Characteristics of Parkinson's Disease in Patients with Childhood-onset Essential Tremor

Joohi Shahed, MD, Alan L. Diamond, MD, Kevin Dat Vuong, MA, and Joseph Jankovic, MD

Parkinson's Disease Center and Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, Houston, Texas

Abstract

OBJECTIVE: To determine the clinical characteristics of patients with Parkinson's disease (PD) and childhood-onset essential tremor (ET). **BACKGROUND:** It is not clear whether ET is a risk factor for developing PD. Diagnostic criteria for ET and PD are not validated. It is not clear what parkinsonian features are allowed in ET or how to diagnose ET in patients with PD. A close temporal association between the onset of ET and PD can cause diagnostic challenge and criticism of prior studies, as action tremor can be an initial PD symptom. Here we characterize patients with typical PD who also had childhood-onset ET. The childhood symptoms are an unlikely presentation of PD. **METHODS:** Patients seen at our Movement Disorders Clinic from 1/00-10/15/04 and diagnosed with PD and co-existent ET with onset before age 20 years were included. All patients had definite ET[1] and probable PD[2]. Age at onset, duration, and characteristics of ET/PD symptoms, and family history (FHx) of ET/PD were recorded. If possible, patients or family were contacted to verify information. **RESULTS:** Of 225 patients with co-existent ET and PD, 22 (77.3% male) met inclusion criteria. Clinical data was verified by interview in 14. In 10 of 22 subjects accurately recalling the onset, the mean age at onset of ET was 13.8 years (range 8–20). Most common ET symptoms were kinetic (86.4%), postural (72.7%), and head (45.5%) tremor. Tremor improved in 8/14 subjects with alcohol, 6/13 with beta-blockers, and 3/7 with primidone. Average age at PD onset was 59.5 years (range 43–85). Of 11 reporting asymmetric ET (73% on the right), PD began on the same side in 10 (χ^2=0.66, p=0.024). Average duration of PD symptoms at 1st evaluation was 3.9 years (range 0.13–23.3); 68.2% reported change in tremor as their 1st PD manifestation. PD was tremor-dominant in 18 (81.8%). 81.8% had a FHx of ET in 1st degree relatives, 13.6% of PD. **CONCLUSION:** This study confirms the presence of a population of PD pts with definite ET. The same side-predominance of ET and PD suggests the two are associated. Over 80% with ET-PD had tremor-dominant PD. Most subjects had a FHx of ET, suggesting a genetic predisposition to tremor. The progression and pathogenesis of the ET-PD syndrome require further study.

REFERENCES: [1]Mov Disord 1998;13 (suppl 3):55. [2]Arch

Introduction

- While essential tremor (ET) and Parkinson's disease (PD) often co-exist in the same individual or family, it is not yet established whether this association is merely co-incidental or whether ET is a risk factor for subsequent development of PD.
- There is no consensus on the degree of parkinsonism allowable in ET, or how ET is diagnosed in a patient with PD.
- Prior studies are difficult to interpret, since it is not clear whether action-postural tremor prior to the onset of other PD symptoms represents ET or early PD.
- Several clinical features suggest the presence of PD in patients with ET. [Table 1]

Objectives

- To determine the clinical characteristics of patients with PD and childhood-onset ET
- The presence of ET symptoms since childhood should eliminate the possibility that this tremor is an initial presentation of PD

Methods

- Charts of patients seen at the Baylor College of Medicine Movement Disorders Clinic between 1/00 and 10/04 were reviewed
- Inclusion criteria:
  - Diagnosed with definite ET [Deuschl et al, 1995] and probable PD [Gelb et al, 1999]
  - ET onset before age 20 years
- Age at onset, duration, and characteristics of ET/PD symptoms, and family history of ET/PD were recorded
- If possible, information was verified by a structured interview

Table 1. Features in ET Patients Suggesting Co-existent PD

Rigidity, bradykinesia, postural instability
New onset rest tremor in a patient with previous postural/action tremor
Tremor worsens with mental concentration
Re-emergent tremor with maintenance of posture
Jaw or lip tremor
Asymmetric postural tremor at onset or new asymmetry of symptoms

Table 2. Patient Characteristics (Total n=22)

	n	%	
Sex			
Male	17	77.3	
Female	5	22.7	
Handedness			
Right	20	90.9	
Left	2	9.1	
Family history in 1st degree relatives			
ET	18	81.8	
PD	3	13.6	
Age at symptom onset	**Mean (SD)**		**Range**
ET (n=10)*	13.8 (4.2)		8 – 20
PD (n=22)	59.5 (11.6)		43 – 85

*10 of 22 patients could report an exact age at onset of their childhood ET symptoms

Results

- 225 patients were diagnosed with co-existent ET and PD [Table 2]
  - 22 met inclusion criteria
  - 14 patients or their relatives were interviewed by telephone
- Characteristics of ET [Table 3]
  - 10 recalled with "reasonable certainty" an exact onset of ET
  - Mean age at onset: 13.8 years (range 8–20, SD 4.2)
  - Average duration of ET at the time of first evaluation in our clinic: 42.7 years (range 31.1–61.0, SD 9.7)
- Characteristics of PD [Table 4]
  - Average age at onset: 59.5 yrs (range 43-85; SD 11.6)
  - Mean latency from onset of ET: 39.7 yrs (range 29–60, SD 9.9)
  - Mean PD duration at initial evaluation: 3.9 yrs (range 0.1–23.3, SD 4.8)
  - 15 (68.2%) reported onset of rest tremor as their first PD manifestation
  - 18 (81.8%) had tremor-dominant PD
- 11 (50%) patients reported asymmetric childhood ET
  - Symptoms were more prominent on the right in 8 (72.7%)
  - PD symptoms began on the same side as their more prominent ET symptoms in 10 (χ^2=0.66, p=0.024)

Table 3. Characteristics of Essential Tremor (ET)

	n	%
Tremor (n=22)*		
Kinetic	19	86.4
Postural	16	72.7
Handwriting	15	68.2
Head	10	45.5
Rest	6	27.3
Voice	5	22.7
Medication Repsonse		
Alcohol (n=14)	8	57.1
Mysoline (n=7)	3	42.9
Beta blocker (n=13)	6	46.2

Table 4. Characteristics of Parkinson's disease (PD)

	n	%
Initial PD Symptom (n=21)*		
Rest tremor	15	71.4
Bradykinesia	4	19.0
Gait disturbance	2	9.5
Cardinal PD Features (n=22)		
Rest tremor	21	95.5
Bradykinesia	21	95.5
Rigidity	20	90.0
Gait Disturbance*	14	66.7
Postural Instability*	10	47.6
Medication Repsonse		
DA or LD (n=16)	15	83.8
LD-induced dyskinesias (n=15)	5	33.3
Anticholinergic (n=5)	1	20.0

*UPDRS data was not available on one patient
DA = dopamine agonist, LD = levodopa

Conclusions

This study provides evidence that some patients with ET later develop PD. The same side-predominance of ET and PD suggests the two are associated. Most subjects had a family history of ET, indicating a genetic predisposition to tremor. The co-occurrence of ET and PD could be explained by the relatively high prevalence of both disorders in the general population and their increasing incidence with advancing age [Findley, 2000; Strickland et al 2004] However, some patients with ET have an increased risk for development of PD.

A recent study [Chaudhuri et al, 2005] has suggested that asymmetric postural tremor predicts development of subsequent PD, but it is not clear if these patients had ET or PD at onset of tremor. Kindred with ET and PD in different family members have been described [Bertolli-Avella et al, 2003; Jankovic et al, 1997, Singleton et al, 2003; Yahr et al, 2003]. A single genetic mutation, interactions between genes and the environment, or the interaction of multiple genes could account for the phenotypic variability and clustering of ET and PD seen in such families [Bertolli-Avella et al, 2003; Yahr et al, 2003].

Functional neuroimaging studies [Brooks et al, 1992; Lee et al, 1999; Piccini et al, 1997] suggest that as ET progresses, nigrostriatal dysfunction may become more apparent and contribute to tremor genesis or that typical ET may confer a predisposition to parkinsonian neurodegeneration.

The progression and pathogenesis of the ET-PD syndrome require further study. The issues can be fully addressed only by prospectively following a large sample of ET patients

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Disclosures

None