

Chapter

Transient ischemic attacks and stroke mimics and chameleons

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In most cases the diagnosis of transient ischemic attacks (TIAs) and strokes is straightforward. However, there are non-vascular disorders that can present with neurologic deficits that simulate cerebrovascular disease (mimics), and TIAs and strokes that can present in unusual ways that resemble something else (chameleons) (Tables 1.1 and 1.2). In this chapter, eight clinical scenarios highlight some of the most common stroke or TIA mimics and chameleons. Careful history gathering through clinical examination, and appropriate imaging tests are needed to identify these mimics and chameleons.

Case 1. Patient with focal neurologic deficits

Case description

A 72-year-old man was found by his wife lying on the ground. She noticed he was rather sleepy, did not answer questions, and was unable to move his right side. She had last seen him well 20 minutes earlier. Past medical history was remarkable for arterial hypertension, dyslipidemia, and a left middle cerebral artery (MCA) stroke 2 years earlier. He had recovered with only minor sequelae in performing fine movements with his right hand.

When he arrived at the emergency department, half an hour later, he was awake, had a global aphasia, right central facial paresis, right-sided hemiparesis (Medical Research Council grade 3), and bilateral Babinski signs. The National Institutes of Health Stroke Scale (NIHSS) score was 12. According to his wife, he was improving clinically. He had no lateral tongue biting, urinary or fecal incontinence, or trauma. He was afebrile. Blood pressure was 160/70 mmHg. Blood

glucose, full blood count, electrolytes, C-reactive protein (CRP), INR, and a PTT were unremarkable. Brain computed tomography scan (CT scan) showed an old left insular infarct (Figure 1.1). Otherwise, the CT was unremarkable without signs of an acute infarct.

As he was leaving the CT-scan room, he had brief involuntary movements of the right hemibody, with twitching of the right side of the face, and right gaze deviation. The involuntary movements lasted for approximately 20 seconds. Brain magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) sequences showed no evidence of acute ischemic lesions.

Diagnostic reasoning

In the emergency department, physicians have to decide promptly what is the most probable diagnosis and what the next action will be. When our patient arrived at the emergency department, his neurologic examination and presentation were compatible with an acute ischemic stroke of the left MCA territory. He had sudden onset of focal neurologic deficits and had multiple vascular risk factors. As the patient was last seen without symptoms within 50 minutes before arriving at the emergency department, the patient was well within the 4.5 hour time window from symptom onset or from last seen well to administer intravenous thrombolysis with recombinant tissue plasminogen activator (tPA). The CT was also unremarkable for acute ischemic stroke and excluded other disorders that could mimic an acute ischemic stroke such as primary central nervous system (CNS) tumors, metastasis, brain abscess, or hemorrhages.

However, the adventitious movements experienced by the patient as he was leaving the CT-scan

Chapter 1: TIAs and stroke mimics and chameleons**Table 1.1** Examples of TIA and stroke mimics

- Intracranial mass lesions (tumors)
- Intracranial infection (abscess, encephalitis)
- Subdural hematoma
- Seizures and Todd's paralysis
- Acute peripheral vestibulopathy (benign paroxysmal positional vertigo [BPPV] or acute labyrinthitis)
- Transient global amnesia
- Peripheral neuropathies including Bell's palsy
- Migraine with aura including sporadic or familial hemiplegic migraine
- Metabolic disturbances that may cause new neurologic deficits or re-expression of previous deficits (hypoglycemia, non-ketotic hyperglycemia, hyponatremia, hypoxia, hepatic encephalopathy, Wernicke–Korsakoff syndrome, alcohol and drug intoxication, systemic infection)
- Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS)
- Psychiatric disorders (conversion disorder, anxiety or panic attacks, malingering)
- Acute demyelination (multiple sclerosis)
- Alternating hemiplegia
- Syncope
- Retinal/ocular pathology

Table 1.2 Examples of TIA and stroke chameleons

- Bilateral thalamic infarcts
- Cortical stroke or TIA
- Limb shaking TIA
- Capsular warning syndrome
- Bilateral occipital strokes or TIAs
- Lateral medullary strokes or TIAs

room raised concerns for a possible seizure secondary to an acute ischemic stroke, or a seizure with a Todd's paralysis since the very onset. Partial or secondary generalized seizures may occur in the acute phase of ischemic stroke. Initially described in the nineteenth century by Robert Bentley Todd, Todd's paralysis refers to a post-seizure event, defined as a transient weakness and depression of motor ability lasting hours to days. It usually affects one or more limbs and follows a focal seizure, or more rarely a generalized tonic-clonic seizure [1]. Sometimes, there may be other neurologic signs such as aphasia, neglect, or psychosis depending on the epileptic focus and surrounding focal areas involved. Therefore, features of post-seizure Todd's paralysis may be similar to an acute ischemic stroke. Several clinical series present unwitnessed or unrecognized seizures with the post-ictal state misdiagnosed as stroke being the most common stroke mimic.

**Figure 1.1** Brain CT scan showing an old infarct in the left middle cerebral artery territory.

Some small series suggest that patients with structural lesions, such as those with previous brain infarcts and the elderly, may be more likely to have transient focal weakness following a seizure. Although there is no consensus regarding the pathophysiology of Todd's paralysis, hypotheses regarding its pathogenesis include: neuronal desensitization, neurotransmitter depletion, active suppression and exhaustive neuronal

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firing, and localized cerebral hypoperfusion resulting from motor cortex exhaustion.

A detailed description of the onset of symptoms is critical to distinguish between Todd's paralysis and an acute ischemic stroke. However, patients are often unable to report onset of symptoms either because they are aphasic or unaware of their deficits. In these cases, accompanying family members may provide valuable information. However, in our patient, symptom onset was not witnessed, and doubts regarding the precise diagnosis remained. This diagnostic uncertainty has a clear repercussion in management, as interventional stroke therapies have potential serious side effects such as intracranial bleeding. Also, although patients with seizures at stroke onset were excluded from thrombolytic trials due to the possibility of confusion with Todd's paralysis, case series suggest that thrombolysis could be useful if there is evidence of a new ischemic stroke. Therefore, it is currently recommended by the European Stroke Organisation that intravenous tPA may be used in patients with seizures at stroke onset, if the neurologic deficit is related to acute cerebral ischemia (Class IV, Good Clinical Practice – GCP) [2]. Guidelines from the American Heart Association/American Stroke Association (AHA/ASA) [3] state that “intravenous tPA is reasonable in patients with a seizure at the time of onset of stroke, if evidence suggests that residual impairments are secondary to stroke and not a postictal phenomenon” (Class IIa, Level of Evidence C).

The elderly have a high incidence of epilepsy that may be related to cerebrovascular disease [4]. In our patient, there were subtle symptoms in favor of a seizure with Todd's paralysis such as his sleepiness, his neurologic improvement, and the past history of a cortical infarct.

However, our patient was found lying on the floor with an acute focal neurologic deficit. He had multiple vascular risk factors including hypertension, dyslipidemia, and a previous stroke, all of which could have been in favor of a new stroke. However, our patient did not have a prior history of seizures.

In these situations, MRI with DWI/ADC sequences can be useful to exclude the presence of acute cerebral lesions not yet detectable with a CT scan. DWI/MRI is the most useful exam to differentiate between an acute ischemic stroke and stroke mimics. Of note, there are reports of hyperintensities on brain DWI/MRI in Todd's postepileptic paralysis described as gyriform cortical hyperintensities that do not necessarily reflect

ongoing seizure activity. These image changes are not associated with a particular vascular distribution, and rather reflect the epileptic foci and surrounding tissue.

Brain CT angiography may be an indirect useful modality in differentiating Todd's paralysis from early seizure and ischemia by detection of intracranial occlusions, which would favor a diagnosis of an ischemic lesion [5]. Electroencephalography (EEG) does not help in differentiating these entities, as focal slowing and epileptiform activity can occur in both acute ischemia and in the post-seizure period.

Tip

An adequate clinical history that properly characterizes time of symptom onset is critical to distinguish TIA or stroke from other pathologies that can also present with focal neurologic deficits.

Case 2. Headache and hemiparesis

Case description

A 21-year-old woman noticed that upon standing up from a chair, her left side became weak and numb. One hour later, she had a throbbing left-sided headache and felt nauseous. She had a history of recurring unilateral throbbing headaches of moderate intensity accompanied by nausea, photophobia, and sonophobia. Headaches were severe enough to interfere with her daily activities. One year earlier, she had a similar episode of headache, preceded by a feeling of heaviness of the right arm which subsided in a few hours. Her sister and mother had a similar history of headaches and occasional weakness. On admission, her blood pressure was 105/60 mmHg. When she arrived at the emergency department she had a left central facial paresis, a left hemiparesis (Medical Research Council grade 4), and left hemisensory loss. Blood glucose was 110 mg/dL. Brain MRI was unremarkable. The headache resolved within 3 hours, but her left hemiparesis persisted for 5 more hours.

Diagnostic reasoning

The young age of our patient and the lack of traditional vascular risk factors raised the possibility of an alternative diagnosis to a TIA. TIAs are rare in young patients without vascular risk factors. The presence of recurrent transient neurologic deficits followed by an evanescent headache led to the diagnosis of migraine with aura. Migraines usually start in the first or second decades

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of life. Our patient had a past history of pulsatile, moderate intensity, unilateral headaches with nausea and photophobia that suggest a diagnosis of migraines [6]. Migraine is a common disorder that can be accompanied by aura in about a third of patients. Migraines with aura can present with neurologic symptoms resembling a TIA or stroke. An aura is defined as transient focal neurologic symptoms that usually precede, or sometimes accompany, the headache. The symptoms usually last minutes and are fully reversible, and are usually followed by a headache and other associated migrainous symptoms [7]. However, the headache may sometimes be absent masking the correct diagnosis. The typical migraine aura is most commonly visual, but it may also be characterized by sensory, speech, or language difficulties. Visual symptoms may be characterized by positive features such as zigzag lines or flickering spots with or without negative features such as scotomata. Basilar migraine may present with double vision, unsteadiness, fainting, or losing consciousness. Retinal or ophthalmic migraine typically affects only one eye. Whenever the aura includes weakness as a symptom, it is classified as hemiplegic migraine, as in our patient. Distinguishing motor from sensory auras can be challenging at times. The motor aura should be a clearly characterized motor deficit such as weakness with difficulty moving one hand, arm, or leg. Some patients with a sensory aura may report dropping objects. A population-based epidemiological survey found a prevalence of 0.005% for hemiplegic migraine [8]. Patients with hemiplegic migraine may, in addition to motor aura, have any of the aura symptoms of migraines with aura or basilar migraine [7]. Most patients also have attacks of migraines with typical aura – without weakness. The most common accompanying aura symptom besides weakness in these patients is sensory. The typical sensory aura is characterized by tingling involving one of the digits that gradually progresses to involve other digits, up to the arm, and then affects the face, tongue, and later the body and leg. The different aura symptoms progress slowly over 20–30 minutes and occur successively, mainly in the following order: visual, sensory, motor, aphasic, and basilar disturbances.

Migraine aura is considered to be caused by cortical spreading depression, which is characterized by a brief neuronal excitation that initiates a depolarization wave that moves across the cortex followed by a prolonged inhibition of neuronal activity [9]. Hemiplegic migraine can occur as a sporadic or a familial disorder.

Patients with sporadic hemiplegic migraine lack a family history of at least one affected first-degree or second-degree relative. The sporadic and hemiplegic migraine forms have a similar prevalence of 0.002–0.003%. Familial hemiplegic migraine (FHM) is dominantly inherited. The presence of similar symptoms in both her sister and mother suggest this type of inheritance in our patient. FHM1 is caused by mutations in the *CACNA1A* gene located in chromosome 19, FHM2 by mutations in the *ATP1A2* gene located in chromosome 1, and FHM3 by mutations in the *SCN1A* gene located in chromosome 2. All the involved genes take part in ion transport. Both sporadic and familial forms of hemiplegic migraine have similar clinical presentations. The mean frequency of episodes is approximately three per year; the frequency and severity tend to decrease with advancing age.

Imaging and cerebrospinal fluid (CSF) studies done during or after an episode of migraine are unremarkable, except in FHM1 where cerebellar atrophy may be present.

Headache is a common feature of acute ischemic stroke. Twenty-seven percent of patients experience a headache at stroke onset. Sometimes, headache in patients with stroke may point to a cervical artery dissection as the cause. There is also a specific type of stroke related to migraine – migrainous infarction. In migrainous infarction the symptoms associated with the typical aura are not fully reversible. The International Classification of Headache Disorders, 3rd Edition (ICHD-3) beta version defines migrainous infarction as one or more otherwise typical auras persisting beyond one hour with neuroimaging confirmation of an ischemic infarction in the affected territory [6]. Meningitis and intracranial venous thrombosis may also present with headaches and focal neurologic deficits, but usually other diagnostic clues are present.

Tip

Diagnosis of hemiplegic migraine relies on a careful description of the aura and on the exclusion of other symptomatic causes. The diagnosis is often made only after recurrent, stereotypic attacks.

Case 3. Sudden memory impairment**Case description**

A 65-year-old woman was admitted to hospital due to a sudden onset of memory impairment. Early in the

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morning, she telephoned her husband telling him she had vertigo and was not feeling well. Five minutes later, when her husband found her, she made him repeat questions: Where am I? What happened? What am I doing here? What day is this? Although he answered appropriately, she did not seem to remember his answers, as she repeated the same questions over and over again. She also did not remember what she had done the day before. This episode lasted 5 hours, with a gradual improvement in her ability to recall information. During the episode, she never lost contact with her husband. He did not notice any involuntary movements or automatisms. When she was seen at the emergency department, she was able to recall new information. However, she could not remember what had happened early in the day. She had a past history of hypertension and was under treatment with lisinopril. There was no history of recent head trauma. She did not take any drugs or new medications. On admission, she was afebrile. Blood pressure was 113/70 mmHg. Neurologic examination was unremarkable, including her ability to recall new information, tested by the three-word test/word list and evocation of recent events. Blood glucose was 120 mg/dL. Brain MRI with DWI and ADC sequences were unremarkable. EEG showed focal slowing or epileptiform activity. Follow-up brain MRI with diffusion sequence performed 3 days later showed a rounded image restriction in the CA1 segment of the right hippocampus (Figure 1.2). She did not have further symptoms.

Diagnostic considerations

This sudden impairment of memory is consistent with transient global amnesia (TGA). The incidence of TGA ranges between 3 and 8 per 100 000 people per year [10]. TGA is characterized by sudden onset of anterograde and retrograde amnesia lasting for up to 24 hours, but usually lasting substantially less. There should be no loss of personal identity, personality, language, or visuospatial functions during the amnesic episode. Also, no other neurologic deficits, recent head trauma, or signs of a seizure should be present. After the episode, anterograde memory returns to normal, but the patient may never remember what happened during the period of amnesia. TGA most commonly occurs in patients in their sixth or seventh decade of life. Headaches, dizziness, or nausea may be present during an episode of TGA. Strenuous physical activities or strong emotional events may antedate onset

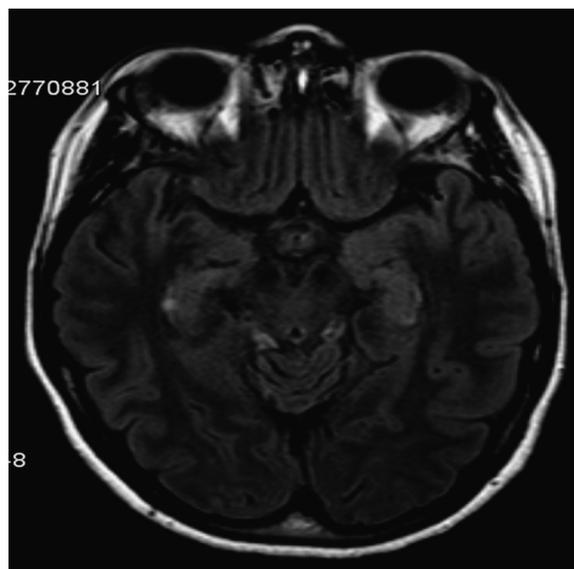


Figure 1.2 Brain MRI showing a rounded image in the CA1 segment of the right hippocampus.

of symptoms [11]. Neuroimaging studies following an acute TGA event show transient perturbation of specific hippocampal circuits involved in memory processing. Focal diffusion lesions can be selectively detected in the CA1 field of the hippocampal cornu ammonis on brain MRI with DWI/ADC when done approximately 72 hours after symptom onset.

Although migraine, focal ischemia, venous flow abnormalities, and epileptic phenomena have been implicated in the pathophysiology of TGA, the factors triggering these unique events remain unknown. Recent data suggest that the vulnerability of the CA1 neurons to metabolic stress plays an important role in the pathophysiological cascade, leading to an impairment of hippocampal function during TGA [12].

There are cases of transient amnesia due to focal seizure activity also known as transient epileptic amnesia. Transient epileptic amnesia has clinical presentation similar to TGA episodes and tends to occur in the morning hours, but it can be distinguished by the shorter duration and repeated amnesic periods.

TIAs or strokes with memory impairment are rare. Every region of the limbic system involved in memory processing may be damaged by strokes, but very rarely in isolation. The combination of amnesia with other acute associated neurologic deficits often leads to the suspicion of a cerebrovascular event in these patients [13].

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Tip

TGA leads to an isolated temporary memory impairment that can last up to 24 hours.

Case 4. Focal neurologic deficits due to metabolic disturbances**Case description**

A 60-year-old woman was admitted to hospital half an hour after her husband noticed increased somnolence, confusion, and decreased strength in her left arm and leg. She had taken her medications during the morning and had gone jogging. Two hours later, her husband found her to be somnolent, with confused speech and difficulty moving her left arm and leg. She had a past history of diabetes mellitus type 2 and ischemic heart disease; she was on metformin, glibenclamide, aspirin, and bisoprolol. Upon admission, neurologic examination showed impaired alertness, confusion, and left hemiparesis (Medical Research Council grade 3). Blood glucose level was 50 mg/dL. She immediately received intravenous 10% glucose. Brain CT scan was unremarkable. Approximately 20 minutes following correction of her blood glucose levels, she started to improve, and made a complete recovery 5 hours after symptom onset. It was later determined that the patient had taken a higher dose of glibenclamide.

Diagnostic considerations

Hypoglycemia and less often hyperglycemia (blood glucose concentration >400 mg/dL) can cause focal neurologic deficits that can mimic a TIA or stroke [14]. Hypoglycemia is a very important differential diagnosis of TIA and stroke. Generally defined as a blood glucose level <70 mg/dL (3.9 mmol/L), it is more common among patients with diabetes mellitus. However, any patient can have hypoglycemia. Causes of hypoglycemia include medications (insulin or sulfonylureas), exercise, fasting, alcohol, insulin secreting tumors, and endocrine disorders such as Addison's disease. In our patient, a personal history of diabetes mellitus and antidiabetic medications namely with sulfonylureas (glibenclamide) should lead to the suspicion of a broad differential diagnosis including hypoglycemia. Glucose is an obligate metabolic fuel for the brain under physiologic conditions, and it is essential for brain metabolism as the brain cannot synthesize glucose or store more than a few minutes' supply as glycogen. Therefore, the

brain needs a continuous arterial supply of glucose. As the plasma glucose concentration falls, blood-to-brain glucose transport becomes insufficient to support brain energy metabolism and function. If hypoglycemia is severe and prolonged and remains untreated, it can lead to a life-threatening situation. Acute effects of hypoglycemia are primarily neurologic. Symptoms of hypoglycemia are initially related to catecholamine release, and later, if untreated, due to neuroglycopenia. Autonomic symptoms include tachycardia, diaphoresis, tremor, anxiety, and hunger. These symptoms are important warnings; however, they may be lacking, for example, among diabetic patients with autonomic insufficiency or in patients on beta-blockers like our patient. Beta-blockers may mask the sympathetic nervous system manifestations of hypoglycemia, and therefore, patients may manifest only symptoms of neuroglycopenia. Neuroglycopenic symptoms are usually present when levels of blood glucose are <50 mg/dL (<2.8 mmol/L). However, these thresholds are dynamic, and in patients with poorly controlled diabetes mellitus, these thresholds are shifted to higher blood glucose concentrations. Neuroglycopenic symptoms include impairment of consciousness that can progress to coma if untreated, confusion, abnormal behaviors, seizures, headaches, and focal neurologic symptoms [15]. Therefore, measurement of blood glucose levels should be part of the initial evaluation of all patients presenting with focal neurologic deficits. Focal neurologic deficits in hypoglycemia may include aphasia, homonymous hemianopsia, hemisensory deficits, hemiparesis, unilateral hyperreflexia, and Babinski sign(s). Both the American Heart Association (AHA) and the European Stroke Organisation (ESO) recommend determination of blood glucose concentration in their guidelines for the evaluation of stroke patients [1,2]. When hypoglycemia is detected, treatment should be started as soon as possible. Both intravenous dextrose and infusion of 10–20% glucose can be used to correct hypoglycemia. Thiamine, 100 mg intravenously or intramuscularly, is given to patients with alcohol dependence to prevent Wernicke's encephalopathy before administering glucose. If intravenous therapy is not possible, subcutaneous or intramuscular glucagon may be used. For non-hypoglycemic patients, excessive dextrose-containing fluids have the potential to exacerbate cerebral injury. Therefore, normal saline is more appropriate if rehydration is required. Of note, there can be a delay of hours to days between correction of blood glucose concentration and improvement

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of neuroglycopenic symptoms. If abnormalities persist longer than 30 minutes following glucose administration and hypoglycemia has not recurred, other causes should be investigated with brain imaging and appropriate laboratory evaluation.

Imaging abnormalities in patients with hypoglycemia are uncommon but very variable, weakly associated with the neurologic deficits, and about a fifth may mimic an acute ischemic stroke. Diffuse and extensive injury observed on DWI with MRI predicts a poor neurologic outcome in patients with hypoglycemic injuries [16].

Other metabolic disturbances that may account for focal neurologic deficits include hyponatremia, hypernatremia [17], and hepatic encephalopathy [18].

Tip

Always check blood glucose concentration in patients presenting with impaired consciousness or focal neurologic symptoms.

Case 5. Recurrent stroke?

Case description

A 78-year-old woman was admitted to hospital due to worsening left-sided hemiparesis. Past medical history was remarkable for diabetes mellitus, dyslipidemia, atrial fibrillation, hypertension, and a right MCA infarct 2 years earlier. She was on metformin, simvastatin, enalapril, and warfarin. As a result of her stroke, she had a left hemiparesis (Medical Research Council grade 4) that allowed her to do most of her daily activities. On the day before admission, her son noticed she was more sleepy and confused, and on the day of admission, he noticed she had increased difficulty moving her left side, shortness of breath, and cough. On admission, she was afebrile. Respiratory rate was 20 cycles per minute. Blood pressure was 137/72 mmHg. Oxygen saturation was 92% on room air. Her breath sounds were decreased over the left lung base. She was somnolent and had a left hemiparesis with a left Babinski sign. There was a neutrophilic leukocytosis. CRP was 7 mg/dL. Blood glucose concentration was 233 mg/dL. Electrolytes and renal function tests were unremarkable. INR was 2.3. Chest X-ray showed consolidation of the left lung base. Brain MRI showed an old right MCA infarct with no new acute lesions on DWI or ADC sequences. She received antibiotics for community-acquired pneumonia,

and her neurologic deficits returned to baseline after 3 days.

Diagnostic considerations

In our patient it was important to consider if the patient had a new stroke. The presence of vascular risk factors, such as hypertension, dyslipidemia, and atrial fibrillation, a previous stroke, and worsening of previous neurologic deficits suggested the possibility of a new stroke. Moreover, the patient was on warfarin, raising concerns for a possible intracranial hemorrhage, one of the most feared complications of anticoagulants. Furthermore, elderly patients with motor deficits may also suffer frequent falls, and when under anticoagulant therapy, they are at increased risk of having subdural hematomas caused by rupture of intracranial bridging veins. Chronic subdural hematomas may present weeks to months after mild head trauma although a history of head trauma may not be remarkable. The neurologic examination showed she had worsening of her previous neurologic deficits, apparently without new neurologic signs. She also had symptoms of a respiratory infection such as cough and shortness of breath. Many times, elderly patients lack fever or other clear signs of infections, and an underlying infection may present as an acute confusional state or worsening of previous neurologic deficits. While a systemic infection can account for re-expression of previous focal neurologic deficits, sepsis by itself may be a risk factor for stroke, as it can induce a hypercoagulable state or be associated with infective embolism. In our patient's brain, MRI with DWI/ADC sequences showed no new lesions, and her physical examination, blood analysis, and chest X-ray confirmed she had pneumonia. Few scientific studies have directly analyzed the underlying reasons why metabolic insults may cause re-expression of neurologic deficits in patients with previous stroke. The most common culprits include urinary tract infections, pneumonia, hypoxia, hyponatremia, medication overdose, hypoglycemia, and non-ketotic hyperglycemia. All patients evaluated for a possible acute stroke require a set of laboratory tests, including a complete blood count, basic metabolic profile, coagulation studies, urinalysis, toxicology screen when appropriate, and chest X-rays. The laboratory tests assist in identifying stroke mimics, determine whether patients may be eligible for intravenous thrombolysis, and also assist in screening for conditions that may influence stroke outcomes.

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Two main hypotheses have been preferred regarding the re-expression of neurologic symptoms in patients with previous strokes:

1. Pathways formed during stroke recovery may be more susceptible to intercurrent metabolic derangements.
2. The penumbral region may be more susceptible to intercurrent metabolic changes than healthy tissue.

Tip

Metabolic insults may cause re-expression of neurologic deficits in a patient with previous stroke. Patients usually regain their baseline status following correction of the precipitating insult.

Case 6. Difficulty in using hand**Case description**

A 28-year-old woman was admitted to hospital due to decreased right-hand strength. She had been well on the previous day. However, upon awakening she noticed difficulty performing some activities with her right hand. Past medical history was unremarkable. Blood pressure on admission was 120/90 mmHg. Neurologic examination disclosed paresis of the right hand with impaired extension of the fingers and dorsiflexion of the right hand, and decreased sensation on the dorsum of the first and second digits of the right hand. The rest of the neurologic examination including muscle stretch reflexes was unremarkable. Brain MRI with DWI/ADC sequences did not disclose acute ischemic lesions.

Diagnostic considerations

Focal neurologic deficits may have other causes than stroke. Our patient had a right radial neuropathy. The signs and symptoms included wrist drop, finger extension weakness, thumb abduction weakness, and sensory loss over the dorsal web between the thumb and index finger. Patients with radial nerve compression at the spinal groove of the humerus may wake up with a wrist drop after a sound sleep. The triceps reflex is often intact. Sometimes, there may be a history of alcohol intoxication. Patients undergoing surgical procedures may also present with mononeuropathies due to compression during limb positioning. In these instances, the ulnar and peroneal nerves are more commonly affected.

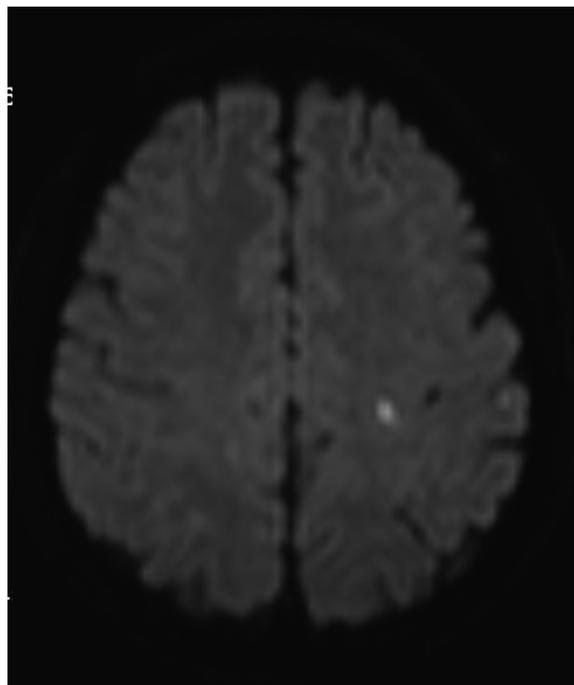


Figure 1.3 Brain diffusion-weighted MRI showing restriction in the left precentral gyrus.

Isolated monoparesis is the main clinical presentation in 5% of all strokes [19]. Cortical strokes may be distinguished from a radial neuropathy due to weakness or sensory changes outside of the territory of the radial nerve and alteration in muscle tone and muscle stretch reflexes. Sometimes, the differential diagnosis may be challenging, and in these instances, brain MRI can be quite useful (Figure 1.3). Strokes simulating a radial neuropathy often involve the “hand-knob” area of the cerebral cortex [20]. This omega-shaped region within the precentral gyrus referred to as the cortical “hand-knob” is the site of hand motor function.

Electromyography (EMG) with nerve conduction studies may be unremarkable in the first 2 to 3 weeks after symptom onset, and therefore may not be helpful for differential diagnosis in the acute phase. In most cases, radial neuropathy improves spontaneously after 6 to 8 weeks.

Tip

It is important to perform a thorough neurologic examination in patients presenting with focal neurologic deficits and establish if the pattern of neurologic deficit suggests a particular lesion site.

Case 7. Shaking movements of the left hemibody

Case description

A 57-year-old man was admitted to hospital due to involuntary “shaking” movements of his left hemibody. He had had several previous episodes, which were only noticed when standing or walking. These “non-marching” involuntary and non-rhythmic shaking movements lasted an average of 2 minutes, and simultaneously involved the upper and lower limbs. There was no alteration in the level of consciousness. He had a personal history of hypertension, dyslipidemia, and smoking, and was under treatment with losartan. On admission, blood pressure was 120/90 mmHg. Neurologic examination was unremarkable, except for a right carotid bruit. Brain MRI showed old watershed infarcts between the right anterior cerebral artery (ACA) and right MCA and between the right MCA and the right posterior cerebral artery (PCA) (Figure 1.4).

Carotid Doppler ultrasound showed a subtotal stenosis of the right internal carotid artery (ICA) (Figure 1.5), later confirmed by magnetic resonance angiography.

Transcranial Doppler (TCD) showed a post-occlusive flow on the right MCA. Interictal EEG showed no epileptiform activity.

The patient was started on aspirin and simvastatin. A right carotid endarterectomy was performed and the patient did not have further symptoms.

Diagnostic considerations

Transient ischemic attacks usually present with neurologic deficits such as loss of muscular strength, reduced sensation, speech and/or language disturbances, or loss of vision. However, they can also present with unusual symptoms such as involuntary movements. Limb shaking TIA, first described by C. Miller Fisher in 1962, has been associated with severe ICA stenosis. Limb shaking TIAs manifest as rhythmic or arrhythmic involuntary hyperkinesias affecting the hand, arm, leg, hand–arm, or hand–arm–leg unilaterally. The movements can be mistaken for focal motor seizures; however, there is no Jacksonian march or involvement of the face. The involuntary movements usually have a low frequency (about 3 Hz), and are frequently described as shaking, jerking, twitching, or trembling [21]. There may also be other associated symptoms

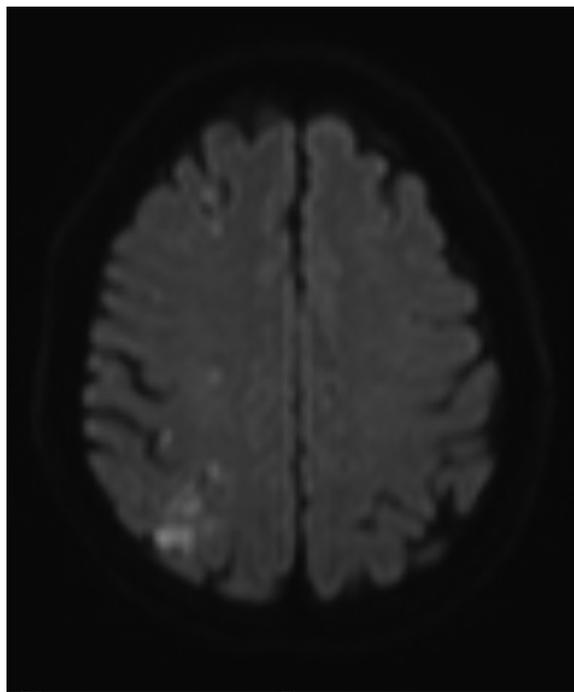


Figure 1.4 Brain MRI in DWI sequence showing watershed infarcts between the right anterior cerebral artery and right middle cerebral artery and between the right middle cerebral artery and the right posterior cerebral artery.

including ataxia, myoclonus, or dystonic limb posturing. Transient aphasia and/or dysarthria, ipsilateral hemiparesis, and numbness of the shaking extremity may also be present. Symptoms are often precipitated by postural changes such as standing or hyperextending the neck, and relieved by sitting or lying down.

The mechanism underlying limb shaking TIA is considered to be hypoperfusion. The critical ICA stenosis leads to decreased blood supply to watershed territories. The involuntary movements are provoked by maneuvers that further compromise cerebral hypoperfusion [22]. Additional studies suggest reduced vasomotor reactivity of corresponding cerebral territories. Some case reports have had normal carotid angiographies; in these instances, ACA stenosis, small vessel disease, and thalamic and midbrain infarction have been reported in association with limb shaking TIAs. Limb shaking TIAs have also been associated with moyamoya disease, and in these instances they can be elicited by hyperventilation.

EEG in patients with limb shaking TIAs does not show epileptiform activity. Some patients have contralateral slowing in the EEG.

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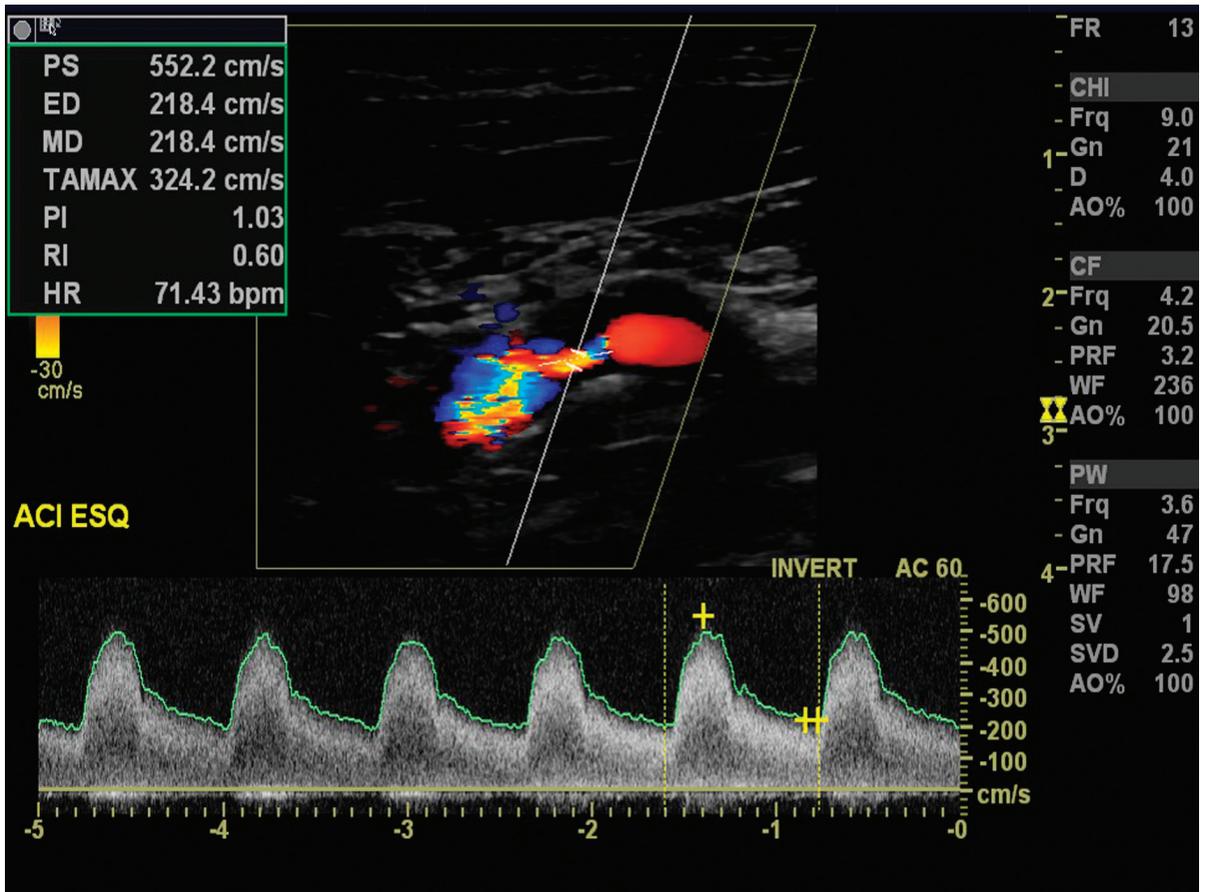


Figure 1.5 Carotid Doppler ultrasound showing stenosis of the right internal carotid artery.

It is important to recognize limb shaking TIAs as they are generally associated with a high-grade carotid artery stenosis that may benefit from reperfusion procedures.

Hemiballismus, chorea, or unilateral dyskinesia may result from acute vascular lesions in the subthalamic nucleus or connections.

Tip

TIAs and strokes may present with less frequent symptoms such as involuntary movements.

Case 8. Altered mental state

Case description

A 55-year-old man was admitted to the hospital due to increased somnolence. His wife noticed he did not

wake up in the morning, and he had been sleeping for 10 hours. She attempted to wake him up but he did not react. Past medical history was remarkable for hypertension, diabetes mellitus, and cigarette smoking. He was on metformin and ramipril. There was no history of drug abuse, alcohol intake, or recent head trauma. Blood pressure was 155/90 mmHg. Heart rate was 74 beats per minute. On admission he was somnolent, reacting only to vigorous verbal stimuli. He had bilateral miotic pupils and upward gaze palsy. Blood glucose was 90 mg/dL. Brain MRI with DWI disclosed paramedian bilateral thalamic infarcts (Figure 1.6). Cerebral angiography showed a stenosis of the medial and upper third of the basilar artery with occlusion of the left PCA. EEG showed a pattern of sleep with abnormal architecture with increased stage 1 and reduced stage 2 sleep; neither slow wave sleep nor sleep spindles were registered.