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Clinical Features of Patients with Blepharospasm: A Report of 240 Cases

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Abstract

Background and Purpose—To characterize patients with benign essential blepharospasm (BEB) by diagnosis, environmental risk factors and family history.

Methods—240 patients with BEB were evaluated through a clinical examination and questionnaire. The questionnaire reviewed personal medical history, demographic factors, risk factors for the development of blepharospasm and family history of dystonia and other neurological conditions.

Results—BEB was more commonly found in females (2.8:1) and 93% of the patients were Caucasian. Fifty percent had pure BEB, 31% had BEB/Meige's syndrome, and 4% had BEB and eyelid opening apraxia (+/- Meige's syndrome). A minority of patients reported preceding photophobia (25%) or other eye conditions (22%). The majority were non-smokers, had no exposure to anti-emetic or antipsychotic agents, had a normal birth history and had no history of head trauma. Seventy-two percent did report a stressful event immediately prior to the development of symptoms. Treatments reported included botulinum toxin (BoNT), oral medications, surgical procedures and acupuncture. Thirty-two percent of patients reported a family history of focal dystonia and BEB was the most commonly reported.

Conclusion—This study confirms previous reports of usual age, sex, caffeine and tobacco use and family history in patients with blepharospasm. New findings include a report on occupation, lower reports of preceding eye conditions and photophobia, and higher reported stressful events. Further, this study shows a change in treatment with an increase in BoNT use and decrease in surgical procedures.

Introduction

BEB was recognized as early as the 16th century in a painting by Pieter Breughel, the Elder(1). Originally, BEB was deemed as psychogenic, but this was refuted by two physicians, J.W. Henderson(2) after observation of 21 cases in 1956 and then by C. David Marsden (1) after evaluation of 39 patients in 1976. Marsden concluded that BEB may be a focal representation of adult onset torsion dystonia secondary to dysfunction of the basal ganglia. Symptoms of BEB include involuntary closure of the eyelids that may develop into severe spasms rendering patients functionally blind(2). A support group, the Benign Essential Research Foundation (BEBRF) was founded in 1981 by a BEB patient, Mattie Lou Koster, to raise awareness and fund research for this disabling condition. In this study, we sought to characterize clinical features of patients with blepharospasm by general demographical information, environmental risk factors and family history of dystonia.

Materials and Methods

Two hundred and forty patients with BEB were recruited primarily in coordination with the BEBRF and examined in Alabama, Texas, Utah, Virginia, Maryland, Pennsylvania, Ohio, and South Carolina. The research protocol was reviewed and accepted by the National Institute of Aging (NIA) at the National Institutes of Health (NIH) prior to enrollment of any patients. In each instance written informed consent was provided by patients prior to participation in the study. Each patient was consented by a named investigator on the NIA

protocol. Each patient had a neurological examination by a movement disorder specialist, a blood sample drawn for genetic analysis and completed a questionnaire. The genetic results will be discussed in future papers. All patients had a full neurological exam to rule out other underlying neurological conditions. Specific criteria for diagnosis of blepharospasm included observation of involuntary bilateral increased blinking with intermittent eye spasms. Patients were also asked about photophobia, dry eyes and sensory tricks. If present, these symptoms were helpful to make the diagnosis, however, they were not deemed essential. Patients were also examined specifically for other focal dystonias. Three patients were excluded after the physical examination as two were thought to have psychogenic blepharospasm and one patient had suspected undiagnosed progressive supranuclear palsy with eyelid opening apraxia. The questionnaire was divided into three parts: general characteristics (gender, age, educational level, occupation), medical history (age of development of symptoms and age at diagnosis by a physician, stressful events, related eye conditions, sensory tricks, birth history, head trauma, other neurological or psychiatric diagnoses requiring treatment, anti-emetic or antipsychotic medications (Table 1), caffeine and tobacco use, current treatments), and family history of neurological conditions.

Results

General Characteristics

BEB was more common in females than males with a 2.8:1 ratio (177 females: 63 males). Ninety-three percent of patients were Caucasian, with <2% of African American, Native American, Asian, Multiracial, and Other represented. Ethnicity was 98% non-Hispanic and 2% Hispanic. The majority of patients (28%) completed high school, followed by 19% college/ bachelors degree, 18% masters degree, 17% associate degree (2 years of college), 7% doctorate degree, 6% other education, 3% trade school and 1% completed grade school only. The most common occupation was clerical work (28%), followed by teaching (21%), health care (15%), other (13%), manufacturing, metals (5%) and <5% of patients in each category of construction, manufacturing, accounting/finance, military, and engineering.

Medical History

For diagnosis, 50% of patients evaluated had BEB, 31% had BEB/Meige's syndrome (M) and 4% had a combination of BEB and eyelid opening apraxia (EOA) (+/- M). Meige's syndrome was defined by the authors as involuntary movements involving the lower face, throat and jaw. The remaining 15% had a combination of BEB and one or more focal dystonias (table 2). The median age of onset of symptoms noted by the patient was 50 years and nine patients reported having symptoms before the age of 24 years. The median age of diagnosis by a physician was 53 years and the earliest age of diagnosis was 26 years. Fifty-six percent of patients were diagnosed within the first year of symptoms, followed by 14% at 2 years, and 8% at 3 years. Eight percent of patients were diagnosed after having symptoms for 10+ years and one patient had symptoms for 38 years before a formal diagnosis was given. When asked about stressful events prior to development of symptoms, 28% reported none, 15% death of a parent, 14% moving, 11% problems at work, 8% divorce and 5.5% illness of a family member. Less than 5% of patients reported medical condition or surgery, relationship problems, other deaths, death of a child, death of a spouse, and separation from loved ones. Only 22% of patients reported having blepharitis, iritis, conjunctivitis or corneal disease prior to the development of BEB. Photophobia was only present in 25% of patients prior to the onset of symptoms; however, when asked about photophobia during the neurological exam, 74% of patients report this symptom. The majority of patients (87%) reported a sensory trick and most patients had more than one sensory trick. The most common trick was touching above the eyes, followed by singing, talking and humming (table 3). Thirty-two patients (13%) reported no sensory tricks.

Regarding birth history, the large majority of patients (75%) reported no problems with their birth history. Six percent of patients reported problems during labor and delivery, 4% of patients were born premature and 4% of the patient's mothers had problems during their pregnancy. Seventeen percent of patients reported a history of head trauma either with or without loss of consciousness at some time prior to the onset of symptoms. For other neurological or psychiatric conditions, 26% of patients reported depression, 14% reported anxiety and 4% had panic attacks. Other concurrent neurological conditions were uncommon. Three percent of patients had a history of a stroke and one patient each had Parkinson's disease, myotonia, brain tumor, and Sydenham's chorea (during childhood, now resolved). Patients were given a list of typical and atypical anti-psychotics and anti-emetic medications to review (Table 1). Twelve percent of patients reported taking an anti-psychotic medication and 19% reported taking an anti-emetic medication prior to the development of symptoms. When asked about tobacco (cigarette) use, 70% of patients never smoked cigarettes, 19% reported prior use of 100 or more cigarettes in their lifetime and 11% were current users. For caffeine, 72% of patients consumed caffeinated beverages regularly. Of these, 29% drink < or =1 cup per day, 32%, 1-2 cups per day, 21%, 2-3 cups per day and 18% more than 3 cups per day. For treatment, almost all patients (97%) were using some form of BoNT. All patients sampled were using Botox, except for one patient that was on Myobloc. Most patients, 73%, reported that symptoms improved with BoNT, but did not completely resolve. Ten percent of patients reported complete resolution between injections, 8% agreed with the statement that they developed resistance to BoNT and 3% reported no benefit. When asked if the movements have spread since the onset of injections, 15% of patients agreed with this statement. In our sample, 13% of patients reported having a myectomy procedure performed. In addition, other treatments included, 63% using artificial tears, 30% clonazepam, 15% diphenhydramine, 9% diazepam, and 8% trihexyphenidyl. Eight percent of patients also reported acupuncture as part of their treatment regimen.

Family History (Figure 1)

In our sample, 32% of patients reported having a family history of focal dystonia. Of these BEB was most commonly reported at 21% (16% were thought to occur in a first-degree relative and 5% in a second-degree relative), focal hand dystonia in 4%, spasmodic dysphonia in 3%, cervical dystonia in 2% and foot dystonia in 1%. One patient also reported a family history of generalized dystonia. Regarding other neurological conditions, 25% of patients reported a family history of tremor: 20% in first-degree relatives, 5% in second-degree relatives. The next most commonly reported condition was Parkinson's disease with 19% of patients reporting a family history (14% in first-degree relatives, 5% in second degree relatives). Dementia was the third most common at 4%. A family history of Huntington's disease, restless legs syndrome, and muscular dystrophy were reported each in one patient.

Discussion

The results above support previous findings in blepharospasm patients with the average age of onset in the 50's and a female predominance (3-6). About half of all patients were diagnosed within the first year of symptoms. The top three occupations were clerical work, teaching and health care and occupations have not been reported in previous studies. It is difficult to determine the significance of this without a control group. However, these occupations most likely reflect that of a middle to later age group of females where this was the most common occupation for women in the United States(7). Environmental factors of anti-emetic/antipsychotic exposure and history of head trauma are in line with previous studies and may pose a risk to development of symptoms(3) Possible mechanisms to explain head trauma resulting in dystonia include damage to the sensitive areas of the basal ganglia

or peripheral trauma inducing maladaptive reorganization of cortical and subcortical circuits of the brain(8). Caffeine use was high in our group sampled; however, it is unclear whether this had a possible protective effect (9) without additional information. In this study, 72% of patients reported one or more stressful events preceding the development of symptoms which is much higher than the 24% reported in a prior study of 250 patients(3). In our cohort the prevalence of photophobia (25%) and eye disease (22%) prior to symptoms was less than observed in prior reports where the estimates were 57% (4) and 50%, (6) respectively. When compared with previous studies, the majority of patients were utilizing BoNT as the primary treatment and overall having improvement in symptoms(10). In our sample 13% of patients reported having a myectomy procedure performed which is a large change from the 1984 study(3) where over one-third of patients had a surgical procedure performed for treatment. Further, the majority of the patients in 1984 had a facial nerve section which is uncommon today due to complications, a high recurrence rate(4), and the increased availability of treatments with a favorable benefit-risk profile. Acupuncture was reported in a relatively high number of patients for treatment, considering the only evidence available for this is a case report of five patients(11). Family history of focal dystonias in our sample was 32% which was similar to 27% reported by a more recent study by Defazio(12). Earlier reports had lower rates of familial focal dystonia reported, 7%(13) and 10%(14), respectively. In our study, this may be due to increased awareness of BEB and in other recent studies it is speculated to be higher due to direct examination of the family members. The majority of patients noted symptoms in a first degree relative which is consistent with the thought that BEB is an autosomal dominantly inherited condition with reduced penetrance(10). It is hypothesized that many, if not all, of the focal dystonias have a genetic background, with common etiologic factors contributing to phenotypic expression(15).

Limitations of the study include lack of a control group to assess the effect of environment and recall bias due to the questionnaire format. Further, the questionnaire was not validated. In future studies, the questionnaire should be more specific regarding the timing of exposure to environmental factors and development of symptoms. The majority of patients were recruited through the BEBRF representing a sampling bias and in most cases family members reported to have dystonia were not available for examination.

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Figure 1.
Family History of Neurological Conditions:

Table 1

Anti-emetic and antipsychotic list of medications

Anti-emetic medications	Compazine (prochlorperazine)
	Phenergan (promethazine)
	Reglan (metoclopramide)
	Zofran (ondansetron)
Antipsychotic medications	Haldol (haloperidol)
	Thorazine (chlorpromazine)
	Orap (pimozide)
	Stelazine (trifluoperazine)
	Mellaril (thioridazine)
	Moban (molindone)
	Seroquel (quetiapine)
	Trilafon (perphenazine)
	Navane (thiothixene)
	Prolixin (fluphenazine)
	Risperdal (risperidone)
	Clozaril (clozapine)
	Zyprexa (olanzapine)

Table 2

Patient Characteristics

Diagnosis	Number of Patients
BEB	121
BEB/M	75
BEB/M/CD	7
BEB/M/SD	7
BEB/CD	6
BEB/M/EOA	5
BEB/EOA	4
BEB/M/FHD	3
BEB/FHD	3
BEB/SD	2
BEB/CD/SD	2
BEB/M/CD/FHD	2
BEB/CD/EOA	1
BEB/M/CD/SD	1
BEB/M/CD/SD/FHD	1

Abbreviations: blepharospasm (BEB), Meige's (M), cervical dystonia (CD), spasmodic dysphonia (SD), eyelid opening apraxia (EOA), focal hand dystonia (FHD)

Table 3

Sensory Tricks

Sensory Trick	Number of patients
Touching above the eyes	72
Singing	63
Talking	60
Humming	50
Other	31
Touching face	26
Relaxing/breathing deeply	23
Concentrating/technical work	17
Touching other areas near symptoms	14
Opening eyes/mouth	12
Coughing	7
Tugging ears	6
Touching neck	6
Whistling	4
Touching arm	4
None	32