

# Atypical presentations of acute cerebrovascular syndromes

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Correct diagnosis of acute stroke is of paramount importance to clinicians to enable selection of correct treatments and to ensure prevention of acute complications, including recurrent stroke. Timely diagnosis can be difficult in some cases because patients with acute stroke can present with atypical or uncommon symptoms that suggest another cause altogether. Publications on these patients suggest that the following strategies could help to reduce misdiagnosis. First, clinicians should suspect stroke in any patient with abrupt onset of neurological symptoms. Second, clinicians should be aware that some patients will initially present with various uncommon and atypical stroke symptoms. Third, a complete and systematic neurological examination should be routinely done in patients presenting with acute neurological symptoms because this might shed light on the true nature of the problem. Finally, clinicians should be aware that even with the most sophisticated neuroimaging tests, stroke might be missed in the early hours after the event.

## Introduction

Worldwide, about 15 million people have a stroke every year, of whom 5 million die and 5 million have a permanent deficit.<sup>1</sup> In high-income countries, stroke is the most common cause of disability and is the third most common cause of death. When patients present with acute neurological symptoms, physicians must distinguish between stroke and other causes that mimic it. Accurate and prompt diagnosis is crucial because implementation of time-dependent therapies, identification and treatment of the underlying vascular mechanism, and attention to the underlying risk factors can improve outcomes and prevent subsequent events.

Patients who present with acute neurological symptoms can be divided into four groups (table). The first group includes patients with obvious stroke—eg, an elderly individual with untreated atrial fibrillation who abruptly develops aphasia and hemiparesis. The second group includes patients whose cause of neurological dysfunction is clearly not stroke, such as a patient without vascular risk factors who develops unilateral weakness of the facial muscles in association with hyperacusis and altered taste consistent with a lower motor neuron facial nerve palsy. In the third group, patients seem to have a stroke, but in fact have a non-vascular cause such as conversion reactions, Todd's paralysis (a disorder characterised by a brief period of paralysis with or without aphasia after a seizure), or migraine. Hypoglycaemia is a particularly important stroke mimic because its treatment is simple and effective. In the era of thrombolysis for acute ischaemic stroke, these stroke mimics have received much attention.<sup>2–5</sup> The final group of patients includes those with actual strokes, but whose presentations are unusual or atypical, suggesting a non-vascular cause. Huff has referred to these patients as “stroke chameleons”.<sup>2</sup> Compared with stroke mimics, this group of patients with missed or delayed diagnosis of stroke has received much less attention and is the focus of this Review.

Patients with stroke can present with atypical symptoms for various reasons. First, in the first minutes

to hours after the event, all the diagnostic information might not be available to the initial health-care providers. Additionally, patients' symptoms can evolve with time. Second, there is substantial variability in the classic cerebrovascular territories that can also result in non-classic presentations. Patients with small strokes, early presentations, young age, posterior circulation location, and deficits that do not result in lateralising motor or speech findings might be more difficult to diagnose clinically.<sup>6–9</sup>

In this Review, we aim to help clinicians improve the accuracy and timeliness of their diagnosis of patients with acute stroke by reviewing causes of misdiagnosis and non-classic symptoms of acute stroke (panel 1). Although much of the focus is on acute ischaemic stroke, we also discuss some aspects of misdiagnoses of haemorrhagic strokes, including intracerebral haemorrhage (ICH), subarachnoid haemorrhage (SAH), and haemorrhage resulting from cerebral venous sinus thrombosis (CVST). Panel 2 provides a glossary of terms of atypical symptoms of stroke.

## Non-localising symptoms

Stroke is usually characterised by the sudden onset of focal neurological deficits, such as hemiparesis, aphasia, or hemianopia, depending on the affected brain structures and vascular territory. However, some strokes can present in a non-localising manner without clear-cut focal deficits.

## Neuropsychiatric symptoms

About 3% of patients with stroke can present with delirium, a delusional state, acute onset of dementia, or mania mimicking a psychiatric illness.<sup>10</sup> Neurological signs are often absent or mild and transient, and therefore might be easily missed. This presentation is usually seen in patients with right-sided (non-dominant) focal strokes in the frontal and parietal regions. Several stroke-related symptoms and signs, such as anosognosia, aphasia, akinetic mutism, abulia, and aprosodia, can be misinterpreted as manifestations of depression. For example, a patient with a right frontal or parietal stroke

	Stroke-like presentation	Atypical stroke-like presentation
True stroke	Stroke	Stroke "chameleons" <sup>22</sup>
Not a stroke	Stroke mimic	Non-stroke

**Table: Diagnosis of patients presenting with acute neurological symptoms**

might be unable to correctly perceive or express the appropriate emotional inflection owing to aprosodia and could have monotonous speech; therefore, these patients might be misdiagnosed as having an affective disorder.<sup>11</sup>

Caudate strokes in the territory of the anterior lenticulostriate arteries might present with only mild neuropsychological and behavioural symptoms, such as abulia, mental and affective stagnation, and impairments in initiative for action, speech, and usual daily activities.<sup>12</sup> Similar features have been reported in patients with isolated strokes in the frontal lobes and underlying subcortical structures, presumably due to interruption of the limbic-frontal connections, and connections to the thalamus. Mania-like presentation, with associated psychosis, might occur in patients with focal strokes in the right orbitofrontal cortex, thalamus, and temporoparietal region.<sup>13</sup> Partial complex seizures due to temporal lobe injury might account for the psychotic symptoms in many patients with temporoparietal strokes.<sup>14</sup>

Although pathological laughing and crying and uncontrollable fits of laughing and crying inappropriate to the context are common sequelae of stroke, these symptoms are relatively rare at stroke presentation. This disorder is most common with strokes that affect the supranuclear motor pathways, bilateral pontine, basal ganglia, or periventricular subcortical areas, and with focal strokes in the frontal or temporal regions.<sup>15</sup> Catastrophic reaction, a collection of symptoms indicative of a patient's desperation and frustration and that include anxiety, aggression, and refusal of treatment, are also not uncommon in patients with stroke, particularly those with left anterior subcortical strokes and premorbid depression.<sup>16</sup>

### Acute confusional state

Delirium can be the presenting feature in a few patients with stroke,<sup>17</sup> particularly after a hemispheric stroke; this state is more frequent in haemorrhagic stroke than in ischaemic stroke (figure 1).<sup>18</sup> Strokes involving the right temporal gyrus, right inferior parietal lobe, or occipital lobe can present with acute confusional states, agitation, restlessness, and easy-to-miss neurological signs, and can be misdiagnosed as delirium. Rarely, vertebrobasilar ischaemia leading to involvement of the thalami, particularly the paramedian nuclei, can present as unexplained rapid onset of confusion with amnesia and minimal neurological deficits.<sup>19</sup> This form of

### Panel 1: Non-classic presentations of acute stroke

#### Non-localising symptoms

- Neuropsychiatric symptoms
- Acute confusional state
- Altered level of consciousness

#### Abnormal movements or seizures

- Abnormal movements
- Limb-shaking transient ischaemic attacks
- Seizures
- Alien hand syndrome
- Localised asterixis
- Isolated hemifacial spasms
- Disappearance of previous essential tremor

#### Peripheral nervous system symptoms

- Acute vestibular syndrome
- Other cranial nerve palsies (especially third and seventh cranial nerves)
- Acute monoparesis
  - Cortical hand syndrome
  - Cortical foot syndrome
- Isolated sensory symptoms

#### Atypical symptoms

- Isolated dysarthria
- Isolated dysarthria-facial paresis syndrome
- Isolated visual symptoms
  - Anton's syndrome (cortical blindness with denial of deficit)
  - Balint's syndrome
  - Isolated visual field disturbances
- Foreign accent syndrome
- Isolated dysphagia or stridor

#### Isolated headache

- Subarachnoid haemorrhage
- Cerebral venous sinus thrombosis
- Cervical artery dissections
- Cerebellar infarction

#### Acute neurological syndrome with negative brain imaging

- Negative non-contrast CT in subarachnoid haemorrhage, cerebral venous sinus thrombosis, arterial dissection, and acute ischaemic stroke
- Negative MRI in acute ischaemic stroke

amnesia is not to be confused with transient global amnesia, the acute onset of transient loss of memory for recent events and impaired ability to retain new information with an otherwise normal neurological examination.<sup>20</sup>

Patients with strokes of the corpus callosum can present with symptoms that are difficult to localise or neurological symptoms and signs attributable to associated interhemispheric disconnection syndromes and can be misdiagnosed as being confused.<sup>21</sup> Patients

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