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Hemifacial spasm in correlation with electrophysiological and radiological findings

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Abstract

Objective : To investigate the correlation between the electrophysiological and radiological findings of primary hemifacial spasm patients

Subjects : Patients with primary hemifacial spasm who had had no botulinum toxin treatment previously were included in the study.

Design : In this prospective study patients underwent cerebral magnetic resonance imaging,a magnetic resonance angiography investigation and an electrophysiological examination after informed consent had be given by the patients. The facial nerve distal latency, amplitude and blink reflex responses were recorded as well as clinical and demographic data.

Results : Twenty five patients completed radiological and electrophysiological investigations. The radiological investigations disclosed neurovascular compromise which can cause hemifacial spasm in twelve patients (48%) while the findings of two patients were not considered as a certain cause of hemifacial spasm. All patients except two had at least one electrophysiological abnormality (92%). The most frequent finding was an increased R1/D ratio which suggested an increased central conduction time.

Conclusion : In this study, an increased R1/D ratio suggests that there is a functional impairment in the brain stem even if it is not possible to disclose structural abnormalities in some hemifacial spasm patients. Combining magnetic stimulation may be a useful tool for further investigations.An inadequate radiological investigation might be the cause of relatively low radiological abnormalities in comparison with the electrophysiological ones.

Key words : Hemifacial spasm ; facial nerve ; blink reflex ; ephaptic transmission ; MR imaging.

Hemifacial spasm is characterized by the clonic movement of the facial muscles on one side of the face. It is a relatively frequent movement disorder. The differential disorder includes tic disorder, clonic seizures, psychogenic spasm, facial paralysis, blepharospasm, facial myokimia and tardive dyskinesia. The prevalence was 11/100000 in a study in Olmsted County and 10/100000 in Oslo (Auger *et al.*, 1990 ; Nilsen *et al.*, 2004). It is more common in some Asian populations than in Caucasians, but there have been no epidemiological studies in these populations to support this observation. Women are affected more than men and the left side more than the right (Tan *et al.*, 2002). Abnormal responses and synkinetic responses of the blink reflexes are useful to confirm the diagnosis. These abnormal responses result from hyper excitability of facial nerves/neurons.

High blood pressure is suggested to be an etiological factor causing arterial abnormalities that cause compression of the facial nerve at the exit zone. Contradictory to this hypothesis, arterial abnormalities are thought to cause both hemifacial spasm and high blood pressure through brain stem and facial nerve compression. Supporting this hypothesis surgical decompression is suggested to lead to normalization of blood pressure in hypertensive patients with neurovascular syndromes (De Fazio *et al.*, 2003).

Possible radiological findings in HFS patients include arterial abnormalities such as a dilated and elongated basilar artery, small arterial branches which compromise the exit zone of the facial nerve and demyelinating lesions. However, neurovascular compromise (NVC) of the facial nerve may not always lead to symptoms as NVC has been demonstrated in normal controls without HFS and in the asymptomatic side in HFS. Some patients who had bilateral or unilateral HFS radiological evaluations disclosed no vascular compromise. It is conceivable that higher cortical modulation of the facial motor nucleus may partly explain why only some patients with NVC develop symptoms and others do not (Tan *et al.*, 2004). In a case control transcranial magnetic stimulation study, electrophysiological evidence of a cortical influence on HFS could be demonstrated. Clinical observations have shown that stress and emotional factors are known to precipitate HFS or facial spasms (Tan *et al.*, 2001). Genetic susceptibility could also determine whether NVC result in clinical symptoms. Familial HFS with presumed autosomal mode of inheritance has been described (Carter *et al.*, 1990).

Patients and methods

The aim of this prospective study is to disclose any relationship between the electrophysiological and radiological findings if it is ever present in HSF patients. In our clinic, cerebral magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) are standard procedures to examine patients with HFS diagnosis. Except for patients 3 and 17, who were investigated radiologically in an outside institution, all patients were examined in our hospital. We used a 1.5 T MR scanner, TSE T2 and T1 axial slices with a slice thickness of 5 mm, FLAIR T2 coronal images and SE T1 sagittal images to study the brain. We also performed cranial MRA using 3D Time-of-flight technique. Source images were reconstructed using MIP and they were also carefully evaluated to demonstrate the relationship of the posterior fossa vascular structures with the facial and vestibulocochlear nerves. To ascertain the HFS diagnosis we used the presence of blink reflex responses in facial nerve innervated muscles other than orbicularis oculi. Patients who had unilateral primary HFS were included in this study after informed consent was obtained, while patients with HFS secondary to Bell's palsy, trauma or surgery were excluded. The primary HFS patients who had previously been treated with botulinum toxin were also excluded from the study. A four channeled electromyography machine was used for the electrophysiological examinations (Medelec Sapphire 4ME).

Facial nerve action potentials were recorded from bilateral orbicularis oculi muscles with surface cup electrodes, which were placed lateral to the lateral cantus and at the middle of the lower part of orbicularis oculi muscle. Supramaximal stimulation was delivered over the facial nerve close to the stylomastoid foramen with bipolar surface electrodes. Blink reflex responses were also recorded from the same sites and also from the mentalis muscle using the same kind of electrodes. The latency (D) and amplitude of facial nerve action potentials, latencies of R1, R2 were recorded ipsilaterally and R2' responses were recorded from the contralateral orbicularis oculi muscle. Using the R1/D ratio we compared the conduction through the distal segment of the facial nerve within that of the entire reflex arc which includes the trigeminal nerve and the proximal segment of the facial nerve. The latency difference of R1, R2 and R2' responses of the two sides were also calculated. We used the normal values that were reported by Kimura (Kimura 2001). The upper limits of normal, defined as the mean latency plus 3 SD include 4.1 ms for direct response, 13.0 msn for R1. Additionally,the latency difference between the two sides should not exceed 0.6 ms for direct response and 1.2 ms for R. The R/D ratio should not fall outside the range of 2.6-4.6, 2 SD above and below the mean in normal individuals. With stimulation of the supraorbital nerve, R2 latency should not exceed 40ms on the side of the stimulus and 41 ms on the contralateral side. In addition, the ipsilateral and contralateral R2 simultaneously evoked on one side should not vary more than 5 ms in latency. A latency difference between R2' evoked by right-sided stimulation and corresponding R2' evoked by left sided stimulation may show a slightly greater value, but not more than 7 msn (Kimura 2001).

Results

Twenty five of 32 patients who had been clinically diagnosed with HFS between the years 2003-2005 were included. Four patients were excluded due to incomplete radiological or inadequate electrophysiological investigations. In one patient blink response could not elicited from the mentalis muscle therefore she was also excluded. Another one of the excluded patients had blepharospasm and hemifacial spasm.

There were 9 male, 16 female patients and the age range was 42-75. Eleven patients had hypertension and were on medication, 5 had normal blood pressure, 9 were reported to have had high blood pressure on more than one occasion at least. Thirteen patients had left HFS. Twenty of the patients had both cerebral MR and MRA ; three had only MR while two had only MRA. Radiological findings are shown on Table I. Twelve patients had abnormal findings, which can cause HFS spasm on the affected side. All of these patients had at least one abnormal electrophysiological parameter. The imaging of patients 3, 9 and 24 had some abnormalities but the causal relationship was uncertain. All had increased R1/D ratio and patient 9 also had a late R1 response (16.5 ms) on the affected side. When direct or reflex response latencies were compared there was no statistically significant difference between the pathologic and the normal side. Except for patients 12 and14 who had neither radiological nor electrophysiological abnormality, all the other patients had some abnormal electrophysiological responses. Increased R1/D ratio was found in 16 patients (64%) and in 13 patients it was bilateral. In nine patients a neurovascular compromise was seen on the symptomatic side. However in patient 15 the finding was on the asymptomatic side. Three patients (Patient 20, 24, 25) had an increased R1 latency difference while another three (patients 6, 19, 20) had an increased R2' difference. There was a mild compression of pons on the symptomatic side of patient 24, which was considered an uncertain finding. However, when it is combined with the increased R1 difference and SR1/D ratio it can be considered a meaningful finding. An early and long R2' response was seen in patient five on the affected side which was not included in the statistical analysis. The results of electrophysiological

Table I

The radiological findings. MCA : Middle cerebral artery, VA : Vertebral artery, AICA : Anterior inferior cerebellar artery, PICA : Posterior inferior cerebellar artery. The findings of the patients who had relevant abnormality were printed in italic characters

Patient No :	Affected Side	Cerebral MRI	Cerebral MRA
1	*Left*	*Small ischemic gliotic lesions in bilateral periventricular white matter and frontal subcortical white matter. Dolicoectatic vertebrobasilar artery, compressing the left anterolateral side of the brain stem. Bilateral aneurysms of MCA and anterior communicating arteries*	*Right M1 aneurysm 5 × 8 mm in diameter. Left MCA aneurysm 5 mm in diameter. Small anterior communicating artery aneurysm. Tortuous basilar artery*
2	*Right*	*No relevant finding*	*Left tortuous anterior inferior cerebellar artery is close to the cisternal part of the facial nerve*
3	Right	No relevant finding	Prominent tortuosity of both vertebral arteries towards right side. Slight atherosclerotic changes of left MCA and branches
4	Right	No relevant finding	Hypoplasia of posterior communicating artery
5	Right	No relevant finding	Not performed
6	*Right*	*No relevant finding*	*Right AICA is close to the facial nerve at the level of its exit from the brain stem*
7	*Right*	*Both anterior inferior cerebellar arteries extend to internal acoustic canal and slightly compress the facial nerves, more prominent on the right side*	*Normal*
8	*Right*	*Normal*	*Right posterior inferior cerebellar artery is close to the facial nerve at the level of its exit from the brain stem*
9	Right	Normal	Prominent tortuosity and ecstasies of all cerebral arteries. Left ICA shows tortuosity and kinking in the intracranial portions. Tortuosity of right vertebral artery
10	Left	No relevant changes	Normal
11	Left	No relevant findings	Normal
12	Left	Normal	Not performed
13	*Left*	*Tortuousity of basilar and left VA, 7th-8th nerves are minimally compressed at the exit zone*	*Proximal basilar artery is close to the 7th-8th nerves at the exit zone on the left*
14	Left	Normal	
15	*Right*	*Tortuousity of BA and left VA and some compression to 7-8th nerves on the left side*	*Tortuosity of all vascular structures and fusiform dilatation of BA*
16	*Right*	*Normal*	*Right VA is in close proximity to 7-8th nerves*
17	Left	Normal	Normal
18	*Left*	*Normal*	*Left AICA is in close proximity to cerebellopontine cistern and mildly tortuous*
19	Left	Normal	Normal
20	Right	Normal	Normal
21	*Left*	*Mildly dilated and ectatic vertebral and basilar arteries*	*Left VA and BA are mildly dilated and ectatic. PICA creates a loop immediately after leaving left VA. 7th nerve might be compressed by left VA and PICA*
22	*Left*	*Not performed*	*Tortuous and kinking left VA, compressing left lateral side of medulla oblongata, pons and cerebellar peduncle and the contents of left internal acoustic canal*
23	Right	No relevant findings	Posterior cerebral artery is occluded
24	Right	Basillar artery is mildly tortuous, there is mild compression of pons on the right side	
25	*Left*	*Not performed*	*Mild dilatation and tortuosity of vertebrobasilar arteries. Left VA is compressing facial nerve at the level of its exit from the brain stem*

Table II

Electrophysiological findings. Missing values could not be calculated due to absence of responses. S :symptomatic side, C :contralateral side. The abnormal findings are printed in bold characters

Patient No	S-R1	S-R2	C-R2'	C-R1	C-R2	S-R2'	S-D	SR1/D	C-D	CR1/D
1	**No response**	34.80	33.10	11.00	32.0	35.60	2.17	Missing	2.4	4.58
2	11.60	35.80	32.40	12.00	30.90	26.30	2.26	**5.13**	2.49	**4.82**
3	10.90	35.10	35.80	10.10	36.00	36.00	2.2	**4.95**	2.02	**5.00**
4	9.70	34.90	38.40	11.20	39.70	**50.40**	1.89	**5.13**	1.89	**5.93**
5	11.20	29.50	30.30	11.20	32.40	19.00	3.4	3.29	2.8	4.00
6	12.00	30.40	30.40	11.40	36.80	37.90	2.01	**5.97**	2.17	**5.25**
7	9.60	36.80	35.80	9.50	33.10	36.00	2.02	**4.75**	1.84	**5.16**
8	10.30	28.30	28.90	10.50	28.00	28.00	1.81	**5.69**	2.11	**4.98**
9	**15.20**	34.30	31.10	11.50	37.80	36.90	2.95	**5.15**	2.76	4.17
10	10.90	36.20	35.40	11.30	33.40	33.30	2.02	**5.40**	2.14	**5.28**
11	11.30	30.30	30.30	**No response**	32.30	31.30	1.17	**9.66**	1.98	Missing
12	10.00	26.30	30.90	10.10	32.00	30.70	2.17	4.61	2.53	3.99
13	**16.50**	34.70	34.70	**No response**	33.00	33.00	2.74	**6.02**	2.74	Missing
14	9.70	35.10	34.20	9.10	35.50	34.50	2.74	3.54	2.08	4.38
15	11.40	31.60	32.40	11.00	34.20	32.80	1.92	**5.94**	2.1	**5.24**
16	11.90	27.60	32.00	11.20	29.60	29.50	1.81	**6.57**	1.92	5.83
17	11.00	37.70	40.10	10.50	**No response**	**No response**	2.25	4.89	2.49	4.22
18	10.40	30.20	31.10	11.10	31.80	31.80	1.87	**5.56**	1.95	**5.69**
19	**No response**	**45.60**	**48.80**	10.10	37.60	37.60	2.34	**Missing**	2.38	4.24
20	12.00	25.00	26.20	10.70	34.70	34.60	2.46	4.88	2.4	4.46
21	11.80	29.30	32.00	**No response**	31.30	31.30	2.84	4.15	2.08	Missing
22	12.80	36.00	38.10	13.90	36.40	37.90	2.22	**5.77**	2.43	**5.72**
23	11.30	36.70	36.10	10.10	34.70	37.60	2.78	4.06	2.18	4.63
24	**13.70**	32.80	30.00	12.00	29.70	33.10	2.25	**6.09**	2.29	**5.24**
25	10.80	36.70	37.30	9.00	31.00	31.50	2.3	**4.70**	2.34	3.85

investigations are shown on Table II. In three patients there was no R1 response on the asymptomatic side (Patients 11, 13, 21) and two (Patients 1, 19) who had no R1 response on the symptomatic side.

Conclusion

The classic hypothesis is that ectopic firing and ephaptic transmission occur at the site of vascular compression. The vascular contact with the portion of the facial nerve, which is covered by central (oligodendrocyte) myelin, injures the myelin thereby allowing bare axons to contact each other closely. It is this close contact between the bare axons which promotes direct electrical communication between the individual nerve fibers (Nilsen *et al.*, 1984-A, Møller 1991). An alternative hypothesis is that there is hyper excitability of facial motor neurons presumably provoked by excessive afferent activity or antidromic stimulation or by both. Recent evidence shows that in human peripheral nerves, sensory axons have substantially greater persistent NA^+ currents than motor axons do, and consequently the firing threshold is significantly lower in sensory than motor axons. This is also possibly the case for the facial and trigeminal axons. This study revealed that trigeminal reflexes are exaggerated in HFS, supporting the idea of hyper excitability of the facial motor neurons at the level of the nucleus. Their results did not show direct evidence of hyper excitability of the facial motor neuron pool. However, the presence of an abnormally exaggerated trigeminal facial reflex, which is not evoked in normal subjects cannot be explained by changes in peripheral facial nerve excitability (Misawa *et al.*, 2006). It is most probable that these patophysiological mechanisms result in abnormalities that can be shown electrophysiologically. Lateral spreading is one of the prominent findings. In normal subjects the zygomatic branch of the facial nerve innervates the orbicularis oculi muscle. In hemifacial spasm cases when the zygomatic branch is stimulated the mandibular branch

innervated muscles and the orbicularis oculi muscle contracted (Nilsen *et al.*, 1984-B). A prerequiste for the occurence of ephactic transmission is that the neural conduction velocity at the site of the lesion is slowed down to values which enable an action potential to have a sufficient amplitude at the end of the refractory period to excite neighboring fibers (Møller 1991). Therefore, the latency of blink reflex responses and the R1/D ratio which show central conduction are useful means to evaluate HFS.

In our study at least one electrophysiological parameter abnormality was present in all of the patients but one. It is interesting that some patients had an increased R1/D ratio on the asymptomatic side and also on the symptomatic side, which partly explains the absence of a difference between the symptomatic and the asymptomatic side. Direct response latency was normal in all these patients, therefore increased R1/D ratios suggest an abnormality involving the proximal segment of the reflex arc. In three patients there was no R1 response on the asymptomatic side (Patients 11, 13, 21) and two (Patients 1, 19) who had no R1 response on the symptomatic side. These findings suggest that even symptoms are unilateral, the functional abnormality may be present in pontine levels on both sides. In a previous study using a blink reflex recovery curve method ,decreased inhibition attributed to facial motor neuron and brain stem interneurons is more predominant on the side of the spasm, but it was also present to some extent on the contralateral side (Uzun *et al.*, 2005). Another study supporting bilateral involvement suggests that patients with HFS may have both an increased excitability of the facial motoneurons of the symptomatic side and an increased excitability of the brain stem inerneurons of the blink reflex pathways on both sides (Valls-Sole *et al.*, 1989). Radiological investigations did not show any other abnormality except vascular compromise , most of them were unilateral. Although it falls short of explaining bilateral abnormality, this finding can be an etiological factor of the HFS. It is not clear enough whether the unilateral presence of NVC was related to limitations of imaging techniques. Perhaps the patophysiology of the hemifacial spasm may include more intricate pathways concerning corticopontine pathways. A more elaborate study including functional radiological and electrophysiological investigations would be useful to give new insights.

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