SERTIFIKAT

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Dr.dr. Yuliarni Syafrita, Sp.S(K)

atas partisipasinya sebagai

PEMBICARA

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Prof. Dr. dr. Moh. Hasan Machfoed, Sp.S(K), M.S.

Ketua Panitia

Dr. dr. Syahrul, Sp.S(K)

MOVEMENT DISORDERS IN METABOLIC DISEASE

(Overview)

Yuliarni Syafrita
Neurology Department
Faculty of Medicine
Andalas University/ RSUP Dr. M. Djamil Padang

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Preface

- Movement disorder : neurological syndrome characterized by hyperkinetic or hypokinetic.
- It's a serious problem, related to brain lesion.
- Metabolic disease : disruption of mechanical reaction at cellular level.
- Metabolic disease: Inherit Metabolic Disorders (IMD).
- Most of IMDs involve nervous system (neuro-metabolic disease).

- Cont'd

IMD :

- Symptoms
- Implicate more than one nervous systems
- 1 metabolic disorder : generates more than one movement disorders
- 1 movement disorder type : produced by some IMDs

- Cont'd

- Epidemiology : overall population-based is not available
- Base on type : RLS, Essential Tremor
- Hospital based : parkinsonism, tremor and dystonia

- When we think a movement disorder caused by metabolic disease?
  - Fluctuate of movement disorder
  - Appear almost at the same condition
  - Followed by systemic symptoms
  - Involve various nervous system
  - Displays several types of abnormal movements

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  - Associated with other neurological signs
  - When dystonia involves the orofacial region
  - Brain MRI : bilateral lesions of the basal ganglia
  - Triggered by fasting and exercise

- **Some Metabolic Diseases as Movement Disorders Etiology**

Mineral storage disorder

- Always in form of mineral excess / acculumulation
- Most common : Iron, Cu, Mn

Iron

- Iron deposits especially in the globus pallidus and substantia nigra can cause hyperkinetic or hypokinetic movement disorders .
- It is known as neurodegeneration with brain iron accumulation (NBIA)

- There are some types, including: pantothenate kinase-associated neurodegeneration (PKAN) and phospholipase A2-associated neurodegeneration
- PKAN
  - ✓ caused by mutations in PANK2 gene
  - ✓ regulates coenzyme A production

  Coenzyme A is involved in fatty acid metabolism and dysfunction of this system causes increased oxidative stress in vulnerable areas, primarily the basal ganglia.

- Manganese
  - caused by mutations in SLC30A10
  - The gene product is a manganese transporter
  - Excessive manganese generate ROS causing neuronal injury
  - Hypermanganesemia with dystonia is characterized by gait and speech disturbances, dystonia, and central hypotone
  - Early recognition is important because therapeutic strategies are available with manganese-chelating agents or iron supplementation

- Copper
  - Disorder of copper metabolism is Wilson disease (hepatolenticular degeneration)
  - It should be suspected in individuals with liver disease presenting with any movement disorder
  - It is caused by mutations in the ATP7B gene
  - Result in abnormal copper excretion into plasma and bile and subsequent toxic accumulation of the metal
  - Reduced excretion of copper to bile results in accumulation in liver; kidney; eye; and brain, especially basal ganglia.

- Neurologic symptoms usually develop in the second or third decade
- Common symptom : dysarthria and hyperkinetic MD (dystonia, tremor, and choreoathetosis). An early sign is abnormal handwriting.
- The most common screening method : a 24-hour urine copper test, Kayser-Fleischer rings. Brain MRI shows "face of panda sign"
- Treatment : penicillamine, trientine, and zinc acetate. treatment of the movement disorders is inconsistent

- Causes a variety of movement and psychiatric problems e.g. chorea, dystonia, cerebellar syndromes and parkinsonism.
- Kayser-Fleischer rings are seen, and tests reveal low ceruloplasmin and high plasma and urinary copper.
- Treatable with copper chelating agents such as D-penicillamine.

Neurotransmitter synthesis disorder

- Defect of synthesis, metabolism and neurotransmitter transport (NT)
- Affect monoamine neurotransmitter, like excitation NT : serotonin and catecholamine (dopamine, epinephrine and norephinephrine) and inhibition (GABA dan Glysine)
- Affect monoamine neurotransmitter, can appear as combination of movement disorder, dystonia, epilepsy, cognitive impairment and motor delay

Guanosine triphosphate cyclohydrolase (GTPCH) deficiency

- A hereditary progressive dystonia with diurnal fluctuation.
- Segawa disease and autosomal dominant dopa-responsive dystonia.
- Symptom manifest in the first decade of life, but many cases may present in the adult years.
- Foot dystonia is the most common presenting symptom. Diurnal fluctuation with improvement after sleep is common

- Other symptoms, such as tremor, asymmetric limb dystonia, or spastic diplegia.
- There is significant improvement of symptoms with low-dose levodopa/carbidopa
- Hence a trial of levodopa is diagnostic.
- Often show a complete to near completemotor response to a combination of low-dose levodopa (4–5mg/kg/d) and a dopa decarboxylase inhibitor.

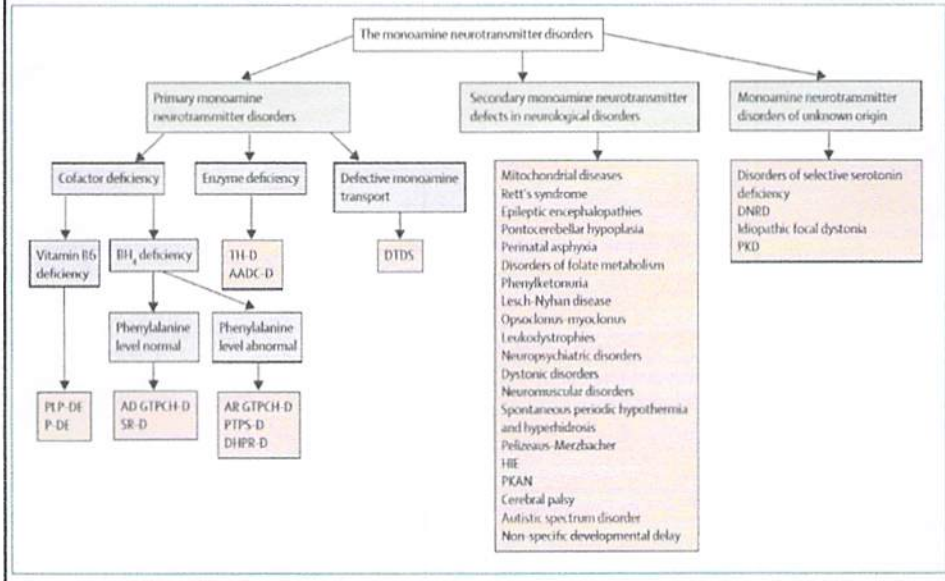

Figure 1: Classification of the monoamine neurotransmitter disorders

- Disorders of energetic metabolism and related diseases

- **Type of Movement Disorder caused by Metabolic Disease**
  - Can appear in various forms
  - Khouja (2010) : the most frequent forms are dystonia and myoclonus. Tic and hemiballism form are not found
  - Several form of movement disorder can occur together

Characteristic:

- Symptoms can not be explained by classic etiology
- Acute or sub-acute onset
- Other neurological or systemic symptoms
- Other neurological or systemic symptoms that appear in childhood

Pathomechanism

- Basal Ganglia has very active metabolism → require sufficient glucose and oxygen.
- Hypoxia, cerebrovascular disease, infection, trauma → lead to disorder

Conclusion

- We must be aware of movement disorders caused by metabolic diseases if :
- ✓ the forms of movement disorders that arise are combination of several forms
- ✓ can not be explained with classic etiology
- ✓ found other systemic symptoms
- Most of the symptoms occur in infant and childhood. Small number of the symptoms occur in adulthood.

THANK YOU