and segmental dystonia- bleparopspams, cervical dystonia and oromandibular occur and extremities can be involved
- M>F (younger age)

- Seen after **chronic** use of dopamine blocking agents(median duration is 5.1years)

Treatment

- Gradually withdraw the neuroleptic
- Substitute atypical antipsychotics
- Serpasil
- Valproate
- Clonazepam
- Baclofen
- Diazepam
- Vitamin E
- BoNT

PISA syndrome

Drug Induced

Tardive Dystonia (Amodiaquine chronic use)

Tardive Dyskinesia

- Stereotyped movements often involving the facial and oral muscles manifest as tongue protrusion , chewing, lip smacking, grimacing
- Trunk and extremities can be involved

- Seen after chronic use of dopamine blocking agents (6 weeks)

- Treatment
  - Gradually withdraw the neuroleptic
  - Serpasil
  - Valproate
  - Clonazepam
  - Baclofen
  - Diazepam
  - Vitamin E

- Post Traumatic Dystonia(Children or adolescence surviving head injury)
  - Hemidystonia
  - Refractory to medical treatment
  - BoNT effective
  - DBS/Thalamotomy

- Paroxysmal Kinesiogenic Dystonia(DYT 11)
  - Childhood onset
  - Episodic dystonia induced by rapid movement to an unexpected stimulus, spells decrease in adulthood
  - Last <1 minute occurring>100times a day
  - Responds well to anticonvulsants

- Paroxysmal NonKinesiogenic Dystonia(DYT8)
  - Infancy onset
  - Episodic, last longer(10mins)and less frequent
  - Episodes precipitated by Stress, Caffeine and ethanol
  - Does not respond to anticonvulsants – benzodiazepines, neuroleptics, anticholinergic

Management of Dystonia

- Consider trial of Dopa in DRD- <40 years, child or adolescent for DRD
- Anticholinergic drugs
  - Benzhexol up to 80mg/day
  - Use other if not helpful
    - Tetrabenazine
    - Pimozide
    - Sulpiride
- BoNT- Focal dystonias
- Thalamic DBS may be an option

BoNT

- For most patients BoNT is the agent of first choice for Dystonia
- For early onset dystonias(<20) drug therapy can be tried
    - Dopa for 3/12-non response rules out DRD
    - Trihexyphenidyl
    - Benzodiazepines
        - Clonazepam
    - Physiotherapy

BoNT

- Several preparations available
  - Botox (Type A)
  - Dysport (Type A)
  - Xeomin (Type A)
  - Neurobloc(Type B)

  - Wide therapeutic range
  - EMG guided techniques.


500 units/vial
2 vials
Dysport
Clostridium botulinum type A
toxin-haemagglutinin complex
IPSEN
Dysport
Dysport


Botulinum
Toxin Type A
BOTOX
Purified
Neurotoxin
Complex
100
UNITS
ALLERGAN
Botulinum
Toxin Type A
BOTOX
100
UNITS


XEOMIN
MERZ
XEOMIN


NeuroBloc
10 000 U

Syringes and needles

- Reconstitute with 1ml N/S for Deep IM injections
- Reconstitute with 2.5Ml N/S for facial injections

Conclusion

- Pattern recognition is the key
- Establish age at onset, family history drugs and psychiatric history
- *It is challenging even to experienced neurologist*
- Use Dopamine in all childhood onset dystonias for up to 3 months if DNA not available- DRD

Thank you