A Comparative Study of Primary and Secondary Hemifacial Spasm

Carlo Colosimo, MD; Matteo Bologna, MD; Simona Lamberti, MD; Lucio Avanzino, MD; Laura Marinelli, MD; Giovanni Fabbri, MD; Giovanni Abbruzzese, MD; Giovanni Defazio, MD; Alfredo Berardelli, MD

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.

Arch Neurol. 2006;63:441-444

EMIFACIAL 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, traumas, and infections.3

Although HFS is a common movement disorder,6,7 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.
ful motions of the face, such as eyelid closure or smiling, were muscles of the face occurring simultaneously when purpose-
synkinesis was defined as contractions of a certain group of
netic movements between upper and lower facial muscles. Facial
bution at the time of examination, and the presence of synki-
sessed the clinical features of the spasm, especially its distri-
months after the last injection of botulinum toxin type A) as-
spasm, and patients with signs of synkinesis without involun-
ticatory spasm, or psychogenic conditions),3,9,10 patients with a
fice, myokymia, focal seizures, hemimasticatory spasm, or psychogenic conditions).3,10 patients with a
ory, facial tics, myokymia, focal seizures, hemimasticatory spasm, or psychogenic conditions),3,10 patients with a

The complete neurological examination (performed ≥ 3
months after the last injection of botulinum toxin type A) as-
ssessed the clinical features of the spasm, especially its distri-
ution at the time of examination, and the presence of synki-
etic movements between upper and lower facial muscles. Facial
synkinesis was defined as contractions of a certain group of
muscles of the face occurring simultaneously when purpose-
ful motions of the face, such as eyelid closure or smiling, were

**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). Hermal facial 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 symp-
toms and the correct diagnosis of HFS was 4.5 ± 5.2 years (range, 0-27 years). When examined, 207 of 214 pa-
tients 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. Neuro-
vascular compression of the seventh cranial nerve was
suspected in 70 (36.5%) 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 dis-
ease 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 in-
volution 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 orbii-
ularis oris muscle. In most patients with focal onset,
twitching gradually extended to the other areas of the ip-
silateral face. In the group with primary HFS, the dura-
tion 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

**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 (39.0)</td>
<td>18 (36.0)</td>
<td>.68</td>
</tr>
<tr>
<td>Age at examination, y</td>
<td>56.9 ± 13.4</td>
<td>65.8 ± 12.4</td>
<td>.90</td>
</tr>
<tr>
<td>Age at onset, y</td>
<td>54.9 ± 13.5</td>
<td>57.0 ± 12.8</td>
<td>.32</td>
</tr>
<tr>
<td>Duration of botulinum toxin type A treatment, y</td>
<td>6.0 ± 4.6</td>
<td>5.2 ± 4.3</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>0 (0.0)</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.

©2006 American Medical Association. All rights reserved.
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.

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.

Because this was not a population-based study, we corrected for a bias in case selection by designing a multicenter investigation and recruiting all consecutive patients who met the eligibility criteria during the study period. 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 women13 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 periorbicular 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,5,5 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.17-19 The fibers become more diffusely arranged as distal levels of the nerve trunk are examined as far as the stylomastoid foramen.18 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

<table>
<thead>
<tr>
<th>Proband</th>
<th>Relative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>Relationship to the Proband</td>
</tr>
<tr>
<td>No./Sex/Age at Exams., y</td>
<td>Side/Age at Onset, y</td>
</tr>
<tr>
<td>1/M/51</td>
<td>Left/45</td>
</tr>
<tr>
<td>2/F/44</td>
<td>Right/38</td>
</tr>
<tr>
<td>3/M/64</td>
<td>Left/39</td>
</tr>
<tr>
<td>4/M/67</td>
<td>Left/59</td>
</tr>
<tr>
<td>5/F/77</td>
<td>Right/67</td>
</tr>
</tbody>
</table>

Abbreviations: O0c, orbicularis oculi muscle; O0r, orbicularis oris muscle; and P, platysma muscle.

©2006 American Medical Association. All rights reserved.
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 ocularis muscle.21 None of the patients with secondary HFS started atypically. Similarly, among 155 cases of primary HFS, Ryu et al.22 found 2 atypical cases (1.3%); Barker et al.23 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.3 Only 1 report described the presence of synkinesis in primary HFS, without providing frequency data.24 In this study, Kim and Fukushima24 found that synkinesis was relieved by facial nerve decompression, suggesting lateral spreading owing to ephaptic transmission in the root entry zone of the facial nerve or, alternatively, owing to hyperexcitability of motoneurons in the facial nuclei.21 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 familial cases of HFS. Nevertheless, the rarity of family history found in our sample was consistent with the rarity of familial cases reported in the literature.11 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.

Accepted for Publication: November 1, 2005.

Correspondence: Alfredo Berardelli, MD, Department of Neurosciences and Neuromed Institute, University of Rome “La Sapienza,” Viale dell’Università 30, 00185 Rome, Italy (alfredo.berardelli@uniroma1.it).

Author Contributions: Study concept and design: Colosimo, Abbruzzese, and Berardelli. Acquisition of data: Bologna, Lamberti, Avanzino, Marinelli, Fabbrini, Abbruzzese, Defazio, and Berardelli. Analysis and interpretation of data: Colosimo, Bologna, and Fabbrini. Drafting of the manuscript: Colosimo, Bologna, Lamberti, Fabbrini, Abbruzzese, Defazio, and Berardelli. Critical revision of the manuscript for important intellectual content: Avanzino, Marinelli, Abbruzzese, Defazio, and Berardelli. Statistical analysis: Lamberti, Marinelli, and Fabbrini. Administrative, technical, and material support: Abbruzzese, Defazio, and Berardelli. Study supervision: Colosimo, Bologna, Avanzino, Abbruzzese, Defazio, and Berardelli.

REFERENCES

Acknowledgment: I thank Fabrizio Doricchi, PhD, for his helpful discussion; and Michel Thiebaut de Schotten, MA, for drawing Figure 2.

REFERENCES


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.”