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Transient Ischemic Disease: Diagnosis and Treatment

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Abstract

A good amount of advancement of transient ischemic attack (TIA) have occurred since it was first recognized as a major risk factor for stroke during the late 1950's. Lately, several studies have constantly revealed that patients who have experienced a TIA constitute a mixed people, with numerous causal factors as well as an average 5-10% risk of suffering a stroke during the 30 days that follow the index event. These two features have driven the most vital alterations in the treatment of TIA patients over the last decade. First and foremost was that more attention was paid to real stroke risk stratification, efficient and complete diagnosis, and the second was an evidence based therapeutic approach, to reduce the risk of subsequent ischemic stroke. This review address some of the salient update on TIA, its diagnosis, treatment and preventive measures that are likely to influence the future care of these patients.

Keywords

Transient ischemic attack, clinical diagnosis, pearls in the management, antiplatelet therapy, anticoagulants therapy

Introduction

Transient ischemic attack (TIA) is defined as "Transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction" [1]. A stroke persists only a short time. TIAs are initiated by a clot or obstruction in the brain. The clot generally melts on its own or is dislodged, and symptoms generally last for a short time. TIAs are at times called "mini-strokes," as their symptoms last only for a few minutes up to 24 hours before vanishing. However, "warning stroke" is a better term, because a TIA often prefigures a full-blown stroke, which needs to be taken seriously. TIA precedes about 15-30% of all strokes [2]. It is reported that on an average 12% of patients who had TIA decease within one year [1]. Within ninety days of TIA, there is greater risk of having a full-blown stroke. About 9 to 17 % of individuals who have a TIA have a stroke within ninety days [1].

TIA Symptoms are similar to other stroke symptoms; however, they are short lived. The symptoms appear unexpectedly, and include numbness or weakness, especially on one side of the body, misperception or difficulty in speaking or understanding speech, visual impairment in one or both the eyes, difficulty walking, giddiness and loss of stability or coordination. Majority of symptoms of a TIA wane within an hour, though they may last for up to twenty-four hours. Since it is difficult to differentiate whether it is TIA or stroke, one should consult a doctor without any delay [3].

Clinical Diagnosis of TIA

Characterized by abrupt onset of focal neurologic insufficiency which are transient lasting for less than 1 hour. These could be due to ischemia involving cerebral cortex, brain stem, cerebellum, retina with complete resolution in under 1 hour. The type of presentation depends on the area of the brain involved [4]. The resolution of signs and symptoms by the time the assessment start is the main challenge for diagnosis of TIA [5].

a) History reveals a sudden onset of a focal neurologic deficit. Symptomatology depends on the site of lesion and type of deficit observed. Usually "negative"

features are observed. Motor deficit such as limb weakness, hemiparesis or monoparesis due to involvement of pyramidal tract or frontal lobe; Sensory deficit due to involvement of parietal lobe; visual deficit due to retinal ischemia causing monocular blindness or temporal or occipital lobe ischemia causing homonymous hemianopia. Amaurosis Fugax characterized by transient or fleeting monocular blindness ("shutter coming down") due to flow of emboli through retinal artery is seen some patients. Depending on the area involved there may be suffer from aphasia or agraphia

b) Findings such unsteady gait, diplopia, vertigo, dizziness, dysphagia are less often seen features of TIA and can be observed in other similar situations and therefore can be suggestive of possible TIA. If they are present in TIA they suggest involvement of the Posterior (Vertebro Basilar) circulation. Drop attacks also known as Atonic Adynamic syndrome characterized by sudden fall on standing without loss of consciousness is also seen in few cases of TIA.

c) Clinical features like amnesia, confusion, incoordination of limbs, sensory deficits like abnormal sensation or deficit in one limb or only in the face. Unusual cortical visual symptoms (lone bilateral blindness and bilateral positive visual phenomena), transient loss of consciousness, headache, complex visual hallucinations suggest that it is unlikely to be TIA.

d) The situations which have "fluctuating" symptoms include metabolic situations like hypoglycemia, hyponatremia, hypokalemia "postural" features like postural hypotension; "marching" symptoms like epilepsy; "positive phenomena" involuntary movements, jerking, scintillating scotoma; "global" phenomena like loss of consciousness; migraine aura, peripheral vertigo are not the manifestations of TIA but suggest TIA mimics. Myasthenia gravis, cervical arthrosis, peripheral-nerve injury, multiple sclerosis, can also present with transient neurologic symptoms mimicking TIA.

The only variance between a stroke and TIA is that with TIA the blockage is short-lived (temporary). TIA symptoms happen suddenly and last a relatively short time. Unlike a stroke, a TIA on resolution leaves no permanent injury to the brain. There's no way to tell if symptoms of a stroke will lead to a TIA or a major stroke [6].

Differential Diagnosis of TIA [6,7]

Features that support the diagnosis of TIA

1. Multiple / single features involving loss of function – Motor (weakness) / Sensory (anesthesia) / Speech problems (aphasia;
2. Specific cerebrovascular territory distribution;
3. Simultaneous onset and resolution of clinical features

History taking that helps to differentiate TIA from other TIA mimics and stroke include are events before, during and after the episode.

A) Events before: Related to comorbid conditions – Confusion: Hypoglycemia (Antidiabetic medications), Hyponatremia (Diuretics, vomiting); Falls soon after standing (Postural hypotension), Prolonged standing (Vasovagal syncope); Transient blackouts with brief loss of consciousness (Syncope) or without loss of consciousness (drop attacks); Past history of noncompliance to treatment (TIA, Seizures)

B) Events associated with the episode: Aura (Seizures, migraine); Involuntary movements (seizures); Incontinence (Seizures); Altered consciousness (metabolic); Headache (Migraine, CVA); BP very high (Hypertensive crisis), very low (Hypotension) [8,9].

C) Events following the episode: Headache (seizures); Motor weakness (Stroke, Metabolic, Seizure); Altered cognition (Metabolic, Stroke, Seizure)

D) Pattern of Recurring TIA Recurrent episodes of same pattern suggest Thrombosis; Recurrent episodes of varying pattern suggest Embolic origin

Diagnosing TIA after the episode has resolved and the clinical examination reveals no clinical features

Cerebral or retinal symptoms consistent with transient ischemic attack (TIA) usually last for seconds or minutes and typically last less than 1 hour. The deficit may be motor (limb weakness); sensory (limb/ face); Visual) uniocular blindness / Homonymous hemianopia); aphasia / dysarthria TIA, or transient ischemic attack, is a "mini stroke" that occurs when a blood clot blocks an artery for a short time.

Importance of general examination in TIA situation

1. Height and Weight BMI-Obesity
2. Cigarette smoking- tobacco stains
3. Dyslipidemia -Xanthoma, Xanthelesma, Arcus juvenilis
4. BP-Hypertension
5. Atherosclerosis – Arterial thickening, Retinopathy
6. Drugs-Oral Contraceptives
7. Bleeding disorders
8. Race-African, south Asian, Caribbean
9. Age-Advanced age > 65 years
10. Family history of TIA
11. Trauma-Head injury

Importance of Cardiovascular examination in the context of TIA [7]

Pulse: Atrial fibrillation

BP: Uncontrolled hypertension, hypotension, postural hypotension

Heart: Murmurs (Valvular heart diseases)

Vessels: Carotid bruit (on the side opposite to the side of deficit)

Fundus: Retinopathy (hypertensive, diabetic), Roth's spots (Infective endocarditis)

Prognosis of TIA [7]

Risk prediction of recurrence

ABCD2 scores: The score on the ABCD2 scale (based on age, blood pressure, the existence of clinical weakness or speech disruption, the length of symptoms, and the presence of diabetes) is used to foresee the threat of stroke. ABCD2 scores range from 0 to 7, with higher scores signifying a more risk of stroke [Table 1a and Table 1b] [10].

The ABCD2 -I score is a refined score that also includes findings on diffusion-weighted imaging of the brain. This score has been shown to improve risk prediction over the ABCD2 score alone [Table 1c].

The addition of carotid-artery stenosis of at least 50% or "dual" TIA (TIA prompting medical attention plus at least one TIA in the preceding 7 days) also improved the performance of the ABCD2-I score

Table 1a: Risk stratification for TIA with ABCD2 score [5]

ABCD2	Criteria	Points
Age	≥60 years	1
Blood Pressure	≥140/80	1
Clinical Features	Unilateral weakness	2
	Speech impairment without weakness	1
Duration of symptoms	>60 minutes	2
	10-59 minutes	1
Diabetes	Yes	1

Importance of prompt diagnosis & treatment of TIA

Prompt diagnosis of provides a critical opportunity to quickly find and treat the cause in order to prevent a devastating stroke. Without treatment, the stroke threat is up to 20% at 3 months, and most of this risk occurs within the first 10 days, particularly within the first 2 days. Prompt clinical diagnosis and immediate preventive measures are associated with a decrease of up to 80% in the 3-month risk of stroke.

How to access the risk of TIA/ Stroke?

If one has more than 3 risk factor in the high risk block, one should consult a stroke specialist. If one has 4 out of 6 factors in caution block, then one should work on life style modification to reduce the risk factors [Table 2].

Investigating TIA [4]

A) Brain Imaging

B) Cardiovascular evaluation

Table 1b: ABCD2 score and risk of TIA [11]

Score	Two day risk for stroke	Recurrence within 90 days
0-3	Low	1.0%
4-5	Moderate	4.1%
6-7	High	8.1%

Table 1c: ABCD2 and ABCD+ score and calculation of risk points of TIA [12]

ABCD2-I	Points
ABCD+	7
I=(Image) MRI:Acute infarction on DWI CT: Acute or old infarction	3

Table 2: Shows the risk factors to access the risk of TIA or stroke

RISK FACTOR	HIGH RISK	CAUTION	LOW RISK
Blood pressure	>140/90 or unknown	120-139/80-89	<120/80
Atrial fibrillation	Irregular heart beat	I do not know	Regular heart beat
Smoking	Smoker	Tying to quit	Non smoker
Cholesterol	>240 or unknown	200-239	<200
Diabetes mellitus	Yes	Boarder line	No
Exercise	Couch potato	Some exercise	Regular exercise
Diet	Overweight	Slightly overweight	Healthy weight
Smoker in family	Yes	Not sure	No
Total Score	High risk	Caution	Low risk

C) Risk factor evaluation

A) Brain imaging

In patients of TIA Non contrast CT scan is usually within normal limits. However, this does not exclude early thrombotic stroke, as the CT can be normal in that situation. Resolution of "TIA" does not mean an infarct has not taken place. It suggested getting a CT/MRI in such patients. Diffusion-weighted imaging of the head is now the preferred test for individauts with a suspected TIA and should be performed immediately [13].

B) Cardiovascular evaluation

Cardiac: Electrocardiography (ECG), inpatient monitoring of the cardiac rhythm, Holter, Contrast transthoracic and trans esophageal echocardiography (TEE) to detect cardiac structural abnormalities such as patent foramen ovale, atrial thrombus, and valvular disease or atherosclerosis of the aortic arch as a source of cerebral embolism.

Assessment of extra cranial and intracranial arteries: Noninvasive imaging (carotid artery ultrasonography, CT angiography, or magnetic resonance angiography) to diagnose a proximal intracranial stenosis, occlusion, or both.

C) Risk factor evaluation

Estimation of fasting and postprandial blood sugar, HBA1c, fasting Lipid Profile, and markers of connective tissue disease such as ANS, ANA Profile. In individuals with headache or transient monocular blindness indicators of inflammation such as C-reactive protein, ESR to rule out giant-cell arteritis.

Management of TIA [4]

A) Goal of treatment

Pharmacologic management for transient ischemic attacks (TIAs) is meant for reducing both short-term and long-term threat of stroke. Antithrombotic therapy should be started as early as intracranial hemorrhage has been ruled out in order to reduce high short term risk of stroke after TIA.

B) Major therapeutic options

1. Antiplatelet therapy: These drugs prevent platelet function by inhibiting the cyclooxygenase enzyme which in turn blocks aggregation. Aspirin blocks prostaglandin synthetase and inhibits prostaglandin synthesis and prevents formation of thromboxane A2. Dipyridamole is a platelet adhesion inhibitor and inhibits red blood cell (RBC) uptake of adenosine, which itself an inhibitor of platelet reactivity. Co- administration of aspirin-dipyridamole prevents cardiovascular incidents following TIAs. Aspirin 25mg and dipyridamole200 mg twice daily is the recommended dose for prevtion of cardiovascular events [14].

Clopidogrel selectively blocks the attachment of adenosine diphosphate (ADP) to its platelet receptor and subsequent activation of the glycoprotein GPIIb/IIIa complex, and inhibits platelet aggregation [8]. Dipyridamole may increase cyclic 3',5'-adenosine monophosphate (cAMP) within platelets and formation of platelet activator thromboxane A2. Dipyridamole may reduce the risk of stroke when used as monotherapy instead of aspirin [15].

Ticlopidine is an alternative antiplatelet therapy for patients who cannot tolerate or do not respond to aspirin therapy.

Anticoagulant therapy

Meticulous inhibition of blood coagulation by means of suitable drugs is indicated for prophylaxis of ischemic stroke in individuals with risk factors for thromboembolism, such as atrial fibrillation. Warfarin acts by preventing the synthesis of vitamin K dependent clotting factors and is used for management of venous thrombosis, pulmonary embolism, and thromboembolic disorders [16]. It is started with 2-5 mg PO/IV qDay × 2 days, OR 10 mg PO × 2 days in healthy individuals. After two days INR will be checked and the is adjusted based INR results. The usual maintenance dose ranges between 2-10 mg/day.

Treatment of significant stenosis

Carotid endarterectomy: Moderately or severe narrowed carotid artery corrected by surgery. This is aimed at clearing carotid arteries of fatty deposits as a prophylactic measure before another TIA or stroke can occur [17]

Angioplasty: In some cases, carotid angioplasty, or stenting, is an option. This involves using a balloon-like device to open a clogged artery and placing a small wire tube (stent) into the artery to keep it open [18].

C. Treatment of associated diseases: Hypertension, Diabetes, Dylpidemia: Appropriate control of blood sugar, blood pressure and blood lipids will be a component of effective management of TIA.

Pearls in Management of TIA [4]

1. TIA is usually characterized by cerebral or retinal features lasting for and clearing completely within 1 hour.
2. Syncope, Seizure (post ictal phase in an unobserved seizure), hypoglycemia can closely mimic TIA
3. Resolution of "TIA" does not mean an infarct has not taken place – get a CT/MRI

4. Diffusion-weighted imaging of the head is now the preferred test for patients with a suspected TIA and should be performed immediately.
5. Presence of "TIA" on waking up – Further workup needed (diffusion weighted MRI Scan) to identify mismatch between Penumbra and infarcted area
6. Non-Focal symptoms – Generalized weakness, numbness, syncope, Incontinence, disorientation-not likely to be TIA
7. Headache preceded by aura and associated with positive visual phenomena suggest migraine rather than TIA
8. Seizures associated with positive phenomena (tonic clonic movements) or negative phenomena (Todd's paralysis) do not suggest TIA
9. A suspected TIA should be evaluated urgently in a TIA clinic or in an emergency department.
10. If possible, immediately after the onset of symptoms, the patient should take aspirin at a dose of 300 mg, followed by 75 to 100 mg daily; Clopidogrel should be added to aspirin during the first 21 days after the TIA (at a 300-mg loading dose, followed by 75 mg per day).
11. The long-term prevention of stroke after TIA typically includes antiplatelet or anticoagulant treatment (depending on etiologic findings), blood-pressure lowering, lipid lowering, glycemic control, smoking cessation, and counseling regarding diet and lifestyle. Carotid endarterectomy.

Conclusion

Suspected TIA is a common and important challenge for the clinician to diagnose and decide on the plan of management. There are many mimics that add to the challenge of diagnosis. Since a significant number of TIA precede a good number of stroke latter, it crucial to diagnose and treat adequately to prevent a stroke. Careful elucidation of history will be useful to differentiate common mimics (syncope, seizers, migraine etc) from TIA. In suspected cases it is reasonable to recommend MRI is assessing TIA. Imaging and careful clinical examination will help in arriving at correct diagnosis. Antiplatelet drugs and anticoagulants either alone or in combination play a role in prevention subsequent stroke.

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