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Letters to the Editor

Cervical Dystonia in Twins

Wunderlich and colleagues[1] presented a pair of monozygotic male twins with cervical dystonia (CD) and then reviewed the literature on twins with dystonia in general. They indicated that there are only five sets of twins reported with dystonia, four of which have cervical dystonia. I have also seen a set of male twins with CD and would like to report on those here.

The twins are from a Caucasian, non-Jewish family of German descent. There is no history of consanguinity. The twins were reported by the mother to be identical, although we had no laboratory confirmation. They were born full-term after an uncomplicated delivery.

Twin 1 was seen at age 35 years (Fig. 1). He had onset of CD at the age of 18 years. The CD had an insidious onset with occurrence initially only while under emotional stress and it gradually progressed until stabilization at age 30 years. There was also a history of stuttering as a child. He had a history of learning disorder and poor school performance requiring special education through high school. He also had a past history of alcohol abuse, which stopped at age 30, and hepatitis. There was no history of head or neck injury or neuroleptic use and no history of remission. In addition to the abnormal postures, he had pain on the right side of his neck. His examination demonstrated rotational torticollis to the right of greater than 60 degrees with no retrocollis. He had mild laterocollis to the left with left shoulder elevation. Range of motion demonstrated diminished rotation to the left and diminished vertical movements. Hypertrophy was observed on the left sternocleidomastoid muscle and left trapezius muscle. The rest of his neurological exam was normal and a work-up for secondary forms of dystonia, including Wilson's disease, was negative.

Twin 2 was also seen at age 35 years (Fig. 2). His weight at birth was low (5 lb. 6 oz.). He had onset of CD at age 17 years after a minor neck injury. While cutting down a tree, a branch from the tree fell and hit him on the right side of the neck. His neck became stiff shortly after the injury and then gradually began turning to the right. It worsened over the years until it plateaued. In addition to the abnormal postures, he had pain on the left side of his neck and no history of remission. Tricks were initially helpful but later lost effectiveness. Like his brother, he also had stuttering as a child and was learning disabled with poor school performance. He had a history of alcohol abuse and was a 4 pack per day cigarette smoker. There is no history of neuroleptic use, but he also had a history of hepatitis. On examination, he had rotational torticollis to the right and retrocollis. There was mild left shoulder elevation. Hypertrophy was present in the left sternocleidomastoid muscle. His range of motion was full. He also had scoliosis and posturing of the left arm with writing. The rest of his neurological exam was unremarkable, and he, too, had a negative work-up for secondary forms of dystonia.

FIG. 1. Twin 1 with cervical dystonia.

Five other family members were examined. Two of them had CD. One of them was a 30-year-old younger brother who did not complain of neck problems but on examination had mild left shoulder elevation and a slight head tilt to the left. The other was a 64-year-old aunt (father's sister) who had onset at age 43 years. She had rotational torticollis to the right and intermittent retrocollis. At age 59, she had onset of spasmodic dysphonia as well. Three other members of the family who were not examined were reported by history to have CD. When possible, the history was confirmed from other family members. One was the father of the twins, who was deceased, but apparently had a history of retrocollis which began at middle age. The other two were daughters of the previously discussed aunt, both of whom were described as having abnormal neck postures.

This family was very similar to that described by Uitti and Maraganore.[2] Unfortunately, more detailed evaluation of this

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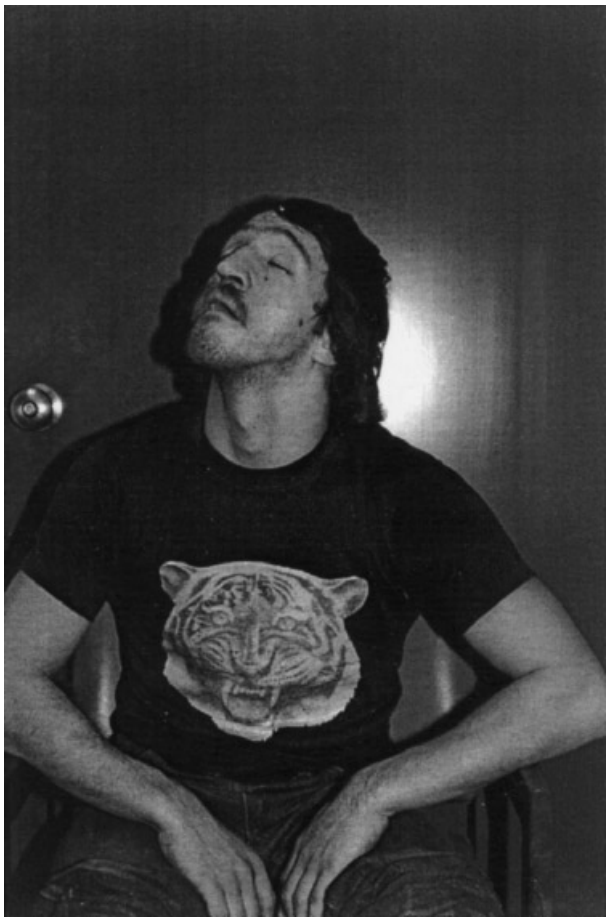

FIG. 2. Twin 2 with cervical dystonia.

family could not be performed as they were lost to follow-up. This represents a fifth set of twins with CD. They, too, had some minor phenotypic variation as described by Wunderlich and associates.[1]

In addition to this set of twins, we would like to bring to the attention of the readers the reports of two other twin pairs not included in the study by Wunderlich and coworkers.[1] Coleman and colleagues and Eldridge[3,4] reported an additional pair of women with onset of dystonia at age 14 and 15 years. Initial symptoms of both were dystonic posturing of the right hand when typing. The dystonia spread to include the right foot and then subsequently the left side after 5 to 6 years. The twin with earlier onset was more severely affected, and no other family members had dystonia. Another pair was reported by Lew and associates[5] in abstract form. They were non-Jewish women who varied greatly in age of onset. One had onset at age 6 years and eventually developed CD with involvement of all four extremities. Twin 2 had onset in the left foot at age 52 years and ended with prominent left foot dystonia and bilateral upper extremity posturing. There were no other affected family members.

These cases add to the list of twin pairs with cervical and other forms of dystonia. The German lineage in our twin pair and family is of interest because families with other forms of focal dystonia including CD have been of German descent as well. It is possible that our family could have their locus in chromosome 18p or chromosome 8. Unfortunately, at the time this family was seen, these two loci had not been reported and the family could not be examined in more detail. Similar families and twin studies should help provide further information on the genotype of CD.

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Survival Duration of Parkinson's Disease Patients Living in Greece Who Carry the G209A α-Synuclein Mutation

We read with great interest the article by Bostantjopoulou and colleagues[1] reporting the clinical phenotypes of 8 Greek parkinsonian patients carrying the G209A α-synuclein mutation. The data in this study confirm the clinical characteristics (younger age at onset and lower prevalence of tremor) described in our previous study[2] of 15 Parkinson's disease (PD) patients living in Greece who carried the α-synuclein mutation (α-synPD). However, the considerably short mean survival duration (6.3 ± 2.5 years from disease onset to death) of 6 deceased Greek α-synPD patients reported by Bostantjopoulou and associates[1] should be interpreted with caution. The number of reported cases is rather small, and our unpublished survival data on deceased Greek individuals with α-synPD may provide a more representative survival duration.

We identified 26 deceased individuals with Parkinson's disease belonging to 10 Greek families recently described by Papapetropoulos and coworkers.[2] To establish a diagnosis for these individuals, we examined medical records, and for individuals without records we accepted a physician's diagnosis of Parkinson's disease or relatives' convincing observations of cardinal signs (bradykinesia, rest tremor, and rigidity). The

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TABLE *The survival duration and age at disease onset for family members of all published Parkinson's disease patients carrying the G209A α-synuclein mutation, including our unpublished data*

Deceased α-synPD patients' family members	n	Mean age at onset, yr (±SD)	Mean survival time, yr (±SD)
Unpublished data	26	57.2 ± 10.3	10.4 ± 3.7
Bostantjopoulo et al.[1]	6	51.3 ± 14.3	6.3 ± 2.5
Combined data on the above cases	32	56.1 ± 1.2	9.7 ± 3.8
Golbe et al.[3]	39	—	9.2 ± 4.9
Markopoulou et al.[4]	11	58.2 ± 9.1	9.0 ± 3.5

α-synPD, Parkinson's disease with the G209A α-synuclein mutation.

historical data on the deceased individuals with Parkinson's disease concerning the date of disease onset and the time of death were obtained by either examining these individuals' medical records or interviewing their physicians or family members. To eliminate family information bias, we confirmed the information by interviewing as many relatives as possible.

The survival duration of our 26 deceased individuals was significantly longer than that described by Bostantjopoulou and colleagues[1] (Kruskal-Wallis test, $P = 0.018$; see Table). However, the mean survival duration for our group of patients combined with the 6 patients described by Bostanjopoulou and associates[1] was remarkably similar to that described by Golbe and coworkers[3] and Markopoulou and colleagues.[4] Furthermore, the mean age at disease onset for our group was not significantly different from that reported by Bostantjopoulou and associates[1] (Kruskal-Wallis test, $P = 0.11$).

The survival difference between the two independently studied groups of Greek deceased relatives of α-synPD patients may be explained by the small number of patients in the study of Bostantjopoulou and coworkers[1] as well as by the early death of 2 individuals due to causes unrelated to Parkinson's disease. It is unlikely to be explained by differences in disease phenotype, because symptoms and signs on examination of 8 and 15 α-synPD patients reported by Bostantjopoulou and colleagues[1] and Papapetropoulos and associates,[2] respectively, corresponded to the same clinical phenotype. Furthermore, patients in both groups lived in the same geographical area.

Historical data are particularly affected by information bias. It is of interest to note that the time from disease onset to examination of the 15 α-synPD individuals we previously described was 10.7 (± 6.1) years[2]; this exceeded the survival duration of our 26 deceased patients. Whether this was due to report bias or more effective treatments of possible concurrent illnesses, or both, is unclear. It is also difficult to explain why the duration of the disease was shorter compared with that of patients with sporadic PD[5] when no difference was found in disease severity, as measured by the Unified Parkinson's Disease Rating Scale, between α-synPD and matched sporadic PD patients.[1,2]

We are currently conducting long-term follow-up of living individuals with α-synPD from diagnosis to death, and also of healthy individuals known to carry the G209A α-synuclein mutation. Hopefully, what we observe during this follow-up will help to clarify the natural history of the disease.

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Hemiballism During Subthalamic Nucleus Lesioning

We read with great interest the report of unilateral ablative lesions of subthalamic nucleus reported by Barlas and colleagues.[1] Subthalamic nucleus (STN) is emerging as the preferred target site for surgical treatment of Parkinson's disease after encouraging results of deep brain stimulation surgery.[2,3] Encouraging findings after STN ablation have also been reported.[4–6] Lesions of STN have conventionally been the site of origin of hemiballism.[7] Therefore, experience of Barlas and associates[1] of absence of hemiballism in eight of nine patients undergoing subthalamic nucleus lesioning is an important observation. They support their observation from a similar experience in 1-methyl 4-phenyl 1,2,3,6-tetrahydropyridine (MPTP)-treated Parkinsonian monkeys undergoing STN lesion for which hemiballism/hemichorea was found to be mild and transient.[8]

We have performed unilateral STN lesions in 3 patients with advanced Parkinson's disease. We encountered transient hemiballism in all three patients after STN lesioning, contralateral to the side of lesion.[6] This hemiballism was of variable severity and duration in each patient. In two patients, it lasted for 2

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weeks and in the third patient, it lasted for 3 weeks. Hemiballism was disabling and severe enough to affect their activities of daily living on the affected side.

We also encountered hemiballism in 2 of 31 patients during macrostimulation, while performing STN stimulation surgery. The stimulation was performed by using a 1 × 0.75-mm electrode at 100 Hz frequency and up to 2 V, to avoid a microsubthalamotomy effect. The postoperative computed tomography scan did not reveal any haemorrhage in the STN area to account for this hemiballism. In both patients, the hemiballism persisted in the postoperative period for 6 months, although the corresponding STN was not being stimulated during this time. In all these patients, there was significant improvement in the motor scores of Unified Parkinson's Disease Rating Scale, once hemiballism settled, similar to that seen by other observers.[4,5,9]

Why did we encounter hemiballism during STN lesioning, whereas others have not? We think that the answer lies in the lesioning technique of STN. The size of the radiofrequency lesion is directly proportional to the size of the electrode, time, and lesioning temperature.[10] We use a very small electrode (0.75 × 1 mm) with a temperature of 70°C for 60 seconds, which produces a 1.5 × 2 -mm lesion. Barlas and coworkers use a larger electrode (1 × 3 mm) and higher temperature (73°C) for 60 seconds, producing a 2 × 4 -mm lesion. The larger lesion is, therefore, more likely to include the surrounding area of the STN: the area dorsal to STN, ansa lenticularis, or the pallidofugal fibers. Carpenter and colleagues[11] showed, in Parkinsonian monkeys, that it was necessary to destroy 20% of STN to induce choreiform movements, whereas if the lesion were large and involved neighboring structures, then these movements were not seen. This finding has also been supported by observations made by Lozano.[12] Our observation of hemiballism in two patients during macrostimulation, persisting in the postoperative period, also confirms that any damage to the STN, even in Parkinson's disease patients, can produce hemiballism. However, the resultant hemiballism is not long lasting. Therefore, we conclude that the hemiballism we saw in all our patients after unilateral lesioning was due to a smaller lesion confined to the STN.

This conclusion raises interesting questions for further exploration of the STN lesioning technique. Should we purposefully make a larger lesion to involve the surrounding areas, or should we confine our lesions to STN only? Which lesion would have a more permanent anti-Parkinson's disease effect? Do we need to use microelectrode techniques with multiple trajectories to find the center of the STN to confine our lesions within the boundaries of STN? These answers would assume more relevance given the theoretical possibilities of cognitive and behavioural deficit, which can follow bilateral lesioning of larger areas.

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