

23. Borojerdi B, Kopylev L, Battaglia F, et al. Reproducibility of intracortical inhibition and facilitation using the paired-pulse paradigm. *Muscle Nerve* 2000;23:1594–1597.
24. Levy LM, Hallett M. Impaired brain GABA in focal dystonia. *Ann Neurol* 2002;51:93–101.
25. Gilio F, Curra A, Lorenzano C, Modugno N, Manfredi M, Bernardelli A. Effects of botulinum toxin type A on intracortical inhibition in patients with dystonia. *Ann Neurol* 2000;48:20–26.
26. Chen R, Wassermann EM, Canos M, Hallett M. Impaired inhibition in writer's cramp during voluntary muscle activation. *Neurology* 1997;49:1054–1059.
27. Orth M, Snijders AH, Trimble MR, Rothwell JC. Variability of TMS paired pulse data within subjects and between subjects—modification of stimulation parameters increases accuracy. *Proceedings of Transcranial Magnetic Stimulation in Movement Disorders Conference; 2003 Mar 14–15; Santa Margherita - Ligure, Italy: Human Movement Disorder Society.*

Alien Limb Syndrome and Moya–Moya Disease

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Abstract: We present the case of a 29-year-old woman with an alien limb and callosal disconnection syndrome who was diagnosed with moya–moya disease. We discuss the potential mechanisms responsible for the alien limb syndrome. © 2004 Movement Disorder Society

Key words: alien limb syndrome; callosal disconnection syndrome; moya–moya disease; mechanism

Alien limb syndrome, which has been well described previously,^{1–3} may result from various underlying pathological conditions. Symptoms may vary, but the hallmark of the disorder is a limb that performs actions contrary to the intention of the patient.⁴ In many cases, the normal

limb attempts to restrain the alien limb. Alien limb syndrome usually results from lesions of the corpus callosum and/or lesions of the anteromedial cortex, including the supplementary motor area.⁵ Here, we report another cause of corpus callosum pathological state resulting in alien limb: a disconnection syndrome resulting from moya–moya disease.

CASE REPORT

A 29-year-old, right-handed woman presented initially with problems speaking, performing complex calculations, and reading. She also complained of frequent involuntary movements of her left arm. She described trying to remove her underwear with her right hand and being thwarted by her left hand uncontrollably bringing her underwear back up. During her hospitalization when showering, her right hand would turn the water off while her left hand would turn it back on. She could not exit the bathroom because her right hand would open the door and her left hand would close it. At initial presentation, the patient also complained of left-sided pain and dysesthesias, as well as headaches and unsteadiness. Examination revealed a unilateral left-sided ideomotor apraxia characterized by an inability to pantomime the use of objects to command, which improved with imitation. The patient showed further improvement with actual object use, although remained slow when demonstrating object use with her left hand compared to her right hand. She had normal repetition but was anomie for objects placed in her left hand. She demonstrated apparent left-hand agraphesthesia and astereognosis, both secondary to left tactile anomia. The patient was able to correctly identify an object placed in her left hand when asked to choose this object from among a series of objects subsequently placed in the left hand. She had a left alien limb syndrome (see Video, Segment 1). She also had finger agnosia, acalculia, and right–left confusion. She had mild motor impersistence but did not display a grasp reflex or Myerson's sign. Motor examination and deep tendon reflexes were normal, but she had an extensor plantar reflex on the left. Cerebellar function and gait were normal.

Lumbar puncture studies and visual evoked potentials were unrevealing. Angiography revealed bilateral high-grade stenosis of the distal internal carotid arteries and collateralization of the lenticulostriate vessels through the posterior communicating arteries and meningeal branches. These findings were consistent with adult-type moya–moya disease (Fig. 1A,B). Figure 1C and D show axial and coronal views demonstrating an enhancing lesion in the anterior mid-body of the corpus callosum (also affecting the septal area and head of caudate) and

This article contains Supplementary Video Clips, available online at <http://www.interscience.wiley.com/jpages/0885-3185/suppmat>.

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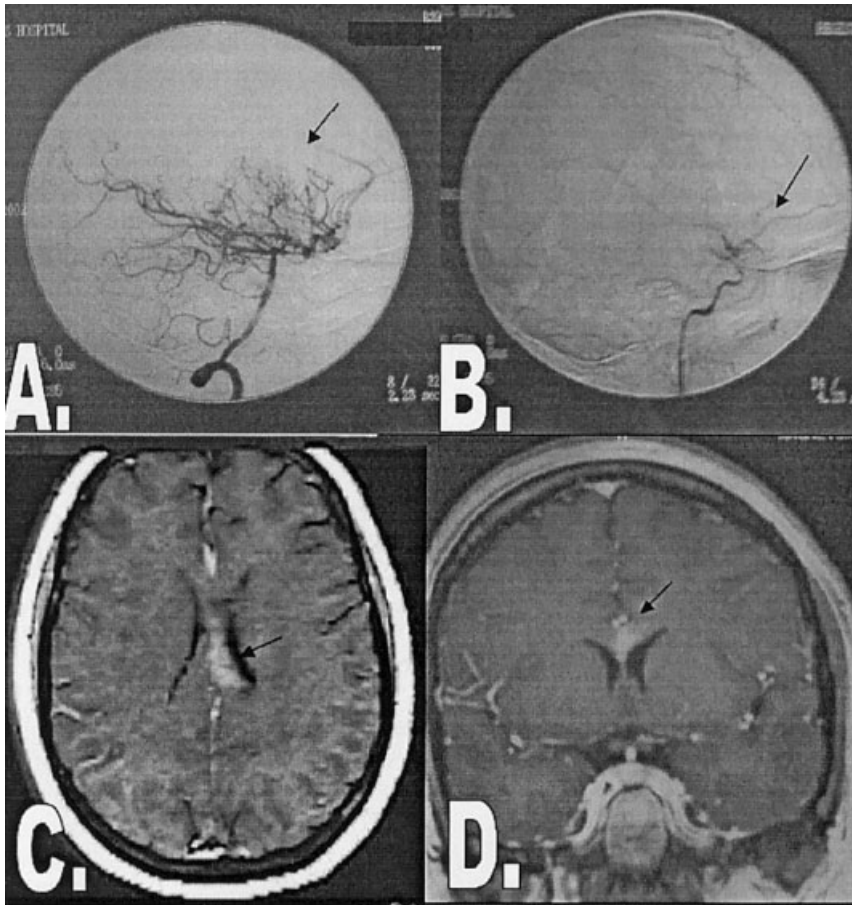


FIG. 1. A and B depict the typical “puff of smoke” appearance (arrows) of moyo-moya disease (left carotid injection, lateral view). An axial (C) and coronal (D) magnetic resonance image depicting the corpus callosum infarction (arrows) at two sites: anterior mid-body comprising the septal area and head of caudate (coronal section) and splenium (axial section). The rostrum and posterior mid-body were also affected (not shown).

the splenium of the corpus callosum, more on the left. In addition, the rostrum and posterior mid-body of the corpus callosum were also affected (not shown).

The patient was examined again at approximately 6 months after her initial presentation. She did not exhibit any interval change upon neurological examination and continued to demonstrate signs of callosal disconnection along with alien limb features.

DISCUSSION

The unilateral tactile anomia and ideomotor apraxia displayed by our patient, along with dissociative phenomena such as intermanual conflict and alien limb, are consistent with a callosal disconnection syndrome.⁶ Brion and Jedynak believed the alien hand sign⁷ was a clinical sign of corpus callosum disconnection. They described a sensory disconnection phenomenon, in which the patient did not recognize his own hand when both palms were placed together out of view, either behind the back, or in front of the patient with closed eyes.⁷ The scope of alien limb syndrome has broadened to include “involuntary” movements that the patients

consider alien to their intent.⁵ Thought to be due to a disruption of the transcallosal fibers and associated supplementary motor areas,¹ the alien hand syndrome was further classified into two types by Feinberg and colleagues.² The first, the frontal alien hand syndrome, may result from damage to the supplementary motor area, anterior cingulate gyrus, medial prefrontal cortex of the dominant hemisphere, and anterior corpus callosum. The symptoms of frontal alien hand syndrome consist of reflexive grasping and groping in the dominant hand. The second type of alien limb requires only a solitary callosal lesion. These cases are characterized by intermanual conflict and apraxia of the nondominant hand. Recently, a posterior alien hand syndrome has been proposed, which spares the corpus callosum and occurs with parietal^{8,9} or thalamic¹⁰ infarcts. In this syndrome, the acting hemisphere is disconnected from sensory input, resulting in purposeless, involuntary behavior such as arm levitation or writhing fingers.¹¹ Additionally, variant cases of alien limb syndrome have been found in patients with partial seizures,¹² Creutzfeldt–Jakob disease,^{13–15} corti-

cobasal ganglionic degeneration,^{16–18} Alzheimer's disease,¹⁹ corpus callosum infarction,^{1,20,21} corpus callosotomy,⁶ bifrontal penetrating cerebral injury,³ anterior cerebral artery territory infarction,^{22–27} anterior communicating artery rupture,^{3,28–30} parietal lobe lesions,^{8,9} posterior cerebral artery territory infarction,^{31,32} capsulothalamic hemorrhage,³³ thalamic infarction,¹⁰ and seizure.³⁴

We report on a case of alien limb resulting from vascular damage secondary to moya-moya disease. Our patient was found to have an ischemic event in the setting of moya-moya disease, which resulted in a callosal disconnection syndrome. Moya-moya disease is a cerebral vasculopathy of unknown etiology³⁵ that is characterized by progressive occlusion of the proximal portion of the carotid arteries, and the development of compensatory collateral vessels. The name moya-moya means a "puff of smoke" and has been used to describe the angiographic appearance of this extensive collateral network of vessels. Although initially thought of as a disease of childhood, moya-moya is well known to occur in adults.^{36,37} The neurological deficits typically result from ischemia produced by arterial occlusion or hemorrhage. To our knowledge, this is the first report of moya-moya disease and alien limb. The patient had nondominant arm involvement and no motor deficits or reflexive grasping. She demonstrated alien limb symptoms similar to the patient of Akelaitis who had undergone callosotomy for intractable epileptic seizures.³⁸ In Akelaitis' report, the patient would attempt to put on clothes with the right hand while pulling them off with the left hand. Similarly, the patient would open a door with the right hand and simultaneously push it shut with the left hand. In another report,³⁹ a patient with callosotomy is described pulling down clothes with one hand and pulling them up with the other, as evidenced in our patient. Akelaitis termed this behavior "diagonistic dyspraxia" to describe the conflict between the intended act and the act actually performed.³⁸ Another patient we observed with a callosal infarction also demonstrated problems with the left hand pulling a blouse off and the right hand putting the blouse back on.²⁰ In these cases and the one reported here, the patients were aware of the alien limb behavior and would express frustration over its interference with routine activities.

The finding of an "alien limb," as in our patient should direct the attention of the treating physician not toward a specific diagnosis, but rather toward a localization of the problem which can be caused by a multitude of pathological conditions. It is not surprising, therefore, that moya-moya disease can result in this phenomenon.

LEGEND TO THE VIDEO

A disconnection syndrome and apraxia is demonstrated.

Segment 1. The patient explains how one hand tries to restrain the other when performing actions.

Segment 2. The segment demonstrates left ideomotor apraxia.

Segment 3. The segment demonstrates the patient's difficulty performing tasks with her left hand.

Segment 4. This segment demonstrates the apparent left-hand agraphesthesia and astereognosis, both secondary to left tactile anomia. The patient was able to correctly identify an object placed in her left hand when asked to choose this object from among a series of objects subsequently placed in the left hand. This finding demonstrates that her right hemisphere is intact and that her apparent agraphesthesia and astereognosis are secondary to the callosal disconnection, which prevents input that is correctly perceived by the right hemisphere from reaching the language region of the left hemisphere (the complete sequence showing intact stereognosis and the ability of the patient to identify objects from multiple choice is discussed in the text but not shown in the video).

REFERENCES

- Geshwind DH, Iacoboni M, Mega MS, Zaidel DW, Cloughesy T, Zaidel E. Alien hand syndrome: interhemispheric motor disconnection due to a lesion in the midbody of the corpus callosum. *Neurology* 1995;45:802–808.
- Feinberg TE, Schindler RJ, Flanagan NG, Haber LD. Two alien hand syndromes. *Neurology* 1992;42:19–24.
- Banks G, Short P, Martinez J, Latchaw R, Ratcliff G, Boller F. The alien hand syndrome. Clinical and postmortem findings. *Arch Neurol* 1989;46:456–459.
- Goldstein K. Zur Lehre der motorischen Apraxie. *J Psychol Neurol* 1908;11:169–187.
- Fisher CM. Alien hand phenomena: a review with the addition of six personal cases. *Can J Neurol Sci* 2000;27:192–203.
- Bogen JE. The callosal syndrome. In: Heilman KM, Valenstein E, editors. *Clinical neuropsychology*. 2nd ed. New York: Oxford University Press; 1985. p 295–338.
- Briou S, Jedynak CP. Troubles du transfert interhemispherique (callosal disconnection) a propos de 3 observations de tumeurs du corps calleux. Le signe de la main etrangere. *Rev Neurol* 1972; 126:257–266.
- Carrilho PE, Caramelli P, Cardoso F, Barbosa ER, Buchpiguel CA, Nitrini R. Involuntary hand levitation associated with parietal damage: another alien hand syndrome. *Arq Neuropsiquiatr* 2001; 59:521–525.
- Marti-Fabregas J, Kulisevsky J, Baro E, Mendoza G, Valencia C, Marti-Vilalta JL. Alien hand sign after a right parietal infarction. *Cerebrovasc Dis* 2000;10:70–72.
- Marey-Lopez J, Rubio-Nazabal E, Alonso-Magdalena L, Lopez-Facal S. Posterior alien hand syndrome after a right thalamic infarct. *J Neurol Neurosurg Psychiatry* 2002;73:447–449.
- Rohde S, Weidauer S, Lanfermann H, Zanella F. Posterior alien hand syndrome: case report. *Neuroradiology* 2002;44:921–923.
- Feinberg TE, Roane DM, Cohen J. Partial status epilepticus associated with asomatognosia and alien hand-like behaviors. *Arch Neurol* 1998;55:1574–1576.
- Oberndorfer S, Urbanits S, Lahrman H, Jarius C, Albrecht G, Grisold W. Familial Creutzfeldt-Jakob disease initially presenting with alien hand syndrome. *J Neurol* 2002;249:631–632.
- Colomer-Rubio E, Sanchez-Roy R, Pareja-Martinez A, et al. Alien hand syndrome in Creutzfeldt-Jakob disease. *Neurologia* 2001;16: 223–226.

15. MacGowan DJ, Delanty N, Petito F, Edgar M, Mastrianni J, DeArmond SJ. Isolated myoclonic alien hand as the sole presentation of pathologically established Creutzfeldt-Jakob disease: a report of two patients. *J Neurol Neurosurg Psychiatry* 1997;63:404–407.
16. Doody RS, Jancovic J. The alien hand and related signs. *J Neurol Neurosurg Psychiatry* 1992;55:806–810.
17. Gibb WRG, Luther PJ, Marsden CD. Corticobasal degeneration. *Brain* 1989;112:1171–1192.
18. Riley DE, Lang AE, Lewis A, et al. Cortical-basal ganglionic degeneration. *Neurology* 1990;40:1203–1202.
19. Green RC, Goldstein FC, Mirra SS, Alazraki NP, Baxt JL, Bakay RA. Slowly progressive apraxia in Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 1995;59:312–315.
20. Watson RT, Heilman KM. Callosal apraxia. *Brain* 1983;106:391–403.
21. Suwanwela NC, Leelachevasit N. Isolated corpus callosal infarction secondary to pericallosal artery disease presenting as alien hand syndrome. *J Neurol Neurosurg Psychiatry* 2002;72:533–536.
22. Ong Hai BG, Odderson IR. Involuntary masturbation as a manifestation of stroke-related alien hand syndrome. *Am J Phys Med Rehabil* 2000;79:395–398.
23. Wu FY, Leong CP, Su TL. Alien hand syndrome: report of two cases. *Changcheng Yi Xue Za Zhi* 1999;22:660–665.
24. Kischka U, Ettlin TM, Lichtenstern L, Riedo C. Alien hand syndrome of the dominant hand and ideomotor apraxia of the non-dominant hand. *Eur Neurol* 1996;36:39–42.
25. McNabb AW, Carroll WM, Mastaglia FL. "Alien hand" and loss of bimanual coordination after dominant anterior cerebral artery territory infarction. *J Neurol Neurosurg Psychiatry* 1988;51:218–222.
26. Goldberg G, Mayer MH, Togliu JU. Medial frontal cortex infarction and the alien hand sign. *Arch Neurol* 1981;38:683–686.
27. Shahani B, Burrows P, Whitty WM. The grasp reflex and perseveration. *Brain* 1970;93:181–192.
28. Starkstein SE, Berthier M, Leiguarda R. Disconnection syndrome in a right-handed patient with right hemispheric speech dominance. *Eur Neurol* 1988;28:187–190.
29. Leiguarda R, Starkstein S, Berthier M. Anterior callosal hemorrhage. *Brain* 1989;112:1019–1037.
30. Tanaka Y, Iwasa H, Yoshida M. Diagnostic dyspraxia: case report and movement-related potentials. *Neurology* 1990;40:657–661.
31. Groom KN, Ng WK, Kevorkian CG, Levy JK. Ego-syntonic alien hand syndrome after right posterior cerebral artery stroke. *Arch Phys Med Rehabil* 1999;80:162–165.
32. Levine DN, Rinn WE. Opticosensory ataxia and alien hand syndrome after posterior cerebral artery territory infarction. *Neurology* 1986;36:1094–1097.
33. Ventura MG, Goldman S, Hildebrand J. Alien hand syndrome without a corpus callosum lesion. *J Neurol Neurosurg Psychiatry* 1995;58:735–737.
34. Leiguarda R, Starkstein S, Nogueira M, Berthier M, Arbelaz R. Paroxysmal alien hand syndrome. *J Neurol Neurosurg Psychiatry* 1993;56:788–792.
35. Takeuchi K. Occlusive diseases of the carotid artery: especially on their surgical treatment. *Shinkei Shimpō* 1961;5:511–543.
36. Suzuki J, Takaku A. Cerebrovascular moyamoya disease: disease showing abnormal net-like vessels in base of brain. *Arch Neurol* 1969;20:288–299.
37. Coakham HB, Duchon LW, Scaravilli F. Moya-moya disease: clinical and pathological report of a case with associated myopathy. *J Neurol Neurosurg Psychiatry* 1979;42:289–297.
38. Akelaitis AJ. Studies on the corpus callosum IV. Diagnostic dyspraxia in epileptics following partial and complete section of the corpus callosum. *Am J Psychiatry* 1944;101:594–599.
39. Sperry EW, Gazzaniga MS, Bogen JE. Interhemispheric relationships: neocortical commissures; syndromes of hemispheric disconnection. In: Vinken PJ, Bruyn GW, editors. *Handbook of clinical neurology*. Amsterdam: North Holland; 1969. p 273–290.

Abnormalities of Dopaminergic Neurotransmission in SCA2: A Combined ^{123}I - βCIT and ^{123}I -IBZM SPECT Study

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Abstract: Extrapyramidal features may occur in spinocerebellar ataxias consistent with neuropathological evidence of nigrostriatal involvement. Recently, striatal dopaminergic neurotransmission was found to be abnormal in the uncommon parkinsonian presentation of spinocerebellar ataxia type 2 (SCA2). We have investigated, therefore, striatal dopamine transporter and D2 receptor function in a series of 9 patients with the more common ataxic presentation of SCA2 using single photon emission computed tomography and $\beta\text{-CIT}$ as well as IBZM. Age-matched healthy subjects and patients with Parkinson's disease (PD) served as controls. All except 1 SCA2 patient exhibited slowness of limb movements without rigidity or rest tremor. In addition, cervical dystonia was present in 5 and dystonic head tremor in 2 SCA2 patients. Striatocerebellar (S/C) ratios of $\beta\text{-CIT}$ binding were significantly reduced in SCA2 patients compared to control subjects, and they were within the range of PD patients. S/C ratios of IBZM binding were significantly reduced in SCA2 patients compared to control subjects. We conclude that dopaminergic neurotransmission is impaired in the ataxic presentation of SCA2, with a prominent loss of striatal dopamine transporter function. Both slowness of limb movements as well as dystonia in the ataxic SCA2 phenotype may reflect dysfunction not only at cerebellar but also at basal ganglia level. © 2004 Movement Disorder Society

Key words: SCA2; dopamine; SPECT; ADCA

Spinocerebellar ataxia type 2 (SCA2) is an autosomal dominant cerebellar ataxia that is progressive and typically associated with slow saccades. The clinical phenotype of SCA2 is caused by an increased number of CAG repeats in the 5' coding region on chromosome 12.^{1–3} Intermediate and/or interrupted CAG repeat expansions

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