The development of the concept of transient ischemic attack (TIA) was an extremely important advance in the understanding and management of cerebrovascular disease, which has been refined over the years to the generally accepted clinical definition of a focal neurological dysfunction which resolves completely within 24 hours. While there is almost certainly a spectrum of pathophysiologies underlying TIA, it is clear that in many cases TIsAs are caused by emboli or microemboli from atherosclerotic plaques and are the harbinger of cerebral infarction. The entity, however, is a clinical concept rather than an anatomical one and includes at least several pathological entities, often with different diagnostic, therapeutic and prognostic implications. In particular, the term TIA is currently used to describe a variety of symptomatically transient neurological disturbances of focal nature due to local ischemia caused by a variety of pathophysiological mechanisms such as hypotension, “hemodynamic crisis,” microembolism, or abnormality of blood constituents. They range from potentially reversible ischemia, on the one hand, to infarction on the other.

It is the purpose of this article to demonstrate that, in some cases, the clinician cannot accurately differentiate between a TIA without infarction and an infarction with minor residua, and to suggest the hypothesis that this distinction may have clinical significance. In this article, we call attention to episodes with the temporal profile of TIA, and a demonstrable pathological substrate, transient neurologic dysfunction in the setting of cerebral infarction.

TIAs are defined as episodes of focal neurological deficit of sudden onset, referable to a specific arterial territory, lasting no longer than 24 hours. As early as 1914, Hunt referred to “cerebral intermittent claudication” due to disease of the carotid artery. Nearly forty years later Denny-Brown described hemodynamic crises or “episodic insufficiency in the circle of Willis of a temporary nature.” Millikan, Siekert, and their colleagues, Fisher, and Marshall among others have more recently elaborated and refined the concept. They have agreed that only transient neurological dysfunction, resolving within 24 hours, can be considered. “Fundamentals of Stroke Care,” published under the sponsorship of the National Institute of Stroke, Vol 14, No 3, 1983

References

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Temporal Profile Resembling TIA in the Setting of Cerebral Infarction
Neurological and Communicative Disorders and Stroke, states that the diagnosis of TIAs is made by the history and occasional observation of an episode by the physician, and that furthermore, during the intervals between episodes, examination reveals no evidence of neurological disorder. This description specifically states that radionuclide and computed cranial tomography (CCT) are normal in patients with TIA unless there is residual undetected infarction. Biller et al noted that CCT is normal in the majority of patients with TIAs. Allen and Preziosi reported abnormal CCT in 12% of patients with a clinical diagnosis of TIA. Buonanno and Toole emphasized that the diagnosis of TIA can only be made retrospectively after the episode has cleared within the arbitrarily set time limit and that it must be made with qualifying terms pending the outcome of special laboratory procedures such as CCT. They believe that the diagnosis of TIA and reversible ischemic neurological deficit (RIND) signify ischemia with preserved viability of neural tissue and that infarction represents ischemia prolonged beyond the length of time that involved tissue can survive. Hossmann and collaborators have experimentally confirmed the reversibility of neuronal dysfunction after transient ischemia, underscoring the importance of the distinction between ischemia and infarction.

This article will focus on the occasional patient who, from a clinical point of view, presents with a neurological syndrome with a temporal profile similar to that seen in TIA, but in whom laboratory investigations show clear evidence of infarction. Representative examples of two such patients, illustrating different aspects of this situation, follow.

Case Reports

Case 1
A 59-year-old hypertensive righthanded man developed a 3 hour episode of slurred speech, weakness and "numbness" of the left arm and leg. The crural weakness was so severe that the patient could not stand. When examined by a neurologist 3 days later, the sole residuum was intermittent left-sided extinction on double simultaneous stimulation. A right carotid bruit was heard by some examiners. The hematocrit was 54, with normal white blood cell and platelet counts. RPR and erythrocyte sedimentation rate were normal. Electrocardiogram was suggestive of ischemia but did not show infarction. CCT revealed a low density area consistent with evolving infarction in the right parietal lobe (fig. 1). Angiography (fig. 2) revealed occlusion of the right internal carotid artery with perfusion of the right hemisphere via ophthalmic retrograde flow from the external carotid artery.

Case 2
A 50 year old professor, while conversing with a friend on 7-7-80, suddenly developed inability to express himself and weakness of the right hand. He walked to his bedroom and lay down. His wife and friend, who had been with him at the initiation of the event, observed that his mental processes seemed slow. For example, when the emergency squad arrived 15 minutes later, the patient was of the impression that only one or two minutes had elapsed. When examined by a neurologist within the hour of onset of the episode, he was noted to have a Broca's aphasia and a right hemiparesis, with a right central facial paresis. It was felt that he had a mild sensory deficit to light touch in the right hand and fingers. Neurovascular examination was normal and he had no bruits in the neck. Blood pressure was 130/80 mm Hg and the pulse regular.

All of these defects resolved completely within 20 hours. CCT performed within 24 hours was compatible with evolving infarction of the left posterior frontal region. Cervical cranial arteriography showed normal extracranial arteries without atheromatosis. In the left posterior frontal region there was a focal area of luxury perfusion involving the short gyri of the insula.

Electroencephalogram, electrocardiogram, echocardiogram, RPR, complete blood count, platelet count and erythrocyte sedimentation rate were all normal. Radioisotopic brain scan on 7-9-80 was normal. Repeated on 7-30-80, it showed increased uptake in the left frontal parietal temporal region, compatible with a small area of infarction. CCT on 8-1-80 demonstrated a hypodense lesion in the anterior part of the left insula, and a dilated frontal horn, suggesting focal infarction which had evolved from the time of the

FIGURE 1. CT scan showing right parietal infarction (arrow) in Patient No. 1.
FIGURE 2. Recent carotid arteriogram showing recent occlusion (arrow) from Patient No. 1.

previous scan on 7-8-80. Speech testing on 7-30-80, with a Porch index of communicative abilities and the Boston Diagnostic Aphasia Examination was entirely normal.

Xenon inhalation regional cerebral blood flow studies were performed seriatum (fig. 3). Baseline Flow Gray pattern and distribution were normal bilaterally on 7-8-80. CO₂ stress test was abnormal with paradoxically reduced flow response in Broca’s area and hyperperfusion responses in adjacent areas. The rest of the left hemisphere was non-reactive. On 7-15-80 the left hemisphere baseline pattern was normal, but the CO₂ response remained decreased in Broca’s area, although improved from the previous test of 7-8-80. On 7-31-80 the left hemisphere was still decreased in response to 5% CO₂, with paradoxical CO₂ response in parietal and occipital lobes. Right hemisphere was normal. In review of all three cerebral blood flow studies, the pattern of baseline flow remained low normal quite consistently over the three studies. Vasomotor reactivity to CO₂ improved dramatically over time.

Of incidental interest is the fact that the patient now remembered that he had had several episodes of tingling as well as numbness and unsteadiness of his right hand which had occurred in the month preceding the acute event.

Discussion

From a clinical point of view, these patients had transient focal neurologic dysfunction with a time course corresponding to that of TIA. The deficit was focal, the time course appropriate and resolution was nearly complete in Case 1 and complete in Case 2. On the other hand, from an anatomical point of view, CCT showed evolving infarction and in one case the regional cerebral blood flow studies were disturbed for six weeks. Should these patients be classified clinical-
ly as having sustained a TIA or pathologically as having suffered cerebral infarction, or both? It is unlikely that the pathogenesis of the cerebral insult in these two patients was identical. Nevertheless, from the point of view of clinical phenomenology, the diagnosis of TIA would be correct, whereas with respect to the structural findings, a more proper diagnosis would be completed infarction. An old "silent" infarct with a new episode of borderzone ischemia resulting in a TIA is another possibility. In the case of cerebral infarction, should the patient with clinical resolution within 24 hours despite infarction in a "silent" region be classified and possibly treated differently from the patient with functional recovery after infarction in a less silent area? In cases such as this, the term "transient ischemic attack" is only partially correct — neurologic dysfunction is indeed transient, but the pathology may be that of a cerebral infarction.

These questions are not purely semantic or academic. Decisions for medical and surgical intervention, as well as prognosis, may differ significantly. The patients described above may be viewed as representing a good surgical risk because of absence of clinical deficits. Yet, from a pathological point of view, the disease process is one of infarction and the risk of surgical conversion of anemic to hemorrhagic infarction must be considered.

Patients such as these are not rare and their classification hinges upon one's decision about CCT findings in TIAs. The interpretation of CCT findings is, of course, also evolving, and with the development of refined imaging methods, it is likely that the accuracy of diagnosis of structural pathology will improve. Few currently available series of patients with TIA take into account the possible differences between those patients with ischemic lesions, and those with infarctions without residual clinical findings. Yet the distinction between pathologically verified TIA, in which the neurological dysfunction is both transient and due to ischemia — a potentially reversible parenchymatous lesion, and cerebral infarction — in which there is irreversible loss of brain tissue — is a crucial, if poorly understood, one. It would not be surprising to find different vascular lesions, prognoses, or response to medical or surgical intervention.

We believe that one root of the problem resides in some cases in inexactitudes of the clinical history and the neurological examination. Regarding history we must, for example, consider the difficulty that patients have in expressing their symptoms, particularly if the event affects the nondominant hemisphere, or if the attack begins during sleep. The moment of beginning of the attack may not be precise and of course, its complete resolution may also be a matter of interpretation. This is illustrated by visual observations described as blurring of vision. Is this partial amaurosis fugax? Another example is provided by the patient with intermittent vertigo. Because of difficulty in its evaluation, clinicians customarily eliminate this symptom from consideration as a TIA unless it is accompanied by other phenomena. Frequently patients will describe visual observations which may include evanescent diplopia. Opinions are divided about whether to classify such patients as TIA. This difficulty with classification is demonstrated by the findings of the cooperative group for study of TIA chaired by Dyken who found that fully 1/3 of patients admitted to the hospital with a diagnosis of TIA were misclassified.

Furthermore, whether the patient has resiud of the attack is again judgmental. We have repeatedly encountered patients who by their own account are completely without sequellae, but whose close associates describe as having altered judgment or a personality change. Cognitive changes as a residuum have not been adequately considered in classification of cerebrovascular events as TIA or cerebral infarction. Nevertheless, this consideration is an important one in decisions regarding classification. The objective modalities used for assessing whether a patient has recovered fully within the 24 hour time constraints are subjective and perhaps arbitrary.

Regarding patient examination for "complete" recovery, this at times is exceedingly difficult. Patients' baseline neurological status, particularly regarding higher cortical function, is often not known so that comparisons cannot be made. What one is left with following examination is a series of observations which, if normal, suggest intact neural function. But if the neurological examination remains abnormal, one must speculate as to whether the ictus or a more remote event(s) caused the abnormality.

This difficulty in classification occurs commonly, with physicians all interested in cerebral circulatory disease disagreeing on the basis of history as to whether an event was a TIA, Ménière's disease, presyncope or even a functional event. This difficulty is magnified when patients consult a physician some weeks after the event. By then the patient's memory has faded and residual deficits may be resolved. Most studies have accepted patients who have had TIA within one to two months of entry. Therefore clinical description and findings may be inexact.

Obviously, there is a need for further careful work in this area. Until further data are available, it seems prudent to us to reserve the term TIA to describe episodes of focal deficit which resolve completely within 24 hours, in which the purported brain lesion is one of an ischemic nature, and which on CCT leaves no visible evidence of its presence. A separate and specific category, cerebral infarction with transient signs (CITS), might appropriately be used to describe patients who (i) fit the temporal profile of TIA but (ii) in whom there is evidence for infarction on CCT. It should be emphasized that this category is an operational one, since the accuracy of diagnosis of structural cerebral lesions is improving with the development of new generation CCT scanners, positron emission tomography, and nuclear magnetic resonance, and may vary from center to center. CCT is only one of a number of laboratory tests that can demonstrate structural pathology, and it is likely that other tests will in
the future be widely available. Nevertheless, this dis­
tinction may prove useful for the diagnosis and study of patients with cerebrovascular disease, because it may permit the explicit differentiation of one type of transient neurological dysfunction with a well-defined basis in terms of parenchymal pathology. While it is unlikely that transient episodes of neurological dysfunction due to cerebral infarctions represent a single pathophysiological entity, it may be important to place patients with such episodes in a different diagnostic category from those with TIA, since this categorization may have important implications for prognosis and therapy.

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References


ERRATUM:


Caption for figure appearing on page 158 was omitted. The caption should have read, “Pathway of Arachidonic Acid.”
Temporal profile resembling TIA in the setting of cerebral infarction.
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