A Comparative Study of Primary and Secondary Hemifacial Spasm

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Background: Hemifacial spasm (HFS) is a common movement disorder.

Objective: To evaluate possible differences in the demographic and clinical features between primary and secondary HFS.

Design: In-person interview using a standardized questionnaire to collect demographic and clinical data.

Setting: A multicenter study that included patients with HFS attending 3 Italian academic centers.

Patients: Two hundred fourteen patients with HFS.

Main Outcome Measure: A complete neurological examination assessed the current muscle distribution of spasm and the presence of synkinetic movements between upper and lower facial muscles.

Results: The study sample comprised 214 patients with HFS, 81 men and 133 women, having a mean±SD age of 65.9±12.3 years; 164 patients were classified as having primary HFS and 50 patients (48 postparalytic and 2 symptomatic cases) were classified as having secondary HFS. Patients with primary and those with secondary HFS had similar mean±SD ages at onset (54.9±13.5 vs 57.0±12.8 years), male-female ratios (63:101 vs 18:32), right-sided–left-sided HFS (77:86 [1 bilateral] vs 21:28 [1 bilateral]), and frequencies of familial cases (2.9% vs 2.0%), respectively. Most patients (65.0%) with primary HFS had initial symptoms of periorcular muscle contractions alone and had subsequent involvement of the lower facial muscles. Most patients (72.0%) with secondary HFS reported initial involvement of the upper and lower facial muscles simultaneously. Signs of synkinesis were present in primary (43.3%) and secondary (58.0%) HFS.

Conclusions: Patients with primary and those with secondary HFS share common demographic and clinical features, including sex distribution, age at onset, affected side of HFS, synkinesis, and rarity of familial cases. Signs of synkinesis were present in significant proportions of patients with primary or secondary HFS. The 2 forms differed in clinical presentation.

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HEMIFACIAL SPASM (HFS) IS a peripherally induced movement disorder characterized by involuntary and unilateral contractions involving the upper and lower facial muscles.1-3 Hemifacial spasm is a long-term disease from which patients rarely recover spontaneously. Primary HFS is commonly attributed to vascular loops compressing the seventh cranial nerve at its exit zone from the brainstem. The facial nerve compression is thought to lead to ephaptic transmission and to hyperactivity of the facial nucleus, resulting in the involuntary facial movements.4,5 Secondary HFS frequently follows peripheral facial palsy or may arise from facial nerve damage produced by tumors, demyelinating disorders, traumatisms, and infections.3

Although HFS is a common movement disorder,4-7 little information is available on possible similarities or differences in the demographic and clinical features between primary and secondary HFS, nor have published reports compared these 2 conditions directly, to our knowledge. To investigate this issue, we conducted a multicenter study that included patients with HFS attending 3 Italian academic centers.

METHODS

The study was based on 214 consecutive outpatients diagnosed as having HFS and attending the movement disorders clinics of the University of Rome “La Sapienza,” the University of Bari, Bari, Italy, and the University of Genoa, Genoa, Italy, from January 1, 2003, to December 31, 2004. To be included in this study, patients needed to have had long-term unilateral involuntary facial muscle contractions affecting 1 hemiface. Patients with bilateral HFS were included if the onset of the spasm was not simultaneous and if the contractions were asynchronous.8 We excluded patients with other facial dyskinesias (such as blepharospasm, oromandibular dystonia, and other orofacial disorders).9-11 The exclusion criteria are described in the online-only Data Supplement available at www.archneur.org.

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Table 1. Demographic and Clinical Features of 214 Patients With Either Primary or Secondary Hemifacial Spasm (HFS)*

<table>
<thead>
<tr>
<th>Demographic and Clinical Features</th>
<th>Patients With Primary HFS (n = 164)</th>
<th>Patients With Secondary HFS (n = 50)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male/female</td>
<td>63/101</td>
<td>18/32</td>
<td>.68</td>
</tr>
<tr>
<td>Age at examination, y</td>
<td>65.9 ± 12.4 (range, 0.5-86)</td>
<td>65.8 ± 12.4 (range, 14-82)</td>
<td>.90</td>
</tr>
<tr>
<td>Age at onset, y</td>
<td>54.9 ± 13.5 (range, 0.5-35.0)</td>
<td>57.0 ± 12.8 (range, 0.5-35.0)</td>
<td>.32</td>
</tr>
<tr>
<td>Duration of botulinum toxin type A treatment, y</td>
<td>6.0 ± 4.6 (range, 0.5-27)</td>
<td>5.2 ± 4.3 (range, 0.5-27)</td>
<td>.30</td>
</tr>
<tr>
<td>Affected side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>77 (47.0%)</td>
<td>21 (42.0%)</td>
<td>.56</td>
</tr>
<tr>
<td>Left</td>
<td>86 (52.4%)</td>
<td>28 (56.0%)</td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>1 (0.6%)</td>
<td>1 (2.0%)</td>
<td></td>
</tr>
<tr>
<td>Muscle spasm distribution at onset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbicularis oculi</td>
<td>106 (64.6%)</td>
<td>14 (28.0%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Orbicularis oris</td>
<td>1 (0.6%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Orbicularis oculi and orbicularis oris</td>
<td>53 (32.3%)</td>
<td>33 (66.0%)</td>
<td></td>
</tr>
<tr>
<td>Orbicularis oculi, orbicularis oris, and platysma</td>
<td>4 (2.4%)</td>
<td>3 (6.0%)</td>
<td></td>
</tr>
<tr>
<td>Muscle spasm distribution at examination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbicularis oculi</td>
<td>4 (2.4%)</td>
<td>2 (4.0%)</td>
<td>.59</td>
</tr>
<tr>
<td>Orbicularis oris</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Orbicularis oculi and orbicularis oris</td>
<td>108 (65.8%)</td>
<td>34 (68.0%)</td>
<td></td>
</tr>
<tr>
<td>Orbicularis oculi, orbicularis oris, and platysma</td>
<td>52 (31.7%)</td>
<td>14 (28.0%)</td>
<td></td>
</tr>
<tr>
<td>Synkinesis</td>
<td>71 (43.0%)</td>
<td>29 (58.0%)</td>
<td>.10</td>
</tr>
</tbody>
</table>

*Data are given as the number (percentage) or as mean ± SD unless otherwise indicated.†Primary vs secondary HFS.

RESULTS

The participation rate was 100.0%. Of the 214 patients meeting the eligibility criteria and participating in this study, 133 (62.1%) were women and 81 (37.9%) were men. The age of the 214 patients was 65.9 ± 12.3 years (age range, 26-86 years), the age at onset of HFS was 55.5 ± 13.3 years (range, 14-82 years), and the disease duration was 10.4 ± 7.5 years (range, 0.5-35.0 years). Hemifacial spasm was left-sided in 114 patients (53.3%), right-sided in 98 (45.8%), and bilateral in 2 patients (0.9%). Among the cohort, the latency between the onset of symptoms and the correct diagnosis of HFS was 4.5 ± 5.2 years (range, 0-27 years). When examined, 207 of 214 patients were receiving treatment with botulinum toxin, the treatment duration was 5.8 ± 4.5 years, and the duration of the beneficial effect was about 3 months.

Primary HFS was diagnosed in 164 patients. Neurovascular compression of the seventh cranial nerve was suspected in 70 (56.5%) of 124 patients who underwent head imaging studies. Among the 40 patients without head imaging studies (disease duration, 12.8 ± 8.4 years [range, 2-24 years]), neither the history nor the neurological signs suggested inflammatory, traumatic, or neoplastic disease of the facial nerve in its intracranial or extracranial pathways. Secondary HFS was diagnosed in 50 patients: 48 had postparalytic HFS, 1 had an acoustic schwannoma, and 1 had multiple sclerosis.

Patients with primary and secondary HFS were similar in sex, age at examination, age at onset, and HFS-affected side of the face but differed in facial muscle involvement at onset (Table 1). Most patients (65.0%) with primary HFS initially had contractions of periorcular muscles alone, whereas most patients (72.0%) with secondary HFS reported involvement of the upper and lower facial muscles simultaneously, including the platysma muscle. Only 1 patient (0.6%) with primary HFS had an atypical presentation, with HFS beginning in the orbicularis oris muscle. In most patients with focal onset, twitching gradually extended to the other areas of the ipsilateral face. In the group with primary HFS, the duration of the disease was significantly longer in patients with involvement of the orbicularis oculi, orbicularis oris, and platysma muscles than in patients with orbicularis oculi and orbicularis oris muscle involvement (13.0 ± 7.7 vs 10.7 ± 7.5 years, P = .03). No difference in the duration of attempted synkinesis was noted.
the disease was found in the group with secondary HFS (8.0±4.9 vs 8.6±7.6 years, P=.76).

In the overall population of 214 patients, examination disclosed synkinesis in 100 patients (46.7%). Signs of synkinesis were more frequent in patients with secondary HFS than in patients with primary HFS, but the difference failed to reach statistical significance (Table 1). The presence of synkinesis did not correlate with sex, age at examination, age at onset, duration of botulinum toxin treatment, HFS-affected side of the face, or muscle distribution at onset and at examination in either group (data not shown). Among patients with primary HFS, however, those with synkinesis were significantly younger at HFS onset than patients without synkinesis (51.1±13.9 vs 57.7±12.4 years, P=.002). On multiple linear regression analysis, there was a significant inverse correlation between the age at onset of primary HFS and the presence of synkinesis. The correlation was independent of sex, age at examination, and duration of botulinum toxin treatment (adjusted regression coefficient, −0.02 [95% confidence interval, −0.03 to −0.005]; P=.006).

A family history of HFS was found in 4 (2.4%) of 164 patients with primary HFS and in 1 (2.0%) of 50 patients with secondary HFS (Table 2). Affected relatives were a parent in 3 cases, a sister in 1 case, and a daughter in 1 case: 3 relatives were diagnosed as having primary HFS and 2 relatives as having secondary HFS. Overall, the age at onset of familial HFS cases was 54.2±14.0 years (range, 38-72 years); there was a slight female (6/10) and right-sided (6/10) preponderance.

In this case series, the demographic features resembled those in the general population of cases.2,3,6,7 As reported in other studies,2,3 HFS was almost invariably idiopathic or post-paralytic, with symptomatic cases being rare. Even the preponderance of unilateral HFS affecting the left side of the face and the frequency of 0.9% of bilateral HFS reported in our series were consistent with other studies.3,11,14

The similarities in the sex distribution, age at onset, and HFS-affected side of the face between primary and secondary HFS are difficult to explain for 2 conditions that differ in origin. However, our findings may reflect the demographic and clinical features of the pathologic conditions that are thought to be more frequently responsible for primary and secondary HFS, namely, vascular loops of the posterior fossa and peripheral facial palsy. Although data on the topic are scant, some evidence suggests that vascular loops potentially compressing cranial nerves and peripheral facial palsy may predominate in women15 and be more frequently left sided.16 Because the facial nerve sustains impairment more often than any other nerve, our findings raise the possibility of a nonspecific sex-, age-, and side-related vulnerability of the facial nerve to different noxae.

In most patients (65.0%) with primary HFS, involuntary contractions started in the perioral muscles and then spread somatotopically to the neighboring facial muscles, involving the orbicularis oris muscle first and the platysma muscle thereafter. Conversely, in most patients (72.0%) with secondary HFS, involuntary contractions simultaneously involved the upper and lower facial muscles, including the platysma muscle. The different patterns of clinical presentation probably relate to causative differences between primary and secondary HFS and to the organization of facial nerve motor fibers. Primary HFS is thought to result from neurovascular compression at the root entry zone of the facial nerve,4,5 whereas damage of the facial nerve along its course from the internal auditory canal to the stylomastoid foramen produces peripheral facial palsy, the most frequent condition predisposing a patient to secondary HFS.3 Anatomical data suggest that the facial nerve motor fibers are topographically organized along their courses into the pons and, probably, at the root entry zones.15,16 The fibers become more diffusely arranged as distal levels of the nerve trunk are examined as far as the stylomastoid foramen.16 Therefore, secondary HFS, which is a condition frequently associated with damage of

| Table 2. Demographic and Clinical Features of 5 Patients With Familial Hemifacial Spasm and Their Affected Relatives |
|---|---|---|---|---|---|---|---|---|
| Patient No./Sex/Age at Examenation, y | Affected Side/Age at Onset, y | Distribution at Examination-Origin | Relationship to the Proband/Age at Examination, y | Affected Side/Age at Onset, y | Distribution at Examination-Origin |
| 1/M/51 | Left/45 | Ooc, OOr, P/primary | Mother/77 | Right/69 | Ooc, OOr, P/primary |
| 2/F/44 | Right/38 | Ooc, OOr/primary | Sister/47 | Right/7 | Ooc, OOr/primary |
| 3/M/64 | Left/39 | Ooc, OOr, P/primary | Father/85 | Left/2 | Ooc, OOr/primary |
| 4/M/67 | Left/59 | Ooc, OOr, P/primary | Mother/89 | Right/72 | Ooc, OOr/secondary to facial palsy |
| 5/F/77 | Right/67 | Ooc, OOr, P/secondary to facial palsy | Daughter/50 | Right/39 | Ooc, OOr, P/secondary to facial palsy |

Abbreviations: Ooc, orbicularis oculi muscle; OOr, orbicularis oris muscle; and P, platysma muscle.

Our multicenter study found several common demographic and clinical features between primary and secondary HFS. These similarities were the sex distribution, age at onset, HFS-affected side of the face, and rarity of familial cases. The 2 conditions differed in muscle distribution at the onset. The frequency of synkinesis, although not statistically significant, was higher in secondary HFS than in primary HFS. In most patients (65.0%) with primary HFS, involuntary contractions started in the perioral muscles and then spread somatotopically to the neighboring facial muscles, involving the orbicularis oris muscle first and the platysma muscle thereafter. Conversely, in most patients (72.0%) with secondary HFS, involuntary contractions simultaneously involved the upper and lower facial muscles, including the platysma muscle. The different patterns of clinical presentation probably relate to causative differences between primary and secondary HFS and to the organization of facial nerve motor fibers. Primary HFS is thought to result from neurovascular compression at the root entry zone of the facial nerve,4,5 whereas damage of the facial nerve along its course from the internal auditory canal to the stylomastoid foramen produces peripheral facial palsy, the most frequent condition predisposing a patient to secondary HFS.3 Anatomical data suggest that the facial nerve motor fibers are topographically organized along their courses into the pons and, probably, at the root entry zones.15,16 The fibers become more diffusely arranged as distal levels of the nerve trunk are examined as far as the stylomastoid foramen.16 Therefore, secondary HFS, which is a condition frequently associated with damage of

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the temporal portion of the facial nerve, is more likely to involve most facial divisions rather than selective regions.

We found only 1 patient (0.6%) with primary HFS in whom spasms started atypically in the orbicularis oris muscle and then gradually spread upward to involve the orbicularis occuli muscle.21 None of the patients with secondary HFS started atypically. Similarly, among 155 cases of primary HFS, Ryu et al22 found 2 atypical cases (1.3%); Barker et al23 stated that up to 8% of 648 patients with HFS had an atypical onset. These differences probably reflect the different selection criteria in these studies. The rarity of atypical onset in primary HFS could also be related to the organization of facial nerve fibers at the root entry zone.

In our sample, patients with primary and secondary HFS had synkinetic movements of facial musculature. Synkinesis is a well-known clinical sign in secondary HFS and is considered to be due to abnormal facial nerve degeneration.24 Only 1 report described the presence of synkinesis in primary HFS, without providing frequency data.25 In this study, Kim and Fukushima26 found that synkinesis was relieved by facial nerve decompression, suggesting lateral spreading owing to ephaptic transmission at the root entry zone of the facial nerve or, alternatively, owing to hyperexcitability of motoneurons in the facial nucleus.27 In neither group in the present study did we find a relationship between the presence of synkinesis and most demographic and clinical features, including duration of botulinum toxin treatment. The lack of a relationship with the duration of botulinum toxin treatment suggests that long-term treatment makes no significant contribution to the presence of synkinesis. The significant inverse correlation between the age at onset and the presence of synkinesis that we found in the primary HFS group alone is difficult to explain.

Because we did not assess a family history of HFS by examining all first-degree relatives, our study may have underestimated the number of family histories of HFS. Nevertheless, the rarity of family history found in our sample was consistent with the rarity of familial cases reported in the literature.21 A noteworthy finding was the similar frequency of familial cases in primary and secondary HFS. Furthermore, 4 of 5 familial index cases had primary HFS, and 2 of 5 affected relatives had secondary HFS. Although we did not compare the frequency of HFS between patients’ relatives and a suitable control population, these observations suggest that few patients, if any, are genetically predisposed to the development of primary HFS and that genetic influences rarely have a pathogenetic role.

CONCLUSIONS

Patients with primary and those with secondary HFS share several common clinical features, including the sex distribution, age at onset, HFS-affected side of the face, and presence of synkinesis. The 2 forms, nevertheless, differ in clinical presentation, presumably because they differ in origin. This study also underlines that synkinesis is present in a significant proportion of persons with secondary HFS as well as those with primary HFS. We failed to find strong evidence supporting a substantial genetic contribution to the origin of HFS.

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REFERENCES


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REFERENCES


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Correction

Errors in Byline. In the article titled “A Comparative Study of Primary and Secondary Hemifacial Spasm,” published in the March issue of the ARCHIVES (2006;63:441-444) on page 441 the first names of Drs Avanzino and Marinelli were switched. The byline should have read as follows: “Carlo Colosimo, MD, Matteo Bologna, MD; Simona Lamberti, MD; Laura Avanzino, MD; Lucio Marinelli, MD; Giovanni Fabbrini, MD; Giovanni Abbruzzese, MD; Giovanni Defazio, MD; Alfredo Bardelli, MD.”