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Short communication

Does acute peripheral trauma contribute to idiopathic adult-onset dystonia?

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ABSTRACT

Background: Acute peripheral trauma is a controversial risk factor for idiopathic dystonia.
Materials and methods: We retrospectively analyzed data from the Italian Dystonia Registry regarding the occurrence of acute peripheral trauma severe enough to require medical attention in 1382 patients with adult-onset idiopathic dystonia and 200 patients with acquired adult-onset dystonia.
Results: Patients with idiopathic and acquired dystonia showed a similar burden of peripheral trauma in terms of the number of patients who experienced trauma (115/1382 vs. 12/200, p = 0.3) and the overall number of injuries (145 for the 1382 idiopathic patients and 14 for the 200 patients with secondary dystonia, p = 0.2). Most traumas occurred before the onset of idiopathic or secondary dystonia but only a minority of such injuries (14 in the idiopathic group, 2 in the acquired group, p = 0.6) affected the same body part as that affected by dystonia. In the idiopathic group, the elapsed time between trauma and dystonia onset was 8.1 ± 9.2 years; only six of the 145 traumas (4.1%) experienced by 5/1382 idiopathic patients (0.36%) occurred one year or less before dystonia onset; in the acquired dystonia group, the two patients experienced prior trauma to the dystonic body part 5 and 6 years before dystonia development.
Discussion and conclusion: Our data suggest that the contribution of peripheral acute trauma to idiopathic dystonia is negligible, if anything, and likely involves only a small subset of patients.

1. Introduction

Although head trauma associated with brain lesions is a well-recognized cause of acquired dystonia [1], it is still unclear whether acute trauma to a specific body part is a risk factor for topographically-related focal dystonia. The few controlled studies addressing this issue provided inconsistent results. An earlier study found a significant association between neck/trunk trauma and cervical dystonia (CD) [2], whereas a later ad-hoc study did not find any association between vault/maxillofacial trauma and cranial dystonia (CRDYT) [3]. A third study detected a nonsignificant trend towards an association between upper limb trauma and upper limb dystonia (ULD) [4]. Recently, a large retrospective cohort study reported an association between peripheral trauma and dystonia [5].

To understand whether trauma to a specific body part contributes to dystonia in the same body part has relevant implications. We here present data from the Italian Dystonia Registry (IDR) [6] in patients with adult-onset idiopathic dystonia and acquired dystonia due to CNS damage, according with the most recent classification scheme [1].

2. Methods

The IDR [6] collected information on several demographic/clinical factors of patients with idiopathic and acquired late-onset dystonia diagnosed and classified according with recent criteria [1]. Lifetime trauma outside the central nervous system that was severe enough to require medical evaluation/hospitalization/surgery was recorded and information was collected on the year/site of trauma and sequelae (contusions, wounds, fractures, dislocations/subluxations, and sprains) [6]. History was supported by medical records and/or informed relatives.

Data were analyzed by Stata 11 (StataCorp, College Station, Texas)

Table 1
Report of traumatic injuries to different body parts in patients with adult-onset idiopathic and secondary dystonia.

	All body parts	Upper limb	Lower limb	Neck/trunk
Idiopathic dystonia group				
Injuries (n)	145	60	60	25
Injuries occurring before dystonia onset	90	38	36	16
Injuries occurring before dystonia onset that affected the dystonic body part	14	5	0	9
Injuries occurring ≤1 yr before dystonia onset that affected the dystonic body part	6[a]	1	0	5
Acquired dystonia group				
Injuries (n)	14	4	6	4
Injuries occurring before dystonia onset	5	2	3	0
Injuries occurring before dystonia onset that affected the dystonic body part	2	1	1	0
Injuries occurring ≤1 yr before dystonia onset that affected the dystonic body part	0	0	0	0

[a] Six injuries from five patients (one patient reported two neck injuries).

and expressed as mean ± standard deviation unless otherwise indicated. Differences between groups were examined by the chi-square test, Fisher's exact test, or Mann-Whitney *U* test as appropriate. The study power for case-control studies with an unequal case-control ratio was calculated assuming threefold modification in the risk of developing dystonia with alpha = 0.05 (two-sided).

3. Results

On April 2019, the IDR included 1382 idiopathic adult-onset dystonia patients and 200 patients with acquired adult-onset dystonia secondary to parkinsonism (n = 120), neuroleptic drugs (n = 55), basal ganglia/brainstem lesions due to cerebrovascular disease (n = 15), tumors (n = 2), and severe head trauma (n = 8). Idiopathic and acquired dystonia groups were similar for age (64.7 ± 12.3 vs. 64.7 ± 11.7 years, p = 0.9) and years of education (9.6 ± 2.1 vs. 9.1 ± 1.9 years, p = 0.7) but differed for sex (912 women/470 men vs. 110 women/90 men, p = 0.002), age at dystonia onset (53.1 ± 10.9 vs. 58.6 ± 11.7 years, p < 0.0001), and focal vs. segmental/multifocal dystonia distribution (1035/347 vs. 133/67, p = 0.01). In the idiopathic group, 49% of patients had CD, 51% had CRDYT, 66% had ULD, and 2% had lower limb dystonia (LLD); in the acquired group, 44% of patients had CD, 32% had CRDYT, 24% had ULD, and 21% had LLD (p < 0.0001).

Acute peripheral injury was reported by 115/1382 (8.3%) idiopathic patients and 12/200 (6.5%) with acquired dystonia (p = 0.3). Thirty idiopathic patients and two patients with acquired dystonia reported two injuries. The number of acute peripheral injuries was therefore 145 for the 1382 idiopathic patients and 14 for the 200 patients with acquired dystonia (p = 0.2).

In the idiopathic group (Table 1), 90/145 injuries (65%) occurred 9.7 ± 3.4 years prior to dystonia onset. Among the 90 injuries, 14 (from 13/1382 patients, 0.9%) affected the same body part that then developed dystonia (time elapsing between trauma and dystonia, 8.1 ± 9.2 years) but only 6/14 injuries (from 5/1382 patients, 0.36%) occurred 5–12 months prior to dystonia onset. In the acquired dystonia group (Table 1), 5/14 injuries (57%) occurred 10.9 ± 4.4 years prior to dystonia onset. Among the five injuries prior to dystonia onset, two affected the dystonic body part (time elapsing between trauma and dystonia, 5 and 6 years) but none occurred one year or less before dystonia onset. There was a nonsignificant trend toward a greater frequency of prior injury in idiopathic than in acquired dystonia group (90/145 vs. 5/14, p = 0.055). However, there was no significant difference in the frequency of prior trauma to the body part affected by dystonia (14/145 vs. 2/14, p = 0.6), even when the trauma occurred one year or less prior to dystonia onset (6/145 vs. 0/14, p = 0.4). The study had an estimated 100% chance of detecting threefold modifications in the risk of dystonia, with alpha = 0.001 (two-sided) for prior trauma to the body part affected by dystonia.

Among the 13 idiopathic patients who experienced prior acute trauma to the dystonic body part, no patient had fixed dystonia, women were predominately affected, age at dystonia onset was in the third to sixth decade, and sensory trick and family history of dystonia were present in 54% and 30% of patients respectively (Table 2).

4. Discussion

Although patients with idiopathic and acquired dystonia had a similar burden of lifetime acute peripheral trauma, there was a nonsignificant greater frequency of prior trauma in idiopathic than in acquired dystonia patients. Focusing on prior trauma affecting the same body part as that affected by dystonia, however, yielded a similar percentage (about 1%) of patients in both groups, regardless of the time elapsing between trauma and dystonia onset. Likewise, there was no difference between idiopathic and acquired dystonia groups in the frequency of trauma (0.36% vs 0%) experienced within the temporal criterion of 1 year proposed by Jankovic [7] to support an etiological

Table 2
Demographic and clinical features of the patients developing idiopathic adult-onset dystonia after peripheral trauma to the same body part.

Patient	Gender	Site of peripheral injury (age at injury, yrs)	Time elapsing between trauma and dystonia onset	Age at dystonia onset (yrs)	Dystonia at onset	Spread to (time to spread)	Sensory trick	Dystonic tremor	Family history of dystonia
1	Male	Upper limb, 25	1 year	26	Cervical dystonia	Upper limb (3 mos), larynx (2 yrs)	Yes	Yes	No
2	Female	Neck, 57	1 year	58	Cervical dystonia	Upper limb (3 yrs)	Yes	Yes	Mother/sister with cervical dystonia
3	Female	Neck, 43	5 months	43	Cervical dystonia	None	Yes	No	No
4	Female	Neck, 43	1 year	44	Cervical dystonia	None	No	No	No
5	Male	Neck, 53	1 year	54	Cervical dystonia	None	Yes	No	No
6	Male	Neck, 42	21 years	63	Cervical dystonia	None	Yes	Yes	No
7	Male	Upper limb, 50	4 years	54	Upper limb dystonia	Neck (2 yrs)	Yes	No	Sister with blepharospasm
8	Female	Neck, 63	2 years	65	Cervical dystonia	No	No	Yes	Brother with cervical dystonia
9	Female	Upper limb, 18	14 years	32	Upper limb dystonia	None	Yes	Yes	No
10	Male	Neck, 21	10 years	31	Cervical dystonia	Upper limb (5 yrs)	Yes	No	Grandfather with upper limb dystonia
11	Female	Neck, 42	3 years	45	Cervical dystonia	None	No	No	No
12	Female	Neck, 16	21 years	37	Cervical dystonia	None	Yes	Yes	No
13	Female	Neck, 18	26 years	44	Cervical dystonia	None	No	Yes	No

relationship between trauma and dystonia in a body part. Of note, this was an arbitrary criterium chosen in the absence of any pathophysiologic basis that has not led to wide acceptance [8].

Previous studies reported peripheral trauma in 1–25% of patients with CD or oromandibular dystonia [9–12]. Studies characterized by higher frequencies of posttraumatic dystonia (9–25%) were based on a limited number of patients (95–166) [10–12], raising the possibility of a chance-associated cluster of posttraumatic cases. In contrast, a study with 892 patients reported a lower frequency estimate (1%) that was closer to our own estimate (0.9%) [9]. At variance with our patients who developed dystonia 4.7 years after trauma in that body part on average, patients from previous series developed dystonia within a few days to weeks after trauma [8–11], that was characterized by fixed dystonia, absence of sensory tricks, poor response to botulinum toxin, and frequent association with complex regional pain syndrome. All these features suggest that at least a proportion of these patients might have had functional dystonia [8], whereas our patients who had prior trauma to the dystonic body part (including those who experienced trauma within one year of dystonia onset) all had clinical features typical of idiopathic dystonia [1].

Most prior controlled studies exploring the association between acute peripheral trauma and dystonia probably suffered from methodological bias. Two studies assessed a large number of variables and were therefore liable to false positive results [2,4]. A recent retrospective cohort study using a population insurance database reported an independent association between peripheral trauma and dystonia [5]. However, investigators could not ascertain the type and etiology of dystonia, nor the sites of trauma and dystonia. We also observed a trend towards a greater frequency of prior trauma in idiopathic patients ($p = 0.055$), regardless of the trauma or dystonia site. However, this difference between groups disappeared when the anatomical correlation between injury and dystonia was considered.

Our study was potentially susceptible to biases inherent in retrospective studies. However, a bias in case selection was unlikely because demographic/clinical features of our population were consistent with those typically observed in adult-onset dystonia [1]. We did not assess trauma in healthy controls but, taking into account that this is a service-based study, it may be appropriate to compare case and control populations from the same setting [2,3]. In this regard, a suitable disease control group should be affected by conditions unrelated to trauma but resembling idiopathic dystonia, even for the degree of medical surveillance required [2,3]. We did not compare trauma frequency in our population and in the Italian population because available population data (https://www.eurosafe.eu.com/key-actions/injury-data/reports) did not allow us to adjust for specificities in age range and posttraumatic sequelae in our population. The greater frequency of men and the higher age at dystonia onset in patients with acquired dystonia were factors which may have favored a greater frequency of trauma in that group, but in actuality this was not the case. The similar age and education level between idiopathic and acquired patients minimized the risk of differential recall. Most reported traumas occurred long before dystonia onset, which also reduced the risk of recall bias. The retrospective assessment prevented us from rating the severity of trauma, but we focused on trauma severe enough to require medical attention and cause local symptoms. Finally, patients were not screened for genes that may predispose to dystonia [1] and may indirectly increase vulnerability to traumas.

Despite these limitations, our data indicated that the contribution of peripheral acute trauma to the pathophysiology of idiopathic dystonia is negligible and may only involve a small subset of patients. This study was controlled, well powered, and representative of idiopathic adult-onset dystonia. These features support the validity of our conclusions that argue against a significant contribution of peripheral acute trauma to topographically-related idiopathic dystonia. A longitudinal study of patients with compressive nerve injuries to estimate the number of individuals with newly developed dystonia would be of help to definitely assess the topic.

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