The natural history and treatment of acquired hemidystonia: report of 33 cases and review of the literature

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Objective: To evaluate the natural history and response to treatment in hemidystonia.

Methods: 190 Cases of hemidystonia were identified; 33 patients in this series and 157 from the world literature. Data was collected on aetiology, age of onset, latency, lesion location, and response to treatment.

Results: The most common aetiologies of hemidystonia were stroke, trauma, and perinatal injury. Mean age of onset was 20 years in this series and 25.7 years in the literature. The average latency from insult to dystonia was 4.1 years in this series and 2.8 years in the literature, with the longest latencies occurring after perinatal injury. Basal ganglia lesions were identified in 48% of cases in this series and 60% of the cases in the literature, most commonly involving the putamen. Patients experienced benefit from medical therapy in only 26% of medication trials in this series and in only 35% of trials in the literature. In the patients reported here, the benzodiazepines clonazepam and diazepam were the most effective medications with 50% of trials resulting in at least some benefit. In the literature, anticholinergic drugs were most effective with 41% of trials resulting in benefit. Surgery was successful in five of six cases in this series and in 22 of 23 cases in the literature. However, in 12 cases, results were transient.

Conclusions: The most common cause of hemidystonia is stroke, with the lesion most commonly involving the basal ganglia. Hemidystonia responds poorly to most medical therapies, but some patients may benefit from treatment with benzodiazepines or anticholinergic drugs. Surgical therapy may be successful but benefit is often transient.

Hemidystonia refers to dystonia which involves the ipsilateral face, arm, and leg. In most cases, a contralateral structural lesion of the basal ganglia or thalamus can be demonstrated by neuroimaging. Common aetiologies include stroke and trauma, and younger patients seem to have a greater propensity to develop hemidystonia after cerebral insults.^{1–3} There is often a latency between cerebral injury and the onset of dystonia. Hemidystonia may be preceded by ipsilateral hemiparesis which often resolves as hemidystonia develops. Some authors have suggested that symptomatic hemidystonia requires preservation of the corticospinal tract,⁴ and may occur as a result of aberrant reorganisation of the motor system after a static lesion.⁵

Both the natural history and response to treatment of symptomatic hemidystonia have not been extensively studied. As hemidystonia usually follows a single cerebral insult, symptoms might be expected to be relatively static. Hemidystonia has been regarded as poorly responsive to medical therapy,⁶ and surgery has been considered an effective treatment option for such patients.⁷ We evaluated our experience with 33 patients with hemidystonia, and compared our results with 157 cases of hemidystonia previously reported in the literature. Our primary aim was to determine the most effective strategy for treating patients with hemidystonia.

METHODS

We reviewed the medical records of 33 patients with hemidystonia evaluated at the Movement Disorders Center of Columbia-Presbyterian Medical Center between 1974 and 1999. Age of symptom onset, type of cerebral injury, latency to onset of dystonia, distribution and severity of dystonia, associated symptoms, lesion site (determined by neuroimaging), and response to treatment (medications, botulinum

toxin injections, and surgery) were recorded. The distribution and severity of dystonia were determined from physical examination and the Burke-Fahn-Marsden dystonia rating scale.⁸ The effectiveness of medications was determined by the response rate—that is, the percentage of medication trials resulting in any beneficial response as reported by the patient. Follow up of 16 patients (48%) by telephone interview included a brief assessment of functional disability.

A Medline search of the world literature revealed 158 cases of hemidystonia reported since 1966. (Case No 15 in our series was previously reported in Burke *et al.*⁵) Data on aetiology, age of symptom onset, latency, results of neuroimaging, and treatment response were collected and compared with our patient series.

RESULTS

Clinical features

In our patients (n=33), aetiologies of hemidystonia included stroke (10 patients), perinatal injury (nine patients), trauma (eight patients), infection (three patients), congenital lesions (two patients), and tumour (one patient) (table 1). The mean age of dystonia onset was 20 years (range 1–69), and the mean duration of dystonia at last follow up was 15.6 years (range 1–58). In 70% of patients, symptoms began in childhood or adolescence. Of the 29 patients with a latent period between cerebral insult and onset of dystonia, the mean latency was 4.1 years (range 2 weeks to 17 years), with the shortest latencies occurring in patients after stroke, usually less than 1 year) and the longest latencies occurring after perinatal injury (table 2).

Onset of dystonia was more common in the arm (48.5%) than the leg (21.2%), and involved the arm and leg simultaneously in 36.4%. The time for dystonia to spread to the

Table 1 Patient clinical data (n=33)

Case/sex/age of onset	History	Latency	Site of dystonia onset	Spread (time period)	Imaging	Associated signs
1/F/52	R thalamic bleed post-thalamotomy for torticollis	4–6 months	L hand/foot	None	R thalamic haematoma	L HP, hemisensory loss pain, cramps
2/F/6	Normal development, stroke at age 6, angiogram/brain biopsy normal	None	R arm	R leg (23 years later)	L frontal/basal ganglia	R HP, aphasia
3/M/70	Stroke at age 70	3 months	L hand/foot	None	R thalamic infarct	L HP, pain
4/F/66	Stroke, L HP for 1 day	8–9 months	L arm	L foot/jaw/pharynx (1 y)	R MCA infarct	L HP, pain, contracture
5/F/2	Stroke at age 2, L HP improved in 5–6 h	Several weeks	L hand	L leg (soon after)	R basal ganglia (putamen/caudate)	L HP
6/M/61	L basal ganglia bleed	None	R hand	R arm/foot	L basal ganglia haemorrhage	R HP
7/M/56	2nd stroke with L HP	5 months	L arm	L foot (N/A)	R parieto-occipital infarct	L HP/hemisensory loss
8/F/27	TIA with L HP (age 24) normal LP, angiogram, imaging. 3 years later, had MVA	3 y	L foot	L hand (soon after)	scan N/A	
9/M/59	L thalamic/basal ganglia haemorrhage	6 months	R arm/foot	None	L thalamic/basal ganglia haemorrhage	R HP, aphasia, dysaesthesia
10/M/6	L HP at age 5, Dx R midbrain tumour extending to thalamus, underwent XRT/shunt	9 months	R leg	R arm/torso (6 months)	L putamen infarct	Pain
11/F/39	MVA with head trauma, age 38	1 y	L hand	L leg (3 years later)	R putamen/parietal insular, ant temp. encephalomalacia	L HP, hemisensory loss, cognitive dysfunction, depression
12/M/13	Fishing pole impaled eye, coma for 2 weeks	4 months	R arm/foot	None	L haematoma	R HP, aphasia
13/F/5	Head trauma without LOC, R parietal laceration	1 month	R arm	R foot (6 months later)	N/A	R HP
14/F/8	Fell off bicycle, head trauma without LOC	3 months	R arm/neck	R foot	L basal ganglia infarct	None
15/F/9	MVA with depressed skull fracture, age 2; coma for 10 days	6 y	R arm/leg	None	N/A	R HP
16/M/11	Fell off horse, head trauma, 3 days later R HP/sensory loss, no LOC, recovery in 2 weeks	2 weeks	R arm/leg	None	N/A	R HP, R HH, hemisensory loss
17/F/23	Fell down stairs, hit right side of head, no LOC	8 months–1 y	L hand	L foot/arm/leg (several years)	Thalamotomy lesion	Increased tone
18/F/24	Fell off horse with mild head injury	10 y	R finger	R arm/leg/voice (1 y later)	L midbrain	Dysarthria
19/F/9	Born at 28 weeks, C-S Apgars 0 and 1, intubated, NICU 2½ months, global delay	9 y	L foot	L wrist/arm, R arm (9 y)	Dandy-Walker (cerebellar/pons hypoplasia) global cerebral atrophy	Cognitive self mutilation behaviour
20/M/1	Forceps delivery, Apgars normal, pneumonia in pregnancy	1 y	L leg	L arm (soon after)	N/A	Shoulder pain
21/M/8	PROM at 5 months, forceps delivery at 6 months, NICU 2½ months, seizures	8 y	L hand	L leg	Deep WM of R temporal lobe superior to putamen	None
22/M/13	Neonatal asphyxia, intubated, seizures, incoordination as a child	13 y	L arm	L foot (7 years later)	FDG-PET: increase in BG (R>L)/motor cortex/ post paracentral region; decrease in thalamus	Tremor
23/M/10	Profuse bleeding at delivery, age 1:R focal seizure and R spastic hemiparesis	10 y	R arm/leg	None	CT: focal atrophy adjacent to frontal horns (L>R) c/w cystic encephalomalacia	R HP, dysarthria, learning disorder
24/F/17	Prolonged labour, delayed motor milestones	17 y	R hand/face	None	L cerebral atrophy	R HP (face/arm), dysarthria
25/M/7	Meconium at delivery, global delay, autism, ADHD, metabolic w/u negative, DYT-1 negative	7 y	L hand/foot	L leg/arm	MRI normal	None
26/F/8	Jaundice (Rh+), normal development, normal ceruloplasmin, slit lamp	8 y	L foot	L hand (10 years later)	CT: R paraventricular lucency	None
27/M/15	Premature at 28 weeks, identical twin had IVH, normal development	15 y	R hand/foot	R arm/leg (3 mos. later)	L basal ganglia	R HP, spasticity
28/M/6	TB meningitis (age 5), recovery in 4 months	9 months	R arm	R leg (9 mos. later)	L basal ganglia, porencephalic cyst	R HP, ADHD, MR
29/F/2	Encephalitis (age 2), residual R HP, resolved	9 months	R hand/foot	R thumb (22 years later)	No imaging	R HP, hemisensory loss
30/F/5	Varicella (age 5), metabolic evaluation negative EBV, strep titres negative brain biopsy c/w with Rasmussen's encephalitis CSF PCR positive for rubella	1 month	L leg	L arm (2 months later)	R caudate/putamen/cortical atrophy, FDG PET: Marked reduction in R lateral frontal/parietal/BG/thalamus	partial seizures, behavioural changes
31/F/5 mos.	Normal pregnancy, birth trauma motor delay, used a brace, R focal seizure at 18 months, EEG: L temporal focus	5 months	R hand	R arm/leg (18 mos. later)	Hemiatrophy of L hemisphere/hemicranium porencephalic cyst (Dyke-Davidoff Mason syndrome)	R HP, seizures
32/F/16	Age 16: episodes of lightheadedness, headaches, L hemisensory loss, HP	Unknown	L hand	L foot/arm/trunk (12 years later)	R thalamic AVM	L HP, hemisensory loss
33/F/8	Age 8: abnormal movements of R arm/leg, Dx: thalamic tumour, Rx with cobalt XRT	None	R arm/leg	Face	L thalamus	Spasms

HP, Hemiparesis; BG, basal ganglia; AVM, arteriovenous malformation; ADHD, attention deficit hyperactivity disorder; c/w, consistent with; Dx, diagnosis; EBV, Epstein-Barr virus; L, left; MVA, motor vehicle accident; N/A, not available; NICU, neurointensive care unit; PROM, premature rupture of membranes; PCR, polymerase chain reaction, R, right; Rx, treatment; TB, tuberculous; TIA, transient ischaemic attack; WM, white matter; XRT, radiation therapy.

Table 2 Summary of clinical characteristics (n=33)

	Age of onset (mean)	Latency (mean)	Site of onset (% of cases)	Lesion site (% of cases)
Poststroke (n=10)	2–69 y (40.5)	3 months–3 y (9.5 months)	Arms: 5/10 (50) Legs: 2/10 (20) Both: 3/10 (30)	5 basal ganglia (55) 3 thalamus (33) 3 cortical (33)
Post-trauma (n=8)	5–39 y (16.4 y)	2 weeks–10 y (27.5 months)	Arms: 5/8 (62.5) Both: 3/8 (37.5)	2 basal ganglia (50) 1 cortical (25) 1 subcortical 1 midbrain (25)
Perinatal (n=9)	1–17 y (9.7 y)	1–17 y (9.7 y)	Arms: 3/9 (33) Legs: 3/9 (33) Both: 3/9 (11)	3 basal ganglia (42) 1 thalamus (14.3) 2 cortical (28) 1 cerebellum/pons (14.3)
Miscellaneous (n=6)	5 months–16 y (6.3 y)	1–9 months (4.5 months)	Arms: 3/6 (50) Legs: 1/6 (16.6) Both: 2/6 (33)	2 basal ganglia (40) 3 thalamus (60) 2 cortical (40)

unaffected limb ranged from 2 months to 23 years (mean 6 years). Severity of dystonia was greater in the arm than the leg in 54.5% of patients, and only 9% had greater leg than arm involvement. Nineteen patients (57%) had an associated hemiparesis which resolved or significantly improved before the onset of dystonia. Eighteen per cent of patients also had preceding hemisensory loss.

Results of neuroimaging were available in 26 patients, and one or more lesions could be identified in 25 cases. Twelve lesions were located in the contralateral basal ganglia (48%), most commonly in the putamen. Thalamic (28%) and cortical (32%) lesions were also seen, and one lesion was in the contralateral midbrain. The thalamic lesions were most commonly haemorrhages and not specifically delineated as being anterior or posterior in location. Cortical lesions were also non-specific and were located in frontal, parietal-occipital, or temporal areas. One patient had basal ganglia abnormalities identified by FDG-PET scan, despite having a normal brain MRI (case 22, table 1).

On follow up telephone interview of 16 patients, most (62.5%) thought that their symptoms were either unchanged or improved. However, six thought that they were worse, and one patient's dystonia became generalised 9 years after symptom onset. Eleven patients had either mild (seven patients) or mild-moderate (four patients) disability. Many were able to remain independent by using their non-affected side for daily activities. All patients remained ambulatory, and most (75%) did not require assistance to ambulate.

Response to treatment

There were 158 medication trials in the 33 patients, most using a single drug (134 trials) and 24 trials using two or more drugs in combination. Five patients did not receive any medical therapy. Effectiveness of therapy was determined by verbal reports from patients or family members. About two thirds (19/28) of our patients had some beneficial response to medication. However, most (95%) required several medication trials (mean 4.7), with 54% requiring five or more trials. Combination therapy was more effective than single drug therapy, with a beneficial response in 41.6% (10/24) compared with 23% (31/134) using monotherapy.

Overall, our patients experienced a beneficial response in only 26% (41/158) of medication trials. The degree of improvement as assessed by the patient was variable; 19 trials resulted in mild to moderate benefit and 22 had more marked improvement. Effectiveness was limited by side effects in 37% (15/41) of these beneficial responses, prompting a change in medication. The most common side effects were sedation, dizziness, confusion, memory loss, and blurry vision, occurring

most often with benzodiazepines or anticholinergic drugs. In a follow up of 16 patients, only six continued to obtain some benefit from medications.

The most commonly used medications were trihexyphenidyl, baclofen, levodopa, clonazepam, diazepam, carbamazepine, ethopropazine, and valproic acid. The best treatment results were seen with the benzodiazepines clonazepam and diazepam, with a response rate (some improvement) of 50%. Anticholinergic drugs were effective in 30% of trials, and antiepileptic medications were only effective in 23%. Both levodopa and baclofen were poorly effective, with response rates of only 12% and 6.6% respectively. Eight patients received botulinum toxin injections and half reported benefit, but in two patients this did not persist with further injections. Five of six patients who underwent thalamotomy reported benefit. However, improvement was transient in three patients, requiring reoperation, which resulted in further benefit. The duration of transient benefit was as brief as 2 months, and as long as 24 months and 5 years.

Review of the literature

We identified 158 reported cases of symptomatic hemidystonia in the literature (table 3). Most were after stroke (48.5%) or trauma (17%), and the remainder were secondary to perinatal injury (8.8%), tumour (5%), infection (5.7%), arteriovenous malfunction (4%), and other miscellaneous causes. The mean age of onset was 25.7 years (range 3–74), and the mean latency between cerebral injury and onset of dystonia was 2.8 years (range 0–40). As in our series, the longest latencies occurred in patients after perinatal injury.^{1 5 42 43 44} Sixty nine per cent were associated with hemiparesis, which usually resolved or improved as the hemidystonia developed.

Eighty seven per cent of available neuroimaging studies identified a lesion; 60% were in the basal ganglia, with the putamen and caudate most commonly affected. Lesions were also present in the thalamus (16%), internal capsule (17.5%), and cortex (25%), often in association with lesions in the basal ganglia.

Data on response to treatment were available in 107 cases, and only 35% of medication trials resulted in any benefit. The anticholinergic drugs were most effective, with a beneficial response seen in 41% of treatment trials. Baclofen, benzodiazepines, and anticonvulsant drugs were less effective, with response rates of 28–30%. Levodopa, dopamine agonists, and dopamine antagonists were only effective in 20% of treatment trials. Surgical intervention was beneficial in 22 of 23 (96%) cases, but in nine of these benefit was transient. Thalamotomy was the most common procedure performed; others included

Table 3 Review of hemidystonia literature: 158 cases from 59 references

Ref (1st author)	No of patients (age in y)	Aetiology	Latency	Lesion location	Treatment (No of patients/response) (dose)
Pettigrew ¹	22 (2–72) (mean 36)	8 stroke 4 perinatal 3 trauma 2 storage d/o 2 neurodegen. 2 post-thalamotomy 1 encephalitis	1 month–32 y	5 basal ganglia 1 frontoparietal 1 porencephalic cyst 1 cerebral atrophy 1 putamen 2 internal capsule 1 striatum 1 thalamus 1 thalamus/basal ganglia 1 pallidal 7 normal scans	Multiple meds (5–) Levodopa (2+, 4–) Trihexyphenidyl (4+, 4–) Haloperidol (2–) Ethopropazine (1–) Propranolol (1–) Levodopa/baclofen (1+) Levodopa/trihexyphenidyl (1+) Baclofen/trihexyphenidyl (1+) Benzodiazepines (1–) Amantadine (1–) Thalamotomy (3tr+)
Giroud ²	18 (mean 10)	Stroke 14 ischaemic 4 haemorrhagic	?	14 basal ganglia	?benzodiazepines (–) Baclofen (–)
Nardocci ³	11 (mean 18.5)	9 stroke 1 perinatal 1 antiphospholipid syndrome	1 month–9 y	6 lenticular 4 IC 3 putamen 4 caudate	Trihexyphenidyl (1+, 4–) 5 thalamotomies (2+, 1+/-, & 1tr+)
Dooling ⁴	4 (12, 20, 5, 2)	Infection	Several months–10 y	3 caudate 4 putamen 3 IC/insula/temporal/ 2 inf frontal/thalamus	Not discussed
Burke ⁵	5 (7, 9, 6, 8*, 55) *(#15 in our series)	3 perinatal 1 trauma 1 stroke	13 months–9 y	1 hemiatrophy 1 focal EEG/spikes 4 CTs normal	Levodopa (tr+) Benzhexol (+) Benzhexol (+) Clonazepam (w) Diazepam? Perphenazine?
Marsden ⁹	18 (1–60) (mean 18) *(Three cases already reported in Narbona, Obeso, and Brett; see below)	2 tumour 2 AVM 6 strokes 3 trauma 1 infection 2 anoxia 2 infantile epilepsy	0–14 y	3 lenticular 1 caudate 2 posterior thalamus 1 capsulolenticular 1 frontocaudate 1 frontolenticular/thalamus/caudate 1 lenticular/IC/caudate 4 hemiatrophy	Not discussed
Lee ¹⁰	6 (53, 55, 74, 71, 23, 4)	4 strokes 1 haemorrhage 1 trauma	0–9 months	Thalamus Subthalamic nucleus	Levodopa (1–)
Leiguarda ¹¹	5 (37, 38, 68, 30, 47)	Stroke/Rx with bromocriptine	Few weeks	Frontotemporal (3) Parietal (4)/lenticular (3)/ Internal capsule (3) Thalamus (1)	d/c bromocriptine (+)
Kostic ¹²	4 (35, 47, 59, 26)	3 strokes 1 AVM	1–2 y 1 y	Lenticular/IC Putamen Lenticular/IC/caudate Temporal/caudate	Not discussed
Rumbach ¹³	1 (3)	Stroke	2 months	Cerebellum Ipsilateral basal ganglia SPECT: frontoparietal	Muscle relaxants (–) Anticholinergic (–) Levodopa (–) Thalamic DBS (–) Botox (tr+)
Ghika-Schmid ¹⁴	2 (?)	Stroke	?	Thalamus/IC/lenticular Parietotemporal	Not discussed
Glatt ¹⁵	2 (62, 68)	1 tumour 1 stroke	3 y 4 months	Parasagittal Occipitotemporal/post lateral thalamus	Anticholinergic (w) Dopaminergic (w) Dopamine blocking agent (slight +)
Lehericy ¹⁶	1 (51)	Stroke	3 weeks	Putamen/caudate/lateral pallidum/insula/IC	Not discussed

Table 3 (cont'd)

Ref (1st author)	No of patients (age in y)	Aetiology	Latency	Lesion location	Treatment (No of patients/response) (dose)
Burton ¹⁷	1 (47)	Stroke	9 months	Putamen/IC/caudate	Not discussed
Hankey ¹⁸	1 (3)	Stroke-mild (Moya-Moya)	20 y	Lentiform nucleus (old infarct)	Levodopa (+)
Oppenheimer ¹⁹	1 (8)	Stroke	Hours	Putamen/caudate	Not discussed
Demierre ²⁰	3 (3, 7, 17)	Stroke	3–4 weeks	Putamen/caudate/IC	Anticholinergic (w) Baclofen/tetrazepam (–) Piribedil/baclofen/clonazepam (+) Piribedil/clonazepam/dantrolene (+) Benzodiazepine or dantrolene (+) Piribedil (+)
Grimes ²¹	1 (9)	Stroke	6 months	Putamen/caudate	Not treated
Sunohara ²²	1 (61)	Stroke	3 months	IL putamen/thalamus CL thalamus	Levodopa (–) Phenytoin (–) Haloperidol (–) Carbamazepine (–) Diazepam (sl. +) Clonazepam (+) (8 mg) 5-HTP (+) (300 mg)
Fross ²³	1 (47)	Stroke	9 months	Putamen (MRI/PET)	not discussed
Factor ²⁴	1 (18)	Stroke	16 y	Frontoparietal Subcortical WM Lentiform nucleus Thalamus	Trihexyphenidyl (+) (9 mg)
*Obeso ²⁵	1 (22)	Hemiplegic migraine	4 months	Thalamus/IC/striatum	Pimozide (UE–, LE+) Propranolol (30%+UE) Propranolol/valproic acid (+) Propranolol/clonazepam (+)
Giroud ²⁶	1 (9)	Stroke	21 days	Caudate/IC/putamen	Benzodiazepines/dantrolene (?)
Krystkowiak ²⁷	2 (39, 52)	Stroke	6 weeks, 4 months	Putamen/caudate/Gpe Caudate/putamen/pallidum/ thalamus	Not discussed
Fernandez ²⁸	1 (38)	Stroke	18 weeks	Right midbrain	Baclofen (–) (30 mg) Benztropine (–) (0.5 mg) Amantadine (–) Valproic acid (–) Levodopa (–) Pimozide (–) Perphenazine (–) Mexilitine (–) Carbamazepine (–) Phenobarbital (–) Clozapine (–) Pallidal DBS (transient +)
Takahashi ²⁹	1 (5)	Stroke	None	Caudate/putamen	Haloperidol (–) (1 mg) Levodopa (–) Diazepam (–) Dantrolene (–)
Gille ³⁰	1 (68)	Stroke	8 months	Posterolateral thalamus	Not discussed
Krauss ³¹	1 (9)	Stroke/trauma	Months	Parieto-occipital lobe Insula/putamen	Thalamotomy (transient +)
Lee ³²	5 (6, 12, 24, 21, 21)	Trauma	Several months–9 y (mean 2 y)	Lenticular/IC/thalamus Posterolateral thalamus Lenticular/IC Inferior frontal None in one case	Clonazepam (+) Trihexyphenidyl (–) Levodopa (–) Propranolol (–) Carbamazepine (–) Tetrabenazine (–) Baclofen (–)

Table 3 (cont'd)

Ref (1st author)	No of patients (age in y)	Aetiology	Latency	Lesion location	Treatment (No of patients/response) (dose)
Krauss ³³	6 (8, 13, 6, 6, 13, 18)	Trauma	3 months–4 y (Mean 1.8 y)	3 caudate 6 putamen 3 pallidum CL hemiatrophy	Trihexyphenidyl, pimozide, tetrabenazine, methyldopa (–) Dantrolene, diazepam, bromazepam (+) Trihexyphenidyl (+) Chlormezepam, phenytoin, biperidin, haldol (–) Thalamotomy (most transient + but three sustained +)
Eaton ³⁴	1 (56)	Trauma	10 weeks	L.subdural haematoma	Removal of haematoma (+)
Mauro ³⁵	2 (7, 8)	Trauma	2 weeks–few days	1 caudate, 1 putamen	Carbamazepine/trihexyphenidyl (–)
Andrew ³⁶	1 (8)	Trauma	1 day	Caudate/IC/lenticular nucleus	Thalamotomy (+)
*Brett ³⁷	1 (5)	Trauma	1 week	Basal ganglia	Not discussed
Perlmutter ³⁸	1 (50)	Trauma	20 min	Basal ganglia by PET CT normal	Clonazepam/iv benztropine (–) Levodopa (w) Haloperidol (tr+) Phenytoin (+) Trihexyphenidyl (+) Phenytoin/trihexyphenidyl (++)
O'Callaghan ³⁹	1 (12)	Trauma	~2 y	N/A	Pallidotomy (tr+) Thalamotomy (+)
Sellal ⁴⁰	1 (16)	Trauma (extradural haematoma)	2 months	Thalamus/IC	Baclofen (–) (50 mg) Levodopa (–) (1 g) Haloperidol (–) (5 mg) Clonazepam (–) (3 mg) 5-HTP (–) (300 mg) Thalamic DBS (+)
Kellner ⁴¹	1 (63)	Trauma	1 y	Lentiform nucleus Frontoparietal WM	Not discussed
Midgard ⁴²	1 (13)	Perinatal	13 y	Striatal atrophy (putamen/caudate)	Diazepam (–), alcohol (+), Propranolol/tetrabenazine (–) Trihexyphenidyl (+)
Saint-Hilaire ⁴³	2 (8, 15)	Perinatal	8–15 y	CL hemiatrophy (CT)	Anticholinergics (+)
Treves ⁴⁴	1 (40)	Perinatal	40 y	N/A	Carbamazepine (+)
Krauss ⁴⁵	2 (9, 15)	Astrocytoma	None	Basal ganglia or thalamus	Steroids (–)
Sciarra ⁴⁶	1 (15)	Tumour	?	Basal ganglia/thalamus	Surgical resection (+)
Krauss ⁴⁷	1 (57)	Tumour	?	Parieto-occipital Compression of basal ganglia	Surgical resection (+)
*Narbona ⁴⁸	1 (8)	Tumour, astrocytoma	?	Putamen	Haloperidol (–) Benzhexol (–) Chlorpromazine (–) Levodopa (–) Carbamazepine (+) XRT (slight +, 10%)
Vandertop ⁴⁹	1 (8)	Tumour	?	Chiasm/hypothalamus	Not discussed
Gordin ⁵⁰	1 (22)	Encephalitis	Days	Putamen/pallidum	Luminal/somnifen (–)
Micheli ⁵¹	1 (11)	Infection (toxoplasmosis)	4 days	None CT/MRI normal	Trihexyphenidyl (–) Delorazepam (–) Antibiotics for toxoplasmosis (+)
Burband ⁵²	1 (14)	Herpes zoster arteritis	6 weeks	Putamen/caudate	Trihexyphenidyl/levodopa (–) Baclofen (+) Botox (+)

Table 3 (cont'd)

Ref (1st author)	No of patients (age in y)	Aetiology	Latency	Lesion location	Treatment (No of patients/response) (dose)
Caviness ⁵³	1 (45)	Sarcoidosis	3 y	None MRI normal	Intravenous steroids (+) Levodopa (slight +) Pergolide Prednisone Baclofen Levodopa/clonazepam (+)
Awaad ⁵⁴	1 (3)	Glutaric aciduria	3 years	FDG-PET: decrease in striatum/frontal cortex/insula MRI: bifrontal temporal atrophy	Baclofen (+) 80%
Jimenez-Jimenez ⁵⁵	1 (47)	Thiethylperazine	None	None CT/MRI normal	biperiden (+)
Angelini ⁵⁶	3 (7, 12, 14)	Antiphospholipid syndrome (stroke)	0–3 months	Posterior IC putamen putamen/caudate	Prednisone (1–)
Friedman ⁵⁷	2 (14, 24)	AVM	?	basal ganglia temporoparietal	Anticholinergics (1+)
Leenders ⁵⁸	1 (7)	Congenital (?AVM)	?	Brain stem/thalamus F-dopa PET: CL striatum	Trihexyphenidyl (+)
Lees ⁵⁹	1 (7)	?	1 y	N/A	Smoking (tr+ 30 min) Benzhexol (+) Benzodiazepines (–) Nicotine (tr+ 1 h)
Quinn ⁶⁰	1 (7)	?	?	L. basal ganglia Bilateral midbrain (L>R)	Not discussed

+, Beneficial response; –, no response; tr+, transient response; w, worsening of dystonia; CL, contralateral, IL, ipsilateral; UE, upper extremity; LE, lower extremity; IC, internal capsule; WM, white matter; Gpe, external globus pallidum; N/A, not available; ?, unknown; 5-HTP, 5-hydroxytryptophan.

thalamic deep brain stimulation (two), pallidotomy (one), and pallidal deep brain stimulation (one). Botulinum toxin injections were beneficial in two of two cases.

DISCUSSION

This retrospective study describes the clinical features and response to treatment in hemidystonia. Our primary aim was to determine the most effective treatment strategy for patients with hemidystonia. There are several limitations to our study. Firstly, in our series many medication trials occurred before the initial visit to our centre, and response to therapy therefore relied on patients' recall. Secondly, most patients were only evaluated at a single office visit, and subsequent response to treatment was primarily determined by follow up telephone calls. We recognise that relying on patients' reports of improvements does not account for a placebo effect. However, we chose to use patients' accounts of treatment response because we were primarily interested in determining which medications patients thought helped them the most. A more objective assessment of response to treatment was precluded by the very limited number of follow up evaluations. Many patients were seen several years ago with most being lost to follow up; only two patients were able to return for another physical examination.

Despite these limitations, we were able to draw several conclusions about the nature of hemidystonia. The most common lesion resulting in hemidystonia occurs in the contralateral basal ganglia. The most common aetiology is stroke, occurring in 48.7% of the cases in the literature and in almost 30% of the patients in our series. Perinatal injury and trauma were nearly as common as stroke in our series, but were less common in the literature. Hemidystonia is rarely a consequence of basal ganglia stroke in adults,^{61, 62} occurring more often in younger patients. Most patients had onset of hemidystonia at less than

25 years of age, supporting the idea that the younger brain is more susceptible to developing hemidystonia.³

There is often a delay between the suspected cerebral insult and the onset of hemidystonia, occurring up to 17 years after the initial injury in our series and as long as 40 years⁴⁴ in the literature. Leenders *et al* proposed that the delayed development of dystonia may be related to "slowly evolving" aberrant neuronal sprouting.⁵⁸ In our review, the latency was longest when hemidystonia was secondary to perinatal injury. This may be related to the greater ability of the developing brain to recover from cerebral insults, or secondary to a delayed recognition of this syndrome in young children.

On follow up evaluation, dystonia had stabilised in most of our patients; none had complete resolution of dystonia. The course of hemidystonia is rarely discussed in the literature. However, Pettigrew and Jankovic reported on one patient who had spontaneous resolution of hemidystonia after 4 years, and another had resolution of dystonia after 3 months of treatment with levodopa and trihexyphenidyl.¹ A handful of reports also describe progression of dystonia over months to years followed by stabilisation.^{32, 35, 42, 57, 58} Thus, the natural history of hemidystonia seems to be initial progression with spread over months to years, followed by eventual stabilisation.

Based on our review, hemidystonia responds poorly to medical therapy. In our series of patients, more than one third of effective medication trials were discontinued because of side effects, and nearly 50% were only partially effective. Benzodiazepines were the most effective medications in our patients. Anticholinergic drugs were less effective, with a response rate of only 30%. In the literature, anticholinergic drugs were the most effective treatment, with a response rate of 41%, similar to previous reports of dystonia therapy.⁶³ Fahn, however, reported five cases of hemidystonia with no response to high dose anticholinergic treatment. In Fahn's series of

patients, those with symptomatic dystonia were less responsive to treatment than idiopathic cases of dystonia with only 36% responding to treatment compared with 59% in the idiopathic group.⁶ This would suggest that patients with symptomatic dystonia do not respond to medical treatment as well as idiopathic cases of dystonia. However, in the report of Marsden *et al*, treatment response of severe dystonia to high dose anticholinergic drugs was independent of aetiology—that is, there was no difference between the response to treatment between idiopathic and symptomatic cases.⁶⁴ The difference between these two studies is difficult to interpret because in both of them there were many fewer symptomatic cases than idiopathic cases. This small sample size may not have allowed for a relevant comparison between the two treatment groups.

Surgical intervention was more successful than medical therapy, both in our series and in the literature. In our patients, results were transient in 60% prompting repeat procedures, whereas in the literature 41% had a transient result. Transient benefit from thalamotomy or pallidotomy suggests that the target is correct but the size of the lesion may be too small. Deep brain stimulation, either in the thalamus or the internal pallidum, may be more successful at producing a longer lasting result as the stimulation parameters can be adjusted to produce maximal benefit. Recently there have been several reports of success using deep brain stimulation of the internal globus pallidus for generalised dystonia,⁶⁵⁻⁶⁸ and even for post-traumatic hemidystonia.⁶⁹ There have been no studies directly comparing thalamic versus pallidal deep brain stimulation for dystonia but as there has been much more experience recently with pallidal deep brain stimulation, we can only speculate that this would be the surgical treatment of choice. However, we think that a randomised study comparing the two techniques would be necessary to determine the most effective surgery for hemidystonia.

In conclusion, hemidystonia usually occurs in the setting of a structural lesion of the contralateral basal ganglia or thalamus. Stroke is the most common cause, followed by trauma and perinatal injury. Hemidystonia typically progresses over years followed in most cases by stabilisation. Response to medical therapy is generally poor and often limited by side effects. However, many patients may benefit from benzodiazepines or anticholinergic drugs. Surgical intervention may be more successful, but results can be transient. Thalamic or pallidal deep brain stimulation may be a reasonable alternative to lesioning. Prospective double blind placebo controlled studies are needed to better evaluate both medical and surgical treatments for hemidystonia.

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