Tics, Myoclonus, Other Movement Disorders

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Gilles de la Tourette Syndrome

Pathophysiology

1. Developmental striatal dopaminergic hyperfunction (terminal hyperinnervation and receptor supersensitivity) - tics respond to antidopaminergics!
2. Monoaminergic dysregulation - obsessional-compulsive disorder (related to serotonergic neurochemistry) is present in 50% patients.

N.B. tics are not mediated through normal motor pathways used for willed movements!

Epidemiology

- relatively common neurological disorder (once considered rare* psychiatric condition) - PREVALENCE: 0.5-3% in childhood, 1% in adolescents, up to 1-3% in boys.
- because most children have mild and undiagnosed symptoms.

- boys >> girls (1.6:10 - 1:1)
- familial pattern of inheritance may be more complicated than previously was thought - boys >> girls (10:1 vs. 3:1) - no asymptomatic period of > 3 months - no specific morphologic changes in brain.

- mean age at onset is 6-7 years, 75% of patients have symptoms by age 11 years.
- tics may present suddenly, however, they usually become recognizable gradually or have intervening spontaneous remissions.

- most common presenting symptoms - simple tics:
  a) motor tics (> 30% facial tic, > 20% neck or shoulder tics) are more common in boys than in girls.
  b) vocal tic (28%) occurs as initial symptoms in only 12-37% of patients (generally noises rather than words).
- vocalizations may simply consist of motor tics that affect vocal apparatus.
- utterance of actual words is virtually pathognomonic of GTS but is very rare as presenting symptom.

- high risk population - children with special education needs (GTS prevalence here ≈ 12%).
- perinatal complications also increase risk.
- incidence of left-handedness or ambidexterity is greater than among normal persons.

Clinical Manifestations

- Multifocal motor > one or more vocal tics lasting > 1 year with no asymptomatic period of > 3 months.

Primary tic disorder - no specific morphologic changes in brain.

1) Gilles de la Tourette syndrome (GTS) - motor and vocal tics for > 1 year.
2) chronic tic disorder - motor or vocal tics (but not both) for > 1 year.
3) transient tic disorder (TTD) of childhood - motor or vocal tics with duration > 1 year - occurs in as many as 24% of school children.

Gilles de la Tourette Syndromes (N. Hyperspecifica)

Paroxysmal Dyskinesia

Painful Legs - Moving Torso Syndrome

Post-Traumatic Movement Disorders
if tics are suppressed voluntarily for time, period of intense tic follows (as if tics were reserved and then released at once)

sudden explosive episodes of uncontrollable rage have been reported in several patients.

most patients show marked improvement after adolescence:

30% - complete remission!! (complete life-long remissions are rare)
30% - no clinically significant tics
30% continue to be symptomatic throughout middle age.

Many patients develop BEHAVIORAL DISORDERS (may dominate clinical picture)

Problems with attention and learning!

1) obsessive-compulsive disorder (in 50% patients!): complex motor tics may be difficult to differentiate from compulsions!

- compulsions are associated with feeling of anxiety, tension, or other discomfort, which is relieved, at least temporarily, by performance of activity (alternatively such activity may be called 'compulsive tic')!

2) attention deficit hyperactivity disorder (in 50% patients!)

- impulsive and self-destructive behavior

- sleep abnormalities (parasomnias, bedwetting, interruption by tics)

- alterations in mood and sexual behavior.

Pure GTS - consists only of motor and vocal tics. Full-blown GTS - also includes coprophrenia, echophrenia, and paliphenia.

GTS plus syndromes - when patient also has ADHD or OCD.

DIAGNOSIS

Neurological observation + videotape taken at home + careful family history.

- to make DSM-IV diagnosis, tics must cause distress or social or functional impairment.

- other diagnostic studies are generally not required.

Neuropsychological testing - to identify patient's strengths and weaknesses - to allow patient to reach maximum academic potential.

TREATMENT

Majority do not require PHARMACOLOGICAL therapy!

- at some point many patients require short-term drug therapy (targeted to troublesome symptoms):

  a) neuroleptics (dopamine receptor blockers) (effective in 70-80% cases); many clinicians prefer PIMozide, FLUPHENAZINE and HALOPERIDOL; doses are tapered as tics wane; atypical antipsychotics also give good results.

  b) dopamine depleters (TETRABENAZINE).

  c) CLONIDINE (effective in 50%) - reduces noradrenergic activity in locus coeruleus.

  d) clonazepam, verapamil, nicotine, deprenyl (selegiline), botulinum toxin.

- PSYCHOTHERAPY mainly used for GTS associated with OCD.

- individual, group, or family counseling helps in facilitating healthy adaptation to illness.

SURGERY - last resort for severely disabled patients: bimedial thalamotomy, bilateral anterior cingulotomy, bilateral limbic leucotomy, coagulation of dorsomedial and intermediate lateral thalamic nuclei.

- DBS of thalamus (centromedian nucleus - substantia periventricularis - nucleus ventro-oralis internus crosspoint in thalamus) - significant beneficial effect? (but adverse effects on oculomotor function and reduced energy levels)

ESSENTIAL MYOCLONUS

- rare disorder (PREVALENCE unknown).

- hereditary (dominant inheritance with variable severity) or sporadic.

- unknown ETIOLOGY.

PATHOGENESIS

SUBCORTICAL origin: small lesions in brain stem / basal ganglia → deafferentation of ipsilateral frontal lobe and contralateral cerebellum.

- DIASCHISIS - sudden inhibition of function - acute focal brain disturbance at distance from original injury site, but anatomically connected with it through fiber tracts.

CLINICAL FEATURES

- onset in 1st decade.

- males = females.

- nonprogressive benign course.

- myoclonus jerks:
  - brief (50-200 msec)
  - may be generalized, multifocal, segmental, or unilateral.
  - mainly involve neck or upper body.
  - exacerbated by action (particularly writing or outstretching of arms).
  - abate during sleep.
  - dramatically ameliorated by alcohol (nearly diagnostic); following alcohol withdrawal, condition becomes worse on rebound.

- absence of other deficits (except dystonia in some patients).

DIAGNOSIS

- normal electrophysiological studies (EEG, somatosensory evoked potentials).

- normal neuroimaging.

- normal blood, cerebrospinal fluid, and tissue biopsies.

TREATMENT

1) benzodiazepines (particularly CLONIDINE) are most effective.

2) anticholinergics (BENZETHIONINE, TRIETHYPHENIDYL).
PALATAL MYOCOLNUS

a) idiopathic
b) dysfunctioning network connecting red nucleus-dentate nucleus-inferior olivary nucleus (triangle of Guilbaud and Mollaret) – dysgenia and hyperventilation degeneration of inferior olivary nucleus.

- continuous synchronous 0-10 Hz contractions of soft palate; persist during sleep.
- patients may notice only persistent ear clicks (repetitive contrasts of tensor veli palatini, which open eustachian tubes).
- generally persist throughout life with infrequent remissions.
- therapy is unnecessary in most patients; disorder is usually resistant to therapy:
  1) 5-HTP
  2) carbamazepine
  3) clonazepam
  4) tetrabenazine
  5) tiotixepinyd

MYOCLODYSTONIC SYNDROMES

- benign autosomal dominant disorder.
- onset in 1-2nd decade of life.
- DYSTONIA = MYOCOLNIC movements.
- no other neurological deficits.
- dramatic response to alcohol combined with benzodiazepines.

STARTLE SYNDROMES (s. HYPEREXPLEXIA)

- pathologically exaggerated normal startle reflexes, i.e. motor responses to unexpected stimuli (auditory, and at times somesthetic or visual):

  1. Hereditary hyperekplexia - autosomal dominant (chromosome 5q) mutations in n-1 subunit of inhibitory GABA 
     receptor.
    - continuous stiffness and flexor posture when infant is handled; disappear with sleep.
    - infants characteristically flex (rather than extend) their arms with Moro response.
    - increased tone gradually disappears during first several months of life, yet startle response can interfere with walking and may result in falls.
    - severely affected patients have startle attacks throughout life.
  3. Startle epilepsy - epileptic seizures triggered by sudden unexpected stimuli preceded by startle (most commonly due to perinatal anoxic encephalopathy).
  4. Culturally based, conditioned behaviors - “Jumping Frenchmen of Maine” (Quebec), "Jumping Sibirs" (Siberia), "Jumping Latah" (Indonesia, Malaysia), "Ragin' Cajun" (Louisiana) - violent startle followed by automatic speech (echolalia, echopraxia, coprolalia), aggressive gestures or defensive postures.
  5. Psychogenic startle (post-traumatic stress disorder, catatonic schizophrenics, newborns with in utero exposure to cocaine) – startle reaction is delayed (measured electrophysiologically).

TREATMENT

Drugs of Choice
1) BENZODIAZEPINES (esp. CLONAZEPAM)
2) GABA agonist (CINANEMI)
Other drugs - valproic acid, 5-HTP, piracetam.

PAROXYSMAL DYKINESIAS

- sudden onset of transient choreoathetosis, dystonia, or both.
- pathophysiologically - interface between movement disorders and epilepsy (EEG may reveal epileptic spikes and phase reversals).
- neurologic examination, neuroimaging, neuropathologic studies are normal.

1. Kinesigenic paroxysmal choreoathetosis (autosomal dominant or recessive) - brief movements (lasting < 3 minutes) induced by sudden voluntary movements (esp. arising from sitting position); occur up to 100 times a day.
   - unilateral or occasionally bilateral.
   - onset typically 8-14 yrs., tend to diminish during adulthood.
   - respond well to anticonvulsants (phenytoin, carbamazepine, phenobarbital).
2. Nonkinesigenic & evertional paroxysmal dyskinesias (autosomal dominant disorders) - more dystonic than choreic; more prolonged (lasting up to 4 hours) and less frequent (3-5 per day); precipitated by alcohol, coffee, fatigue, stress, excitement.
   - respond poorly to most medical therapy (some improve with clonazepam).

PAROXYSMAL MYOCLONUS

2.1. Other drugs

5. Drugs of choice

1. ENZODIAZEPINES
2. THERAPY
- movement disorder with sensory symptoms: writhing movements of toes + pain in legs**
  **continuous throughout waking hours.
  ** mildly irritating = excruciatingly severe.

N.B. pain does not have shooting / electric quality like radicular irritation.

N.B. movements are not response to pain!
- patient feels no relief in moving and instead tires from fruitless attempts to stop movement.
- usually with back pain in context of prior back injury / surgery; sometimes follows herpes zoster.
- posterior roots and ganglia has been suggested to explain syndrome.
- electrophysiological studies are normal.
- no effective treatment: sympathetic blockade, anticonvulsants.

** POST-TRAUMATIC MOVEMENT DISORDERS **

Etiopathophysiology:

a) direct injury to basal nuclei → early movement disorders.

b) sprouting, remyelination, ephaptic transmission, inflammatory changes, oxidative reactions, and central synaptic reorganization in basal nuclei → delayed movement disorders.

cause may be even mild TBI (even without loss of consciousness); incidence after severe TBI = 22% (50% transient, 50% persistent).

N.B. in many cases, TBI is not a cause (e.g. patient may not have noticed mild movement disorder that was present before injury).

movement disorders have been described after peripheral trauma; mechanism - altered sensory input, leading to central cortical & subcortical reorganization; frequently accompanied by reflex sympathetic dystrophy.

Examples: blepharospasm after eyelid surgery; oromandibular dystonia after dental procedures; spasmodic dysphonia after facial injuries; cervical dystonia after neck injuries such as whiplash; foot dystonia after stubbing toe; minor foot and ankle injuries → painful legs and moving toes

Clinically (all types of involuntary movements can occur!) – most common:

1. Parkinsonism (e.g. after repeated head injury as in boxers)
   TBI may result in temporary exacerbation of pre-existing Parkinson's disease

2. Dystonia

3. Low-frequency kinetic tremors


BIBLIOGRAPHY for ch. “Movement disorders, Ataxias” — follow this LINK >>