Transient unilateral weakness: is it a transient ischaemic attack?

Abstract

Transient ischaemic attack is an emergency medical condition that causes brief negative focal neurological symptoms such as unilateral weakness. The symptoms herald a high risk of stroke and hence require urgent assessment. The challenge lies in the brevity and compendium of associated symptoms that can 'mimic' a plethora of other conditions. The result is a high rate of referrals to transient ischaemic attack clinics for these stroke mimics. This article highlights the diagnostic challenges in transient ischaemic attack with relevance to unilateral weakness.

Key words: Stroke mimics; Transient ischaemic attack; Unilateral weakness

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Charles C Southey[1]

Jonathan Birns[1]

Peter Sommerville[1]

Ajay Bhalla[1]

Author details can be found at the end of this article

Correspondence to:
Charles C Southey;
charles.southey@nhs.net

Introduction

Transient ischaemic attack is a brief focal neurological deficit as a consequence of ischaemia affecting the brain, spinal cord or retina (Easton et al, 2009). Having an episode of transient ischaemic attack places patients at significantly greater risk of stroke, the second leading cause of mortality worldwide (Lioutas et al, 2021). The National Institute for Health and Care Excellence and European guidelines emphasise the urgency of identification, diagnosis and simultaneous management of transient ischaemic attack in a timely manner, with tspecialist referrals to be made within 24 hours of symptom onset (National Institute for Health and Care Excellence, 2019; Fonseca et al, 2021). The American Heart Association adds to these guidelines by recommending the use of diffusion-weighted magnetic resonance imaging to differentiate acute infarctions from transient ischaemic attacks without infarction (Winbeck et al, 2004). In addition to these technological advances, all clinicians are able to take a focused history and examination to allow them to act promptly and prevent disabling and even life-threatening consequences.

Importance of transient ischaemic attack with unilateral weakness

Transient ischaemic attacks with motor impairment are associated with up to two-fold greater risk of subsequent stroke than transient ischaemic attack without motor impairment (Lodha et al, 2017). Evidence from diffusion-weighted imaging studies suggests the increased risk may be because of the presence of an established ischaemic lesion (Calvet et al, 2009). Not only are these patients at higher risk of subsequent stroke, but around 50% require rehabilitation for subtle issues following transient ischaemic attack with motor impairment (Verbraak et al, 2012).

Challenges in identifying transient ischaemic attacks

Transient ischaemic attack is a substantial challenge for the physician to manage as it is a condition where the neurological symptoms are no longer evident, with timing being both possibly vague (as a result of patient and/or family member uncertainty and delayed presentation) as well as time-critical (as early proactive management can reduce the risk of stroke). In addition, the condition has a wide range of possible symptoms, depending on the area(s) of the brain affected, which can present diagnostic challenges. Teasing apart these symptoms from other conditions is important, yet levels of agreement between trained stroke-

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trained neurologists assessing the same patients have been found to be fairly low (Castle et al, 2010). The need for diagnostic reliability underscores the importance of the history-taking process, which guides whether or not to perform further investigations, including imaging.

Diagnosis of transient ischaemic attack

In order to overcome the aforementioned diagnostic challenges, history taking is tailored to determining if the symptoms are attributable to focal vascular dysfunction. The sudden nature of the cerebral artery occlusion is much the same as a section of an electrical circuit being damaged, resulting in an immediate breakdown of that particular area's function. As a result, an important feature of history taking is to ascertain that the downstream function of the brain supplied by a particular cerebral artery is being affected (as opposed to the whole of the brain). Additionally, neurological symptoms from transient ischaemic attack usually result in an absence of function. These focal and non-focal neurological symptoms are outlined in Tables 1 and 2.

The following format is vital to cover the key questions to evaluate whether the symptoms are consistent with vascular pathology (and if temporary, a transient ischaemic attack):

1. Are the neurological symptoms focal rather than non-focal?
2. Are the focal neurological symptoms negative rather than positive?
3. Was the onset of the focal neurological symptoms sudden?
4. Were the focal neurological symptoms maximal at onset rather than progressing over a period?

If the answer to all questions is yes, the symptoms are almost certainly caused by vascular pathology (cerebral ischaemia or haemorrhage) (Rudd and Bhalla, 2018).

Having established that transient ischaemic attack is the likely cause of symptoms, the next question is to distinguish the cause, guided by the clinical features and imaging.

Table 1. Focal neurological symptoms attributable to specific locations in the brain that can present as a transient ischaemic attack

Weakness (hemiparesis) or uncoordination of one side of body
Dysphagia
Ataxia
Dysphasia (receptive or expressive)
Dysarthria
Dyslexia
Dysgraphia
Dyscalculia
Hemisensory disturbance
Transient monocular blindness
Hemianopia or quadrantinopia
Bilateral blindness
Diplopia
Vertigo (only in association with other brainstem focal symptoms, unusual for vertigo as an isolated symptom to represent a transient ischaemic attack)
Dyspraxia
Visual spatial dysfunction (visual neglect)
Amnesia (as an isolated symptom does not indicate transient ischaemic attack)

If multiple stereotypical focal events over a period of time with the same symptoms then a diagnosis of transient ischaemic attack is very unlikely: consider seizure activity. From Rudd and Bhalla (2018)

Weakness only indicates the transient ischaemic attack's laterality in the brain, which gives little insight into which vascular territory the ischaemia is occurring in. Furthermore, isolated unilateral weakness is consistent with a transient ischaemic attack syndrome resulting from transient occlusion either in the anterior circulation (the brain regions supplied by the carotid system) or the posterior circulation (the brain regions supplied by the vertebrobasilar system), such as those listed in Table 3. Other clinical features that may help to locate the origin of the transient ischaemic attack include symptoms alongside the unilateral weakness, such as those listed in Table 1.

Limb-shaking transient ischaemic attacks and capsular warning syndromes

In addition to the classical presentation of transient ischaemic attacks, limb-shaking transient ischaemic attacks and capsular warning syndromes are important presentations of which clinicians should be aware. Limb-shaking transient ischaemic attacks are a rare form of brief (<5 minutes), irregular jerking or flailing limb movements, thought to occur as a result of hemispheric hypoperfusion from the internal carotid artery (Rosenbaum et al, 2016). Although

Table 2. Non-focal neurological symptoms that are generalised and can present as a transient ischaemic attack

Generalised weakness
Generalised sensory disturbance
Faints or light-headedness
Blackouts or drop attacks (syncope)
Faecal or urinary incontinence
Confusion
If isolated symptom, in the absence of other focal neurological symptoms: ■ Vertigo ■ Tinnitus ■ Dysarthria ■ Dysphagia ■ Diplopia ■ Ataxia

From Rudd and Bhalla (2018)

Table 3. Transient ischaemic attack symptoms associated with anterior (ie carotid) and posterior (ie vertebrobasilar artery) areas in the brain

Symptom	Carotid territory	Vertebrobasilar territory
Dysphasia	Yes	No
Monocular visual loss	Yes	No
Unilateral weakness	Yes	Yes
Unilateral sensory loss	Yes	Yes
Dysarthria	Yes	Yes
Homonymous hemianopia	Yes	Yes
Ataxia or unsteadiness	Yes	Yes
Dysphagia	Yes	Yes
Diplopia	No	Yes
Vertigo	No	Yes

From Rudd and Bhalla (2018)

these can be easily confused with focal motor seizures, important differences lie in the absence of Jacksonian march, lack of extension into the face and normal electroencephalography, which make a focal seizure more unlikely. Limb-shaking transient ischaemic attacks are associated with severe internal carotid artery stenosis which, when identified, may be surgically corrected to minimise the risk of infarction (Das and Baheti, 2013).

The capsular warning syndromes affect the internal capsular region of the brain, resulting in stereotypical focal neurological deficits that are sudden and maximal on onset (Sen et al, 2020). The syndrome typically presents with unilateral sensory or motor weakness of two of the face, arms or legs. The precise pathophysiology remains unclear but is most likely to be the result of intrinsic cerebral small vessel disease and hypoperfusion (Tassi et al, 2013; Sen et al, 2020). As a result, the management is intensive secondary stroke prevention. The condition's urgency lies in the increasing risk of subsequent ischaemic infarction, which can evolve in up to 60% of cases (Paul et al, 2012).

Risk factors

Prominent risk factors associated with transient ischaemic attack include non-modifiable factors such as increasing age and male sex. Women are more likely than men to have stroke mimics, including initial presentations with headaches (Yu et al, 2021). Modifiable risk factors for transient ischaemic attack include smoking, diabetes, hypertension and dyslipidaemia (Ström et al, 2016; Pohl et al, 2021).

Transient ischaemic attack mimics

Extensive research has gone into transient ischaemic attack or stroke mimics, which present with similar symptom patterns as transient ischaemic attack or strokes but which are associated with different diagnoses. The frequency of mimics range from 9–29%, with the most common being migraines and seizures (McClelland et al, 2019).

Migraines

Migraines are one of the most common stroke mimics (Terrin et al, 2018), with auras of neuronal excitation followed by inhibition gradually spreading along the cortex at a rate of approximately 3–5 mm/min, resulting in a rolling progression of symptoms including visual phenomena, dysarthria, sensory disturbances and, in rare cases, hemiplegia (Russell and Ducros, 2011). Migraines without aura affect around 15% of the population, while 8% have migraine with aura. Hemiplegic migraines are rare with a prevalence of approximately 0.01% (Russell and Ducros, 2011). Migraine patients often first present in the first or second decade and the symptomatic marching progression is a key distinguishing feature from transient ischaemic attacks where symptoms occur simultaneously.

Seizures

Focal seizures can present as stroke mimics with hemiparesis because of the metabolic demand on excitatory neurons in the post-ictal state, known as cortical spreading depression. Seizures tend to differ from transient ischaemic attacks as they exhibit positive neurological symptoms including limb jerking, lip smacking, painful sensory disturbances or dystonic posturing. Moreover, seizures spread to different body parts as per the cortical map, whereas transient ischaemic attacks occur simultaneously. In terms of a temporal profile, seizures and transient ischaemic attacks may be similar in brevity; however, seizures occur in similar patterns recurrently over years. Although seizures can occur early on following a stroke, the numbers remain relatively low at about 4%, with 1.5% being at stroke onset (Pohl et al, 2021). Nevertheless, it is important to bear in mind that up to 30% of new-onset seizures in >60-year-olds are secondary to stroke (Camilo and Goldstein, 2004).

Todd's paresis

Todd's post-ictal paresis is an important stroke mimic thought to occur as a result of electrical overactivity followed by subsequent exhaustion in the primary motor cortex resulting in focal weakness (Anathhanam and Hassan, 2017). Todd's paresis occurs in about 1 in 10 focal

neurological seizures, with the duration usually being between 30 minutes and 36 hours (Rolak et al, 1992). Todd's paresis tends to be associated with recurrent stereotypical symptoms.

Space-occupying lesions

Space-occupying lesions include CNS tumours, metastases and abscesses. As a space-occupying lesion increases in size, a resultant mass effect can impair cerebral blood flow with subsequent neurological deficit and potential for seizure activity. Abscesses may be associated with fevers and headaches and malignancies may have a history of weight loss and night sweats. Despite case reports showing rapid growth of brain tumours resulting in transient symptoms (Schröter et al, 2021), their pattern tends to be slower and progressive.

Cerebral amyloid spells

Cerebral amyloid angiopathy presents with transient focal neurological episodes or 'amyloid spells' that manifest as unilateral motor, somatosensory, visual or language disturbances lasting approximately 30 minutes (Smith et al, 2021). The unilateral weakness presents as a stereotypical spreading weakness across body parts as per the contiguous cerebral cortex. The pathophysiology is thought to occur through deposition of beta-amyloid in the cerebrovasculature, resulting in micro-subarachnoid bleeds in the lobar regions of the brain (Vales-Montero et al, 2019). The phenomenon was only initially identified through histopathological investigations, although Greenberg and his colleagues created the modified Boston criteria in order to identify probable cerebral amyloid angiopathy (Greenberg and Charidimou, 2018). This omits the need for histopathology, although it still remains the gold standard. Cerebral amyloid angiopathy may evolve into subarachnoid haemorrhages which, in some cases, may also be associated with recurrent episodes that are stereotyped in nature with migratory symptoms (Stanton et al, 2020).

Peripheral neuropathy

Peripheral neuropathy is a rare form of stroke mimic that tends to gradually cause unilateral weakness or sensory deficit in a specific anatomical distribution. The condition is caused by changes in the distal nerves causing axonal, segmental or Wallerian degeneration.

Multiple sclerosis

Multiple sclerosis is another stroke mimic characterised by demyelinating lesions across multiple sites in the brain that can present with transient unilateral weakness. The patients tend to present younger than those with transient ischaemic attacks (between 20 and 40 years of age), as well as being predominantly female at 3:1. Being an inflammatory condition, multiple sclerosis tends to present with symptoms more gradually over 72 hours, with the initial presentation often being optic neuritis. It is important to note that patients with multiple sclerosis often have traditional vascular risk factors and that stroke risk is increased by approximately 71% in such patients (Palladino et al, 2020). Magnetic resonance imaging remains a useful tool in supporting the clinical diagnosis, with the McDonald criteria being a structured framework to help with diagnosis.

Functional disorders

Functional disorders are highly common stroke mimics, comprising up to 15% of stroke mimic presentations (Jones et al, 2020). Patients tend to be younger and female, with fewer additional symptoms such as language issues or loss of consciousness. Another factor to consider is traumatic life events or even health problems, such as the functional unilateral limb weakness that further promotes dysfunctional behavioural responses. Functional disorders tend to have inconsistent physical examinations after repeated evaluations and do not tend to fit into vascular territories.

Metabolic stroke mimics

Metabolic disorders including hypoglycaemia and hyperglycaemia are well recognised as stroke mimics, with particular reference to confusion and loss of consciousness (Pohl et al, 2021). A rare example is hypokalaemic paralysis resulting in unilateral hemiplegia, with rapid resolution upon correction of the underlying cause (Liu et al, 2022).

Key points

- Transient ischaemic attack is a medical emergency that places patients at increased risk of stroke.
- Unilateral weakness is a common symptom of transient ischaemic attack and stroke mimics, resulting in diagnostic challenges.
- There are currently no clinically validated tools to diagnose transient ischaemic attacks.
- History taking and clinical examination are fundamental tools to distinguish transient ischaemic attacks from stroke mimics, with supplemental imaging as appropriate.

Conclusions

Transient unilateral weakness is a negative focal neurological symptom that is commonly associated with transient ischaemic attack, despite an array of alternative diagnoses that require careful history taking to establish the diagnosis. The narrative provided by the patient is crucial to elicit with support from collateral histories where applicable, gauging the timing, nature and recurrence of the unilateral weakness in question. Diffusion-weighted magnetic resonance imaging is becoming increasingly useful in aiding the differentiation of transient ischaemic attacks, strokes and the stroke mimic.

Author details

[1]Department of Ageing and Health, Guy's and St Thomas' NHS Foundation Trust, London, UK

Conflicts of interest

The authors declare that there are no conflicts of interest.

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