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Letter to the Editor: New Observation

Transient Alien Hand Syndrome: Thinking Beyond Neurodegeneration

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An 83-year-old, right-hand dominant man with a history of coronary artery disease, chronic kidney disease, hypertension, and cigarette smoking presented to the emergency department complaining of involuntary movement involving his left arm and hand. His symptoms started suddenly while sitting in a chair at home. He first developed an abnormal sensation in his left arm, which then started to drift up in the air without his control. When he tried to hold his left arm down with his right hand, his left hand reached out and grabbed his right wrist forcefully. Being disturbed, he again attempted to pull his left forearm down, at which point the left hand reached across to scratch the right forearm. He then stood up and reached for his walker. To his surprise, the left arm again grasped the right wrist, causing him to lose his grip on the walker and fall. He became alarmed and, fearing that the left arm would reach up and attempt to choke him, called 911.

Each occasion of uncontrollable hand behavior ceased within a few seconds, and the entire episode lasted less than 30 minutes. The patient demonstrated the actions of left hand to the examiner (Figure 1) and was scared to touch it when brought to the ED. He described the arm being entirely out of his control and as having "a mind of its own". During examination, approximately 2 hours from symptom onset, the abnormal sensation and movements of the left hand had resolved. He denied any arm or leg weakness, although subtle left arm pronator drift was observed. The rest of his neurological examination, including testing for cortical sensations, was normal. The National Institute of Health Stroke Scale (NIHSS) score was 1 for left arm drift.

CT head was normal, and CT angiography (CTA) showed mild diffuse atherosclerosis and no large vessel occlusion. Brain MRI showed multiple small acute cortical infarcts in the right parietal and temporal lobe (Figure 1). Despite presenting to the hospital within 4.5 hours, the patient had NIHSS ≤5 with non-disabling deficits, so intravenous thrombolysis was not considered. The patient was treated with dual antiplatelet therapy for 21 days followed by aspirin (ASA) monotherapy and he was started on high-intensity statin (atorvastatin 80 mg daily).[1] A target blood pressure of less than 130/80 was established, and he received stroke-related education.[2]

His pronator drift resolved within 48 hours, and his echocardiogram and 72-hour Holter were normal. Given his age, multiple infarcts, and lack of a clear vascular source of embolism, 14-day Holter monitoring was done, which revealed paroxysmal atrial fibrillation. His ASA was switched to apixaban 2.5 mg twice daily (dose reduced due to age and creatinine clearance). At his 3-month follow-up, he remained recurrence-free.

The presentation described here has been called alien hand syndrome (AHS), an uncommon neurologic syndrome that is characterized by a foreign sensation of the limb in conjunction with involuntary motor actions. Classically, patients describe the limb behaving autonomously or as having "a will (or mind) of its own".[3,4] AHS has been observed in patients with a variety of underlying conditions including tumor, infarction, viral encephalitis, Creutzfeldt–Jakub disease, and neurodegenerative disorders.[3,4] Thus, its presentation warrants thorough investigation. AHS is most often reported in neurodegenerative disorders such as corticobasal syndrome, in which it is a hallmark sign. However, the chronicity of these disorders distinguishes it from other, more acute causes. The abrupt onset and transient course of the patient's symptoms warrant consideration of epileptic, metabolic, and vascular etiologies. Frontal lobe seizures may occur without loss of consciousness, but typically cause brief, repetitive, and stereotyped clonic or dystonic movements. The onset of metabolic conditions is generally slower and is often associated with non-focal neurological manifestations such as altered mental status. Vascular pathology, particularly ischemic stroke, is a distinct possibility, considering the acute onset of symptoms and mild pronator drift. Interestingly, the first description of AHS, by Goldstein in 1908, was in a patient with stroke.[5]

In our patient, the complex motor behavior of the left upper extremity would suggest localization to areas involved in motor planning and programing in the right cerebral hemisphere (Figure 1). These include the motor regions, which provide motor engrams for the movements; cortico-striato-thalamo-cortical loops, which participate in the initiation and control of movement; and parietal areas, which are involved in spatial perception and

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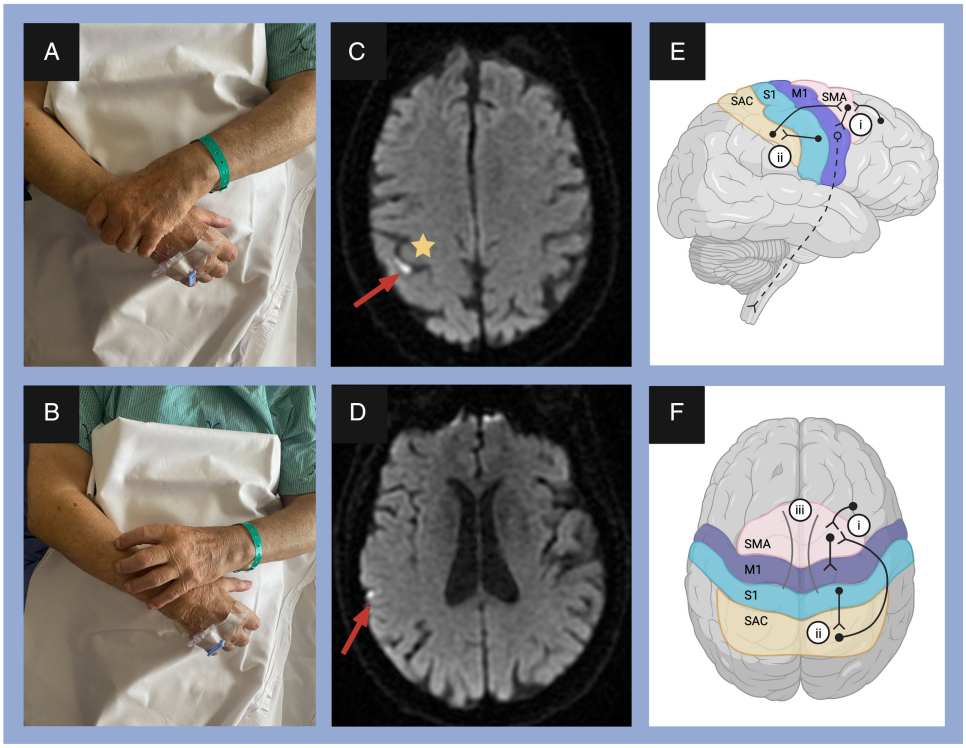


Figure 1: Patient imitating motor behaviors that occurred during the event including grabbing the right wrist (A) and scratching the right arm (B) with the left hand when the patient attempted to put his left arm down. Diffusion-weighted imaging (DWI) axial view shows infarcts (red arrows) in the right parietal near the hand knob area in the motor (precentral) gyrus (yellow star) (C) and right temporal lobe (D). Diagram showing possible sensorimotor regions and pathways involved in alien hand syndrome in sagittal (E) and axial (F) views. i. Frontal cortex; ii. Parietal cortex; iii. Corpus callosum. SMA: supplementary motor area; M1: primary motor cortex; S1: primary somatosensory cortex; SAC: sensory association. Figure created with BioRender.com.

awareness. Historically, three topo-clinical variants of AHS have been recognized, each of which is associated with specific clinical findings that may assist in localization: anterior AHS (which may be further subdivided into frontal and callosal subvariants) and posterior AHS (Table 1).[3,4,6] Despite understanding of the brain regions involved in the expression of AHS, the exact pathophysiology is unclear. It is hypothesized that damage to the supplementary motor area, which is activated during the development of the conscious intention to move and normally functions to inhibit the primary motor cortex, may result in movement of the contralateral hand without intention.[7] Damage to the corpus callosum disrupts interhemispheric connections that normally facilitate synchronization or dissociation of the hands when performing bimanual and unilateral tasks, leading to intermanual conflict.[4] Finally, the parietal lobe is involved in motor planning and integration of sensory signals, including position sense. Damage to this region may impair the ability to perceive motor behavior and, consequently, the ability to recognize one's own movement.[7,8] In the case described above, the patient described abnormal sensation, spontaneous arm levitation, grasping by the nondominant hand, and a feeling of the arm being outside of his control. This presentation suggested involvement of the right parietal or frontal lobe, and imaging ultimately revealed lesions in the right parietal cortex near the hand area as well as a punctate lesion in the right temporal cortex. Overlap in AHS phenotypes, which has also been described elsewhere, may be due to network disruption, highlighting the widespread and distributed network involved in movement planning, programing, and execution.[6]

Although apparently rare, acute intracranial pathology should be suspected in patients presenting with symptoms of sudden onset motor behavior that is outside of conscious control, particularly when it involves the nondominant upper extremity. Localization of the lesion is often possible based on presenting symptoms, which allows accurate analysis of symptoms, appropriate investigations, and early diagnosis. Knowledge of this (and other) uncommon and unusual neurological presentations serves to avoid misdiagnosis, particularly in complex patients such as those with mental health issues or those being investigated for functional neurological disorders. Finally, despite being more commonly associated with

Table 1: Typical features of topo-clinical variants of alien hand syndrome. Note that manifestations can overlap when multiple brain regions are involved, networks disrupted or vary based on hemispheric dominance

Clinical features	AHS variants		
	Anterior		
	Frontal	Callosal	Posterior
Typical lesion location	SMA, CG, medial prefrontal cortex or CC	Anterior CC	Parietal lobe; rarely posterior CC
Classical hand/limb behavior	Reflex grasping, groping and compulsive manipulation of tools	Intermanual conflict	Arm levitation
Hand involvement (typically)	Dominant	Non-dominant	Non-dominant
Limb paresis	May be present	Absent	Absent
Sensory loss	Absent	Absent	Can be present
Other signs	Impaired bimanual coordination	Ideomotor apraxia, tactile anomia and agraphia involving left hand	Triple ataxia (sensory, optic, cerebellar), hemispatial neglect, denial of ownership of hand

CC, corpus callosum; CG, cingulate gyrus; SMA, supplementary motor area.

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neurodegenerative conditions, acute AHS could be a presenting sign of an underlying treatable and preventable condition, as it was for this patient.

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A. Hemy analyzed the data and revised the paper.
R.J. Singh supervised the study and was involved in the conception, design, writing, analysis, and revision of the paper.

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