Orthostatic Tremor – A Review of 40 Cases

Toby C. Yaltho, MD, Joseph Jankovic, MD, and William G. Ondo, MD
Baylor College of Medicine, Houston, Texas

OBJECTIVE

To evaluate the clinical characteristics, associated features, and treatment response of a large orthostatic tremor (OT) series seen over a 23-year period.

BACKGROUND

OT was described in 1984 by Heilman as tremor of the legs and trunk when standing, accompanied by unsteadiness or fear of falling, which is relieved by walking or leaning on nearby objects [1]. OT is a rare condition and its relationship to essential tremor and Parkinson's disease has not been clarified. The characteristic electrophysiological finding of a rapid (frequency 13-16 Hz) regular tremor suggests that despite some overlapping features, OT is a separate entity from essential tremor. The high frequency tremor results in partial fusion of the muscle contractions and may only cause a rippling of the muscle rather than a clinically observable tremor. The diagnosis of OT often relies on electromyography (EMG) recordings, but palpation, and auscultation with a stethoscope can demonstrate the high frequency tremor. Two large series involving 41 and 26 patients suggest that OT is associated with other movement disorders and neurological conditions [2,3].

METHODS

We reviewed the medical records of 40 patients seen at the Baylor College of Medicine Parkinson's Disease Center and Movement Disorders Clinic between 1987 and 2010 who fulfilled the diagnostic criteria for OT. All patients underwent a detailed neurological examination and were evaluated by a movement disorders specialist. Information about demographics, clinical features, and etiology was entered into a database and analyzed.

Table 1. Orthostatic tremor subgroups

	Primary OT (n=34)	OT plus (n=6)	All OT (n=40)
Sex	16F, 18M	3F, 3M	19F, 21M
Age at onset	60.5	57.6	60.1
Duration of symptoms	6.8	4.5	6.4
Postural hand tremor	25 (74%)	2 (33%)	27 (69%)
Family history of hand tremor	19 (56%)	2 (33%)	21 (53%)
Family history of orthostatic tremor	1	1	2
Response to treatment	0.9 (n=22)	1.8 (n=6)	1.1

RESULTS

The mean age at onset was 60.1 years (range 32-77 years) and 21/40 (53%) were men (Table 1). The mean duration of symptoms was 6.4 years. A family history of tremor was noted in 21/40 (53%) patients and 2/40 patients reported a family history of OT, although these relatives were not examined at our center. We found that 34/40 (85%) had idiopathic OT. In this subgroup 25/34(74%) had an additional arm tremor, usually low amplitude. In some cases postural arm tremor occurred only while standing and improved while walking. In our population 6/40 (15%) had OT plus additional neurological features including 1 with Parkinson's disease and restless legs syndrome, 2 with parkinsonism, 1 with ataxia, and 1 with hemifacial spasm (Table 2). One patient was diagnosed with dementia with Lewy bodies preceded by OT for 20 years. Follow-up data was available for 28/40 patients and averaged 53.3 months (range 1 to 196 months). Treatment response was modest and inconsistent, averaging 1.1 (0 = no improvement to 3 = complete resolution). In 9/28 (32%) of cases OT worsened over the follow-up period. Medications found to be most effective for treatment of OT included clonazepam, propranolol, gabapentin, pregabalin, primidone, carbidopa/levodopa, valproic acid, and phenobarbital. One patient had very good improvement with bilateral thalamic deep brain stimulation (DBS) surgery.

Table 2. OT Plus

Pt	Sex	Associated Neurological Disease	Age at Onset	Duration (years)	Hand Tremor
1	F	Dementia with Lewy Bodies	68	5	No
2	F	Essential tremor, Ataxia	55	10	Yes
3	F	Essential tremor, Parkinson's disease	51	5	Yes
4	M	Parkinson's disease, Restless legs syndrome	41	8	Yes
5	M	Hemifacial spasm	66	6	Yes
6	M	Parkinsonism	65	10	No

DISCUSSION

Gerschlager and colleagues described 41 patients with primary (idiopathic) OT (31/41) and OT plus (10/41) if additional neurologic features were present. The OT plus group consisted of patients with Parkinson's disease, vascular parkinsonism, drug-induced parkinsonism, orofacial dyskinesias, restless legs syndrome and periodic limb movements in sleep. OT has also been associated with progressive supranuclear palsy [4]. Piboolnurak and colleagues found additional neurologic signs in 4/26 patients with OT (peripheral neuropathy, poliomyelitis and blepharospam), but none of their patients had parkinsonism or cerebellar dysfunction.

DISCUSSION (cont'd)

The association of OT and parkinsonism and the occasional response to dopaminergics suggest that the dopaminergic system may be involved. In a previous study, presynaptic dopaminergic deficit was found in 9 of 11 patients with primary OT using I^{123}-FP-CIT single photon emission computed tomography (SPECT) [5]. However, this finding could not be confirmed in other studies [6]. Abnormal activation of a central tremor generator by a unilateral structural lesion may cause bilateral OT. There may be dysfunction of the cerebellum and PET studies have demonstrated increased blood flow to the cerebellum and the lentiform nuclei in patients with primary OT [7].

OT has been divided into two main types: (1) fast OT, characterized by 13 to 18 Hz bursts of muscle activity 1; and (2) slow OT, with 70 to 120 ms EMG bursts at frequencies <12 Hz. In addition to idiopathic cases, OT has been associated with Parkinson's disease and essential tremor[8]. OT has been also associated with multiple sclerosis, Graves disease, thiamine deficiency, monoclonal and biclonal gammopathy, and small cell cancer lung cancer with positive anti-Hu antibodies. Other unusual associations include delayed onset OT after head trauma, a nonenhancing structural lesion in the left dorsolateral midbrain, and lesions (schwannoma and tuberculoma) affecting the pontine structures. Many of these disorders, however, probably represent leg tremors other than the classic OT.

CONCLUSION

In our population of OT patients, there was a slight male preponderance and 69% had postural tremor phenomenologically similar to essential tremor. Over half of our patients had a family history of tremor, but a family history of OT was uncommon. Additional neurological features were seen in 15% of patients. Medications were generally unsatisfactory, although one case responded well to VIM DBS. Our series of 40 patients is of similar size as the largest series of OT reported in the literature and contributes to understanding the clinical characteristics of this rare disease.

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