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Cheiro-oral syndrome: A reappraisal of the etiology and outcome

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Abstract

Objective: This is a review of our cases and published literature on cheiro-oral syndrome (COS), to better understand its localization, etiology and outcome. *Methods:* In addition to our database, we reviewed the medical database (including PUBMED, BIOSIS, EMBASE, and SCOPUS) and other sources, searched by the keyword of "cheiro-oral". The definition of COS was a subjective or an objective sensory disturbance confined to the perioral area and the finger(s)/hand without a detectable abnormality in mental, motor or cerebellar function. Only cases of COS where the clinicoanatomic correlation could be identified by neuroimaging study, autopsy or stereotatic surgery was included. *Results:* There were a total of 174 patients; 85 patients from our database, 76 patients from medical database, and 13 patients from other sources. They were 111 men and 63 women. Their age ranged from 12 to 85 years; average being 58.2 years. Stroke is the leading etiology and constituted 74% of the patients. The most common location of lesion was thalamus, followed by pons and cortex. Classical unilateral COS was seen in 81% of patients, atypical COS in 19%. Whereas the lesions were from cortex to cervical spinal cord in unilateral COS, atypical COS was associated with lesions in pons or medulla oblongata. An early deterioration was seen in 16.5% of patients, especially in large cortical infarction and subdural hemorrhage. Structural lesions were found in 85% of patients.
Conclusion: Classical unilateral COS do not have a high localizing value, the atypical COS is associated with lesion in pons or medulla.

INTRODUCTION

Cheiro-oral syndrome (COS) was first reported in literature at 1914 by *Sir* Sittig [1], a German military doctor, who described three young men suffering an acute onset of paresthesia confined to their perioral area and ipsilateral finger(s)/hand. Autopsy showed their responsible lesions to be respectively encephalitis, gumma and vascular malformation, located at contralateral postcentral gyrus of the parietal lobe.[1] Since then, COS has received great interest in Europe. Later, cases were also found to have thalamic lesion.[2-4] Because neuroimaging was not available in first half of last century, COS was thought to be due to involvement of the contralateral parietal lobe or thalamus.

In the last 50 years, the rapid advances in intracranial imaging has facilitated the study in clinicoanatomic correlation, and better understanding of etiology and pathogenesis in a broad variety of neurological disorders, including COS. There were a number of published studies on COS from Italy[5], Japan[6-9], Netherland[10], USA[11-12], Taiwan[13-14] and Korea.[15] In contrast to the traditional concept that COS is localizing and has prognostic value, these studies suggest that COS can involve a wide neuraxis from cortex to medulla oblongata, and clinical deterioration can occasionally be seen.[11-12,16-18] However, most of these studies are based on a single patient or small number of cases. There is yet no comprehensive review of the published literature. In this study, we would like to review of patients with COS, as well as the published literature, to reappraise the etiology and outcome of patients with COS.

METHODS

This was a prospective study since 1989; from 1989 to 2000 at Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, and from 2001 to 2010 at Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan. Patients were inpatients or outpatients of these two medical centers, or referred from local hospital or

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clinic for further neurological investigation or consultation.

1. Definition of COS

COS was defined as a subjective or an objective sensory disturbance confined to the perioral area and the finger(s)/hand without a detectable abnormality in mental, motor or cerebellar function. Patients with mild change of tendon reflex or muscle tonicity without significant decrease of muscle strength, focal seizure or movement disorder, mild brainstem or neuro-ophthalmological symptom, or neurological deficit probably due to other event was not excluded.[16]

There were 4 types of COS.[16] Unilateral or Type I was a sensory impairment confined to the perioral area and ipsilateral finger(s)/hand. Bilateral or Type II was a sensory disturbance confined to the perioral area and finger(s)/hand bilateraly.[19] Atypically bilateral or Type III was a sensory disturbance confined to the perioral area and finger(s)/hand in that one was involved bilateraly whereas the other was unilateral.[16] It was an incomplete and atypical form of the bilateral COS. Crossed or Type IV was a sensory disturbance confined to the perioral area and opposite finger(s)/hand in a crossed pattern.[17]

2. Enrollment of patients

In our previous reports, we excluded cases whose COS was related to migraine ictus, intoxication or pharmacotoxicity in order to clarify the neuroanatomy of COS. In this study, we included all COS patients except migraineur in order to elucidate the actual etiology and location of COS.

Each patient had a detailed review of medical history, neurological examination, cranial computerized tomography (CT) scan or magnetic resonance image (MRI), and somatosensory evolved potential to identify the etiology and localization. When indicated, further appropriate tests were performed and the details were in previous reports.[16-19]

3. Review of literature

Regarding to the COS in literature, we searched the medical databases including PUBMED, BIOSIS, EMBASE, and SCOPUS, and other sources including Google website, open journals such as DOAJ (http://www.doaj.org), BioMed Central, Free Medical Journals (http://www.freemedicaljournals.com), Academic Journals (http://www.academicjournals.org), Bentham Science (http://www.benthamscience.com), Internet Scientific Publications, and references of previous COS papers. Only case of COS who received cranial CT scan or MRI, autopsy, or stereotactic surgery in that a clinicoanatomic correlation could be identified was enrolled. The COS variants, like cheiro-oral-pedal syndrome, cheiro-pedal syndrome[20], or cheirobuccopedal syndrome[21], were excluded. COS cases reported in internet, newspaper or domestic meeting without a formal publication in scientific periodical or monograph were excluded.[22]

4. Definition of responsible etiology

Responsible etiology was defined as the most probable cause of the COS in temporal course or neuroanatomic correlation based on clinical features or other diagnostic investigations such as neuroimaging. The diagnosis of intracranial lesion such as neoplasm, vascular anomaly or others was based on the radiological finding made by Neuroradiologists. In case of stroke, a diagnostic dilemma was the disappearance of the diffuse-weighted image (DWI) and apparent diffusion coefficient (ADC) change on MRI a period of time after index ischemic stroke. Therefore, an ischemic stroke was also diagnosed when there was (1) a positive DWI with or without ADC change; (2) an acute onset of sensory deficit, a lesion with high T2-weighted or FLAIR-weighted intensity but without significant parallel change of T1-weighted intensity situated within the ascending sensory pathway compatible with the neurological presentation; and (3) no other possible cause.

5. Size of lesions

In case of brainstem infarction or hemorrhage, the lesion was considered "large" when the infarction or hematoma was over one-fourth area of the brainstem at the same level. Those with less area were considered "small". The hemispheric infarction was considered "large" when the area of infarction was over one-third area of the middle cerebral artery territory. In subdural hematoma, it was "large" when the thickness of hematoma was more than 1 cm.

RESULTS

1. Number of cases of COS

There were a total of 174 cases included in the analysis, they consisted of 111 men and 63

women; male consisted of 63.8%. Their age ranged from 12 to 85 years; average being 58.2 years (Table 1). Our own database consisted of 85 patients, seen between January, 1989 to December, 2010. They were 59 men and 26 women. Their age ranged from 32 to 74 years; average being 59.8 years. The patients enrolled before 2007 had been reported previous.[13,16-19, 23-25] (Table 1).

There were 76 reports from PUBMED, EMBASE, BIOSIS and SCOPUS searched under the keyword "cheiro-oral". Other than our previous reports, another 35 reports were excluded for the following reasons: (1) Cases presented earlier[15,26] were later incorporated into larger case series[27-28]; (2) The patients did not fulfill the criteria of COS in this study[29]; (3) The patients presented with significant mental, motor, cerebellar, or other sensory deficit[30-33], or an extension of sensory deficit beyond cheek at face or hand beyond wrist.[3-4,12,26] The remaining 35 records were published between 1966 and 2011, which has 76 patients. They were 43 men and 33 women. Their age ranged from 12 to 85 years; average being 56.6 years (Table 1).

From the other sources, we found an additional 12 reports which have 13 patients fulfilling the criteria of COS.[34-45] Two patients with autopsy were excluded due to an extension of their cheiral paresthesia to forearm.[3-4] These reports were mostly local medical journals in non-English languages, using keywords other than COS, or not collected in PUBMED. These 13 patients consisted of 9 men and 4 women. Their age ranged from 34 to 71 years; average being 56.6 years (Table 1).

2. Neurological manifestations

In these 174 COS patients, 141 patients presented as Type I (81.0%), 15 patients as Type II (8.6%), 13 patients as Type III (7.5%), and 5 patients Type IV (2.9%).

3. Etiology

The leading causative lesion was ischemic stroke in all series (52.9%), following by hemorrhagic stroke (21.8%). They accounted for 73.7% of all the patients. Other causes included intracranial bypass complication (3.4%)[46], cervical cord disorder (3.4%)[47], neoplasm (2.9%)[10,44], vascular malformation (1.1%)[18], and abscess[35], aneurysm[48], dermoid cyst[49], seizure[43], stereotactic surgery[5], middle cerebral artery stenosis[50], and drug (0.6%), respectively (Table 2). No etiology cause was identified in 18 patients (10.3%) but most of these patients had had old cerebral infarction.[16]

In our series of patients, one patient experienced a short duration of less than 30 minutes of mild bilateral COS (Type II) shortly after the first ingestion of 5 mg flunarizine for migraine prophylaxis. She did not have other significant past medical illness previously. There was also no other neurological symptoms during the event or any subsequent complication. The etiology of COS was attributed to meningioma in 3 patients[10,18], and brain metastasis in 2 other patients.[44]

We have encountered a few patients who experienced bilateral COS after an ingestion of marine products.[22] Cingulotoxin was identified in these products. However, as these patients were only reported in popular media and were not reported in scientific publications, they were not included in this study.

A structural lesion responsible for the COS could be indentified in 148 out of 174 patients (85.1%). In 141 of these 148 patients (95.3%), further treatment measures could be advised. In the 26 patients, the cause of COS was unknown. (Table 2).

As compared to Type II, III and IV COS patients, where the etiology was predominantly due to ischemic or hemorrhagic stroke (27/33 patients, 81.8%); in Type I COS patients, the

Table 1: The sources of cases of cheiro-oral syndrome reviewed

Series	Total patients	Age (year)	Male gender
Lin *et al*'s series	85	32-74; average 59.8	59/85 (69.4%)
Medical database	76	12-85; average 56.6	43/76 (56.6%)
Other sources*	13	34-71; average 56.6	9/13 (69.2.0%)
Overall	174	12-85; average 58.2	111/174 (63.8%)

*Google website, open journals such as DOAJ, BioMed Central, Free Medical Journals, Academic Journals, Bentham Science, Internet Scientific Publications, and references of previous COS papers

Table 2: The etiology of the cheiro-oral syndrome patients

Etiology/Series	Lin *et al*'s series	Medical database	Other sources	Total (%)
Ischemic stroke	36	48	8	92 (52.9%)
Hemorrhagic stroke	21	15	2	38 (21.8%)
Neoplasm	2	2	1	5 (2.9%)
Infection/abscess	0	0	1	1 (0.6%)
Aneurysm	0	1	0	1 (0.6%)
Vascular malformation	2	0	0	2 (1.1%)
Dermoid cyst	0	1	0	1 (0.6%)
Seizure	0	0	1	1 (0.6%)
Stereotactic surgery	0	1	0	1 (0.6%)
Intracranial bypass complication	0	6	0	6 (3.4%)
MCA stenosis	0	1	0	1 (0.6%)
Drug	1	0	0	1 (0.6%)
Cervical cord disorder	6	0	0	6 (3.4%)
Unknown	17	1	0	18 (10.3%)

responsible causes were stroke in 73.0% (103/141 patients). (Table 3).

4. Location

In a patient with seizure[43], single proton emission computed tomography revealed an increased right parietal lobe uptake with electroencephalogram showing paroxysmal epileptic discharge during the COS episode. As the neuroimaging did not reveal any structural lesion, she was thought to have a nonstructural lesion at her right parietal lobe.

Thus, a total of 26 patients did not show any structural lesion responsible for the COS. They included patients with negative neuroimaging, patients with isolated middle cerebral artery

Table 3: Structural changes according to types of cheiro-oral syndrome (COS)

Etiology/Type	I	II	III	IV
Ischemic stroke	72	9	7	4
Hemorrhagic stroke	31	2	5	0
Neoplasm	5	0	0	0
Infection/abscess	1	0	0	0
Aneurysm	1	0	0	0
Vascular malformation	2	0	0	0
Dermoid cyst	1	0	0	0
Seizure	1	0	0	0
Stereotactic surgery	1	0	0	0
Intracranial bypass complication	6	0	0	0
MCA stenosis	1	0	0	0
Drug	0	1	0	0
Cervical cord disorder	6	0	0	0
Unknown	13	3	1	1

stenosis, intracranial bypass complication, and the patient whose symptom was attributed to drug side effect. Except for one patient with multiple infarct, the responsible lesion was a single lesion in the other 147 patients (Table 3).

The most common location of lesions in COS was at thalamus (25.9%), followed by pons (24.7%), cortex (18.4%), internal capsule (4.0%), cervical cord (3.5%), corona radiata (2.9%), medulla oblongata (2.9%), midbrain (1.7%), and multiple sites (0.6%). The three common sites, thalamus, pons and cortex accounted for 80.8% of the 148 identifiable lesions, and 69.0% of the 174 COS patients overall (Table 4). Thus, there is a wide range of anatomical sites that could account for COS, ranging from cortex to cervical cord, but the most common were at thalamus, pons and cortex.

The most common site of ischemic stroke was thalamus, following by pons and cortex. As for hemorrhagic stroke, the most common was pons, following by thalamus and cortex. Neoplasm was exclusively located in cortex.

There is some differences in the locations of lesions with different types of COS. In 86/141 (60.9%) of Type I patients, the site of lesion was at the thalamus to cortex. In the 28 Type II and Type III COS patients, the location of their lesions was pons in 20 patients (71.4%); thalamus in 2 patients, cortex in 1 patient, and unknown in another 4 patients (Table 5). The single patient who suffered bilateral COS had bilateral subdural hemorrhage. The thalamic lesion was unilateral in the two Type II and Type III patients. In one Type II patient, the responsible cause was drug effect without identifiable location.

5. Outcome

In cases from medical databases and other sources, most of the studies focused on the clinicoanatomic correlation and etiology but the outcome was rarely mentioned. Therefore, we analysed our series to determine the risk factor associated with outcome. In our patients, early deterioration of neurological status within 7 days after index COS was present in 14 (16.5%) out of 85 patients. This was seen in large cortical infarct in 5 (83%) out of 6 patients, subdural hemorrhage in 5 (83%) out of 6 patients, medullary infarct in 3 (75%) out of 4 patients, and pontine hemorrhage in 1 (11.1%) out of 9 patients, respectively.

In the cortical infarct patients, the infarction was large and involved more than half of the middle cerebral artery territory in the 5 patients with early deterioration. In the other patient who did not have deterioration, her infarction was small and located focally at the postcentral gyrus

Table 4: The location of lesions in 148 cheiro-oral syndrome patients with structural lesions

Etiology/Location	Cortex	Corona radiata	Internal capsule	Thalamus	Midbrain	Pons	Medulla oblongata	Cervical cord	Multiple sites
Ischemic stroke	15	5	7	33	3	23	5		1
Hemorrhagic stroke	8			11	1	18			
Neoplasm	5								
Infection/abscess	1								
Aneurysm						1			
Vascular malformation	2								
Dermoid cyst						1			
Seizure	1								
Stereotactic surgery				1					
Spinal stenosis								6	
Total no of patients	32	5	7	45	4	43	5	6	1
(%)*	18.4%	2.9%	4.0%%	25.9%	1.7%	24.7%	2.9%	3.5%	0.6%

Another 26 patients included middle cerebral artery stenosis, intracranial bypass surgery complication, drug, and 18 patients without identifiable etiology or location of lesion

*the frequency of location was expressed as the number of case in one location out of a total of 174 patients

Table 5: The locations of lesions according to the different types of cheiro-oral syndrome (COS)

Etiology/Type	No.	Type I	Type II	Type III	Type IV
Cortex	32	31 (22.7%)	1 (6.7%)		
Corona radiata	5	5 (3.5%)			
Internal capsule	7	7 (5.0%)			
Thalamus	45	43 (31.9%)	1 (6.7%)	1 (7.7%)	
Midbrain	4	4 (2.8%)			
Pons	43	23 (30.5%)	9 (60.0%)	11 (84.6%)	
Medulla oblongata	5	1 (3.5%)			4 (80.0%)
Cervical cord	6	6 (4.3%)			
Multiple sites	1	1 (0.7%)			
Unknown*	26	20 (18.4%)	4 (26.7%)	1 (7.7%)	1 (20.0%)

* included middle cerebral artery stenosis, intracranial bypass surgery complication, drug, and 18 patients without identifiable etiology or location of lesion

at parietal lobe. Therefore, a larger infarct size is associated with higher risk of early deterioration in COS arising from cortex.

As for the patients with intracerebral hemorrhage, the lesions were all subdural, ranging from acute to chronic form. These hemorrhages were all large in size but herniation was not seen. Five out of 6 patients had early deterioration, occurring rapidly after the index COS event. The size of the subdural hematoma did not appear to be a risk factor for early deterioration.

In our 4 patients with medullary infarct, 3 had early deterioration to manifest with Wallenberg's syndrome, whereas the other patient exhibited crossed COS without further neurological deterioration. Sekine *et al*[51] have also reported a 62-year-old man who suffered COS due to contralateral medullary infarction. However, the patient's clinical course was uneventful. In contrast to the 13 pontine infarction patients, 1 out of 9 pontine hemorrhage patients suffered early deterioration.[19] The hematoma of this patient was large.

Table 6 shows the relationship between types of COS and neurological outcome inclusive of cases from published literature, Neurological deterioration occurred in 60% of the Type IV cases, but the number was small. In the 14 COS patients with early deterioration, none died or became vegetative. The functional disability was moderate in 11 patients, and mild in 3 patients.

In our series of patients, none had recurrence of stroke or COS within 1 month to 6 months after their index COS event.

DISCUSSION

In this review, we analysed 174 COS patients from our own database and the published literature. Although we could only find 89 patients in the published literature, this does not necessarily mean that COS is rare, as cases without unusual etiology or location may not have been reported. Nevertheless, as we could collect only 85 patients over 12 years in our own database, COS is thus probably an uncommon neurological syndrome.

Table 6: The relationship between neurological deterioration and types of cheiro-oral syndrome (COS)

Type of COS	Total cases	Cases of neurological deterioration	Ratio
Type I COS	141	9	6.4%
Type II COS	15	2	13.3%
Type III COS	13	0	0.0%
Type IV COS	5	3	60.0%

Stroke, ischemic or hemorrhagic, is the most common cause of COS seen in three quarter of the patients reviewed. Previous cerebral infarctions is also seen in some patients where the cause of COS is unknown.[16] Sasamori *et al*[46] recently reported 6 out of 21 patients experiencing reversible COS shortly after bypass surgery for Moyamoya disease. Navabi *et al*[50] reported a patient with COS having ipsilateral middle cerebral artery stenosis without other identifiable brain lesion. Therefore, these findings support COS as largely a stroke syndrome.

Since the location of lesion ranges from the cortex to cervical spinal cord in COS patients[47], COS differs from the other classical brainstem or cortical syndrome which often predicts a singular location.

Thalamus, pons and cortex are the leading sites of COS and constitute 81% of all patients reviewed with structural lesions, and 69% of patients overall. In contrast to thalamus and pons, where the lesions are nearly exclusively infarct or hemorrhage, for COS from cortex, a variety of non-stroke lesions are also present, including neoplasm[10,44], abscess[35], vascular malformation[18], and seizure.[43] In fact, most of the non-stroke lesions are found at cortex.[10,18,35,43-44] This differences of etiology in cortical lesion versus those from the thalamus/pons may be due to a relative predilection of infarct and hemorrhage at thalamus/pons.

The majority of COS is unilateral, similar to the earliest reported cases.[1-4] The bilateral or atypically bilateral COS[12,15,18-19,41,52-55] constitutes 16.1% of all COS, and crossed COS[17] in 2.9%. In bilateral, atypically bilateral and crossed COS, the responsible etiology is usually from stroke, and the location is mostly at pons in bilateral/ atypical bilateral COS, and lateral medulla oblongata in crossed COS. Thus, in general the bilateral/atypical bilateral/crossed COS is able to predict the lesion location better than the typical unilateral COS.

Although COS is a restricted sensory disorder, an early clinical deterioration is seen in close to one out of 6 patients (16.5%). This is more common than the lacunar stroke. The risk factors of early deterioration are etiology causes of large cortical infarction, subdural hemorrhage, medullary infarction and less so, pontine hemorrhage.[16] In our previous studies, we have found that the volume of large infarction and subdural hemorrhage do not significantly change when neurological deterioration occurs.[18-19,24] In cases of subdural hemorrhage, a removal of hematoma rapidly improves the neurological deficits and also pre-existing cheiro-oral paresthesia.[18-19,24] Therefore, in COS, patients should be observed for clinical deterioration, in particular, those with large cortical infarct and subdural hemorrhage.

In summary, based on this review, firstly COS can generally be regarded as a stroke syndrome. Secondly, classical unilateral COS does not have localizing value. The bilateral, atypical bilateral and crossed COS, on the other hand, better predicts an involvement respectively at pons or lateral medulla oblongata. Thirdly, structural lesions are found in 85.1% of COS patients, and in 95.3% of these patients, more specific treatment measures could be advised based on the etiologies. Fourthly, clinical deterioration occurs in one in 6 (16.5%) patients, where early management may be required. Imaging to elucidate the location and etiology of COS is thus important in the management of COS.

DISCLOSURE

Conflict of interest: None

REFERENCES

1. Sitting O. Klinische Beitrage zur Lehre von der Lokalisation der sensiblen Rindenzentren. *Prager Med Wochenschr* 1914;45:548-50.
2. Strauss H. Über Sensibiliätsstörungen an Hand und Gesicht, Geschmacksstörungen und ihre lokalisatorische Bedeutung [Ger]. *Monatsschrift für Psychiatrie und Neurolgie* 1925;58:265-76.
3. Garcin R, Lapresle J. Syndrome sensitif de type thalamique et à topographie chéiro-oral par lésion localisée du thalamus. *Rev. Neurol (Paris)* 1954; 90:124-9.
4. Garcin R, Lapresle J. 2d. Personal observation of a sensory syndrome of the thalamic type with cheiro-oral topography caused by localized lesion of the thalamus [Fre]. *Rev Neurol (Paris)* 1960; 103:474-81.
5. Testa C, Nizzoli V. Cheiro-oral syndrome appearing after stereotaxic surgery in a thalamic site [Ita]. *Riv Patol Nerv Ment* 1966; 87:387-92.
6. Hirayama K, Narabayashi H. Thalamic sensory disturbances and somatic localization of disturbances due to lesions of the sensory nucleus [Jpn]. *Rinsho Shinkeigaku* 1973;13: 681-8.
7. Hashiguchi K, Igata A. A case of primary pontine hemorrhage with cheiro-oral syndrome (palm-oral sensory disturbance). *Shinkei Naika* 1976; 5:79-80.
8. Tawara S, Terao A, Araki S, Shirabe T. Unilateral medial longitudinal fasciculus (MFL) syndrome with palmar-oral symptoms [Jpn]. *Rinsho Shinkeigaku* 1974; 14:745-51.
9. Fujisawa A, Imaizumi, Nukada T. Clinical study of cheiro-oral syndrome [Jpn]. *Rinsho Shinkeigaku* 1979;19:17-21.
10. Ten Holter J, Tijssen C. Cheiro-oral syndrome: does

it have a specific localizing value? *Eur Neurol* 1988; 28:326-30.
11. Bogousslavsky J, Dizerens K, Regli F, Despland PA. Opercular cheiro-oral syndrome. *Arch Neurol* 1991; 48:658-61.
12. Helgason CM, Wilbur AC. Basilar branch pontine infarction with prominent sensory signs. *Stroke* 1991; 22:1129-36.
13. Ngai WK, Chang YY, Liu JS, Chen SS. Cheiro-oral syndrome: identification of the lesion sites and a proposal for its clinical classification. *Kaohsiung J Med Sci* 1991; 7:536-41.
14. Huang MH, Chu NS. Pure cheiro-oral syndrome due to a small pontine hematoma: report of a case and review of the literature. *J Formos Med Assoc* 1994; 93:636-9.
15. Kim JS, Lee MC. Stroke and restricted sensory syndromes. *Neuroradiology* 1994; 36: 258-63.
16. Chen WH. Cheiro-oral syndrome: a clinical analysis and review of literature. *Yonsei Med J* 2009; 50:777-83.
17. Chen WH, Li TH, Chen TH, *et al*. Crossed cheiro-oral syndrome. *Clin Neurol Neurosurg* 2008;110:1008-11.
18. Chen WH, Lan MY, Chang YY, Lui CC, Chen SS, Liu JS. Cortical cheiro-oral syndrome: a revisit of clinical significance and pathogenesis. *Clin Neurol Neurosurg* 2006; 108: 446-50.
19. Chen WH, Lan MY, Chang YY, Liu JS, Chou MS, Chen SS. Bilateral cheiro-oral syndrome. *Clin Neurol Neurosurg* 1997; 99:239-43.
20. Chen WH, Lin HS, Chui C, Wu SS, Lui CC, Yin HL. Cheiro-pedal syndrome: Clinical analysis and review of literature. *J Clin Neurosci* (in press)
21. Chen WH, Wu YS, Lin HS. Cheirobuccopedal syndrome. *Acta Neurol Taiwan* 2009; 18:34-6.
22. Lien CS, Chen SS. Cingulotoxin. *Central News Agency (Taiwan)*, April 19, 2006.
23. Chen WH, Tseng YL, Lui CC, Liu JS. Episodic pain syndrome restricted cheiro-oral region associated with pontine lesion. *Brain Inj* 2005; 19:949-53.
24. Chen WH, Chang YY, Yin HL, Liu JS. Bilateral cheiro-oral syndrome and traumatic subdural hematoma. *J Trauma* 1995;38:826-7.
25. Chang YY, Chen WH, Liu JS, Chen SS, Wu HS. Unilateral cheiro-oral syndrome in a patient with bilateral subdural hematomas. *J Formos Med Assoc* 1994; 93:727-9.
26. Kim JS. Restricted acral sensory syndrome following minor stroke. Further observation with special reference to differential severity of symptoms among individual digits. *Stroke* 1994; 25:2497-502.
27. Arboix A, Tomàs J. Clinical study of 17 patients with cheiro-oral-pedal syndrome [Spa]. *Med Clin (Barc)* 2002; 118:180-2.
28. Arboix A, García-Plata C, García-Eroles L, *et al*. Clinical study of 99 patients with pure sensory stroke. *J Neurol* 2005; 252:156-62.
29. Takahashi N, Kawamura M, Hirayama K. Motor paresis with cheiro-oral topography due to small infarct in the internal capsule or the corona radiata [Jpn]. *Rinsho Shinkeigaku* 1997; 37:7-12.
30. Yasuda Y, Watanabe T, Tanaka H, Ogura A. Localizing value of bilateral cheiro-oral sensory impairment. *Intern Med* 1998; 37:982-5.
31. Mochizuki A, Eto H, Takasu M, Utsunomiya K, Schoji S. Cheiro-oral syndrome with internuclear ophthalmoplegia and cerebellar ataxia following midbrain infarction. *Eur Neurol* 1994; 34:286-7.
32. Combarros O, Díez C, Cano J, Berciano J. Ataxic hemiparesis with cheiro-oral syndrome in capsular infarction. *J Neurol Neurosurg Psychiatry* 1992; 55:859-60.
33. Hasegawa Y, Okada H, Okamoto S. Neuro-Behçet disease with bilateral cheiro-oral syndrome following simultaneous multiple brain hemorrhage [Jpn]. *Rinsho Shinkeigaku* 1991; 31:754-9.
34. Combarros O, Polo JM, Pascual J, Berciano J. Evidence of somatotopic organization of the sensory thalamus based on infarction in the nucleus ventralis posterior. *Stroke* 1991; 22:1445-7.
35. Chang GY. Cheiro-oral syndrome because of cerebral abscess. *Eur J Neurol* 1997; 4: 521-3.
36. Jeong DS, Lee BR, Cho SG, Park HK, Shin HK, Sung KB. Cheiro-oral syndrome with INO following brainstem infarction. *J Korean Neurol Assoc* 1998; 16:229-32.
37. Sanchetee PC, Venkataraman SVSM, Jena A, Dhamija RM. Lacunar infarct presenting as cheiro-oral syndrome [Letter]. *Neurol India* 1993; 41:183-4.
38. Lu SX. Cheiro-oral syndrome: 2 cases report [Chin]. *Chin J Neuromed* 2005;4:514.
39. Masaya O, Fukashi U, Masakuni K. Microbleed causing thalamic cheiro-oral sensory syndrome was detected by T2-weighted imaging [Jpn]. *Neurol Med* 2005; 62:517-8.
40. Kumral K., Kutluay E., Çolakoglu Z. Cheiro-oral syndrome with cortical sensorial dysfunction fallowing thalamic infarction. *Nörol Bil Der* 1994; 3-4:161-5.
41. Seo JY, Lee JH, Nam DH, Oh SY, Shin BS. Atypical cheiro-oral syndrome presented with bilateral perioral sensory symptoms in unilateral thalamic infarction. *J Korean Neurol* Assoc 2010; 28:298-300.
42. Osamu H, Nara N. Chronic subdural hematoma presenting with repeated transient cheiro-oral syndrome [Jpn]. *Shinkei Naika* 2011;74:367-9.
43. Akiko N, Toshiya F, Mitsuru K, Kojiro S. Paroxysmal cheiro-oral syndrome due to cerebral cortical lesion. A case report [Jpn]. *Neurol Med* 1999; 50:551-5.
44. Noda S, Umezaki H, Nagata S, Kuromatsu C. Cortical cheiro-oral syndrome due to convexity meningioma [Jpn]. *Clin Neurol* 1983; 18:506-9.
45. Tagawa K, Ikeda Y, Hirata Y, Takahashi A, Satoh Y. Cheiro-oral syndrome due to infarction of parietal lobe [Jpn]. *Clin Neurol* 1984; 20:70-3.
46. Sasamori T, Kuroda S, Nakayama N, Iwasaki Y. Incidence and pathogenesis of transient cheiro-oral syndrome after surgical revascularization for moyamoya disease. *Neurosurgery* 2010; 67:1054-9.
47. Lin HS, Yin HS, Chui C, Lui CC, Chen WH. Spinal cheiro-oral syndrome: A common neurological entity in unusual site. *Neurol Neurochir Pol* 2011; 45:583-9
48. Nakayasu H, Sue S, Takahashi K, Hori T, Hokama Y. A mechanism of cheiro-oral syndrome due to brainstem lesions, a case of a dissecting aneurysm

of the basilar artery [Jpn]. *Rinsho Shinkeigaku* 1991; 31:550-3.
49. Nakamura M, Mizuguchi M, Momoi MY, Chou H, Masuzawa T. Transient cheiro-oral syndrome due to a ruptured intracranial dermoid cyst. *Brain Dev* 2001; 23:261-3.
50. Nabavi DG, Zunker P, Mumme T, Georgiadis D. Cheiro-oral syndrome due to severe stenosis of the middle cerebral artery. *J Neurol* 1996; 243:483-4.
51. Sekine T, Kawabe K, Kawase Y, *et al*. Cheiro-oral syndrome associated with lateral medullary infarction. *Neurol Sci* 2011; 32:321-2.
52. Shintani S, Tsuruoka S, Shiigai T. Pure sensory stroke caused by a cerebral hemorrhage: clinical-radiologic correlations in seven patients. *Am J Neuroradiol* 2000; 21:515-20.
53. Kim JS, Bae YH. Pure or predominant sensory stroke due to brain stem lesion. *Stroke* 1997; 28:1761-4.
54. Ikeda K, Iwasaki Y, Kishi H, Imai K, Kinoshita M. Brain stem cheiro-oral syndrome: neurological signs for brain stem lesions. *Clin Neurol Neurosurg* 1995; 97:192-4.
55. Matsumoto S, Kaku S, Yamasaki M, Imai T, Nabatame H, Kameyama M. Cheiro-oral syndrome with bilateral oral involvement: a study of pontine lesions by high-resolution magnetic resonance imaging. *J Neurol Neurosurg Psychiatry* 1989; 52:792-4.