TRANSIENT GLOBAL AMNESIA: A REPORT OF THREE CASES AND REVIEW OF THE LITERATURE

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SYNOPSIS

Three patients aged 53 to 59 from each of the three major ethnic groups in Singapore presented with an acute disturbance of memory. They suffered a retrograde amnesia for all events of the past days to weeks and for 6 to 18 hours could not make new memories. As they recovered their retrograde amnesia shrank but the anterograde amnesia was permanent. They have remained well on follow-up and their attacks of transient global amnesia are probably due to transient ischaemia of the mesial temporal regions.

INTRODUCTION

Imagine youself on holiday in a strange country and you suddenly lose your memory for all the events of the last one or two weeks. You will suddenly realise you do not know where you are and not even how you got there in the first place. You will look confused and even absurd to those around you. To make matters worse, you can't seem to remember anything you are told for more than one or two minutes. Fortunately you still can remember who you are and who your friends and relatives are.

Three patients presented at Tan Tock Seng Hospital within a three month period with this problem of Transient Global Amnesia (TGA), a term first introduced by Fisher and Adams in 1964 (1). Although the pathophysiology remains obscure, the natural history and prognosis of this interesting albeit uncommon entity has become clearer in recent years. This paper will present the details of these three cases and review the literature available.

CASE 1 A WOMAN, AGE 56

The patient, a 56 year old Chinese housewife, presented on 8th August 1985. She woke up on the morning of 6th August 1985 and prepared breakfast for the family as was her normal habit. At 9:00 am she went marketing. On the way there she stopped by at a Chinese medicine shop to buy some herbs. As she did not have sufficient money with her, she telephoned her son at home to bring one hundred dollars to the shop. After buying a wide variety of herbs, she went to the market nearby where she bought both meat and vegetables. She returned home at 12:30 pm and proceeded to pack her purchases. At the same time she laid out on the table some of the herbs, meat and vegetables intended for the midday meal.

She gave instructions to her son, a 22 year old undergraduate, to boil some water for the herbs and went to telephone a relative. A heated argument occurred over the telephone and the conversation became very loud.

On returning to the kitchen after the long conversation, she became very agitated and kept asking who had brought all the herbs, meat and vegetables. Before her son could answer she would again ask the same question over and over again. She was jumpy and restless, and started to chain smoke. She knew who she was and who her son was but could not remember any of the events of that day. She also could not remember she had been hospitalised several days previously.

Six days previously she had been hospitalised for acute onset of vertigo and tinnitus in the right ear. She stayed in hospital for 3 days from 1st to 4th August. When reminded about the hospitalisation she again became very agitated and asked many questions about the hospitalisation. She gradually calmed down and was quite relaxed by 6:00 pm. When asked what she had been doing the whole afternoon she replied she had been taking a nap.

She finally went to bed at 8:00 pm and the next morning, with a lot of help, started remembering some of the events she had forgotten. By the time of admission she still could not remember the details of her earlier hospitalisation. Throughout this period she knew who she was and had no difficulty identifying her children. She could remember telephone numbers she knew before.

There was a history of appendicectomy in 1956 and she smoked 10 cigarettes a day for the last 20 years. She was admitted to Tan Tock Seng Hospital on 1st August 1985 for acute onset vertigo and tinnitus in the right ear. Examination did not reveal any abnormalities and a diagnosis of Meniere's disease was made. There was good symptomatic response to oral prochlorperazine and she was discharged three days later.

On examination she was found to be orientated in person, time and place. Memory of remote events was good and she could remember the events of the morning of 6th August. She had no memory of the period when she was very confused and also no memory of her recent hospitalisation. Short-term memory was excellent and seven-digit recall was normal. Her blood pressure was 140/90 mm Hg and the only abnormalities were a positive Hallpike's maneuvre with nystagmus demonstrating latency and fatigability. A full blood count, urea and electrolytes, ECG, CT scan without contrast enhancement and EEG were normal. She was reassured and discharged.

She has remained well with no similar recurrence.

CASE 2 A WOMAN, AGE 53

The patient was a 53 year old Malay housewife who lived with her daughter, son-in-law and three grandchildren. She woke up at 5:00 am on 4th July 1985 and did some general housekeeping in addition to washing the clothes. Her daughter woke up at 7:00 am and found her looking very confused. She could not remember what she had done that morning and kept asking herself "What is wrong with me? Why am I so confused?" She knew who she was and who her grandchildren were but could not remember the events of the past two weeks — including the mild upper respiratory tract infection she had three days previously.

She laid down on her bed and kept asking the time every few mintues. She appeared unable to remember anything she was told and kept asking the same questions many times. She ignored her grandchildren although she was able to carry on a conversation and did not look dazed. She was rational and speech was not slurred. At 10:30 am her daughter brought her to a government out-patient clinic where the doctor on duty did not detect any abnormalities. She was referred to Tan Tock Seng Hospital. They returned home first and there, at about 12:30 pm, she appeared to have become "normal" again. She could not remember having been to the government outpatient clinic.

She was seen at the Accident and Emergency Department of Tan Tock Seng Hospital that afternoon. No abnormalities were detected on clinical examination and her blood pressure was noted to be 130/90 mm Hg. Except for amnesia for the events of the past two weeks she appeared perfectly normal. There was no medical past history of significance.

She was seen later at the Neurology Department and was admitted. A thoroguh mental state and physical examination revealed no abnormalities. Full blood count, urea and electrolytes, chest x-ray, ECG and a CT scan without contrast enhancement were all normal. An ECG showed intermittent theta activity scattered bilaterally without lateralisation; no potential epileptiform activity was present. A 2-dimensional echocardiogram was normal.

She was reassured and discharged. When next reviewed in September 1985 she remained well although the amnesia remained unresolved.

CASE 3 A MAN, AGE 59

The patient, a 59 year old Indian missionary, became confused at about 7:00 pm on 1st June 1985. He was in Ipoh for a retreat and was having an after dinner chat with some friends when he developed a generalised headache. He had a history of migraine and was prepared for the attack. He took a tablet of cafergot and felt better. He vaguely remembers sitting down and has no recollection of what happened after that.

His friends suddenly found him behaving strangely. He appeared to have lost his memory and behaved oddly. He thought he was in hospital and kept asking who his room-mates were. He refused to go to bed and had to be carried there by his friends. Even then he dangled his legs over the side of the bed and refused to sleep. His speech was normal and he appeared rational. He was, however, unusually quiet and preferred to stare straight ahead as if deep in thoughts. He was observed hourly by a friend till 3:00 am when he fell asleep. At 5:30 am he woke up with absolutely no recollection of any of the events of the previous day.

He shaved and took a bath but conversation seemed impossible. An observer noted that his short term memory seemed almost non-existent. He was, however, still able to shave and take breakfast without any difficulty. He was able to go to the railway station and buy a train ticket to Penang. When he arrived in Penang he remembered the address of an old friend who ran a medical clinic there. He went there and was advised by his doctor friend to return to Singapore as fast as possible. He appeared to have recovered by this time. He returned to Singapore by air and was met at the airport by another doctor friend. He seemed quite his normal self. They went for dinner and he was admitted to Tan Tock Seng Hospital the next day.

He was a full time missionary and did not smoke cigarettes or drink alcohol. There was a 10 year history of migraine with bilateral retro-orbital headaches. He took cafergot when necessary with rapid relief.

Our patient was admitted to Tan Tock Seng Hospital on 3rd June 1985. Clinical examination was completely normal. A full blood count, ESR, urea and electrolytes, chest x-ray, ECG and CT scan without contrast enhancement were all normal. An EEG showed intermittent theta activity in the left temporal region.

He was reassured and discharged; remaining well till the present moment. He still has no recollection of the events of 1st June 1985. He remembers going to the railway station on 2nd June 1985 and then arriving in Penang.

DISCUSSION

Our patients were all middle-aged people without prior major illnesses. They came from all the three major ethnic groups in Singapore and suffered a temporary period of dysmemory suddenly. Patient 1, the Chinese housewife, suffered her attack after an emotional telephone conversation. The Indian missionary, patient 3, had an attack of migraine immediately before his. No precipitating factor could be identified in patient 2, the Malay grandmother.

They all suffered a loss of memory for all events occurring over a variable period immediately preceding the attack. This period of retrograde amnesia varied from days to weeks. The attack itself was characterised by bewilderment and repeated questions about present and recent events. Although they appeared to understand and accept the proferred replies, they kept repeating the same questions as if they forgot the answer (and probably also their question) immediately after they were given. In other words, they could not make new memories.

They appeared rational and speech appeared normal to their relatives and friends. Consciousness was not clouded and there was no motor weakness, sensory disturbance, difficulty in balance, involuntary movements or bladder and bowel dysfunction. There was no apraxia and they had no difficulty whatsoever with activities of daily living.

The attack was transient, lasting about 18 hours in patient 1, 6 hours in patient 2 and 15 hours in patient 3. Patient 1 recovered after a night's sleep while patient 3's attack persisted for several hours more after the night's sleep. After recovering they had no memory whatsoever of the events during the attack. Patient 1 claimed she had been "taking a nap" during that period while patient 2 had no recollection of going out to the outpatient clinic. The added period of retrograde amnesia i.e. loss of memory for events preceding the attack, shrunk in the following days but in none of our patients was there complete recovery.

Neurological examination after the attacks revealed no abnormalities of the central nervous system except for the amnesia. Investigations which included CT scan were normal except for mild abnormalities in the temporal regions on electroencephalography in patient 2 and 3.

An episode of acute transient memory disturbance was described as a complication of vertebral angiography by Hauge in 1954 (2). In 1956 Bender defined a "syndrome of isolated episode of confusion with amnesia" by describing twelve cases (3). It was, however, the extrememly detailed description of 18 personal cases by Fisher and Adams in their classic treatise of 1964 that established the syndrome of "Transient Global Amnesia" into common knowledge. Indeed, Fisher and Adams were not aware of Bender's paper before their landmark classic was published. This was not surprising as the Journal of Hillside Hospital was not widely available.

The condition affects mainly middle-aged and elderly men and women. The attacks occur abruptly and usually last less than 24 hours. Both emotional and physical stress (e.g. a hot shower or a swim in cold water) have been described as precipitants of some attacks. During the attack, the patients retain their personal identities and are able to perform normal activities. They are not able to remember new information and therefore tend to ask the same questions repeatedly. This applies to all forms of memory e.g. verbal, printed word, visual, auditory etc and hence the description of a global amnesia. Memory for the attack is lost forever. The associated retrograde amnesia often shrinks over several days but rarely resolves completely. The attacks usually do not recur although one patient with thirteen attacks of transient global amnesia has been described.

The physiological basis of TGA remains uncertain. Transient cerebral ischaemia (i.e. TIA of the posterior circulation) is favoured by many while others believe it may be epileptic. The development of TGA during angiography in some cases and its association with migraine (as in patient 3 where the attack was immediately preceded by an attack of migraine) would favour transient cerebral ischaemia. Of the more than 13 episodes of TGA occuring during or after angiography, the majority were related to injection of contrast material into the vertebral artery (2, 4). Shuttleworth et al (5) described two cases occuring 4 and 6 minutes after injection of contrast into the coronary arteries. In both cases the arterial pressure measurements were damped and corrected by aspiration just prior to the attacks. Arterial embolism was blamed. More sophisticated imaging techniques appear to support cerebral ischaemia as the physiological basis for TGA. Raichle has demonstrated, with positron emission tomography, a generalised decrease in cerebral blood flow and cerebral metabolic rate for oxygen with a disproportionately severe reduction in cerebral metabolic rate for oxygen in the mesial temporal lobes bilaterally during an attack of TGA. After the attack, cerebral blood flow returned to normal while cerebral metabolic rate for oxygen exceded normal (6). Caplan (7) has proposed the concept of "acute arterial dyscontrol" i.e. a sudden, self-limited alteration in vascular tone precipitated by an external or internal stimulus. He felt that aging or other risk factors for vascular disease could have rendered the arteries more prone to "dysregulation". This concept does provide a basis for the known association between migraine and TGA.

Those who favour epileptic discharge as the cause of TGA have produced encephalographic evidence. In

particular, Rowan and Protass (8) reported mesial temporal spike discharges during drug-induced sleep in five of seven patients studied with nasopharyngeal electrodes. They argue that the disorder in TGA occurs in deep temporal structures and hence the surface recordings used normally (as in our three patients) may not reveal epileptiform discharges. Nevertheless more than 80% of patients with TGA never experience another episode again. This is unlike the nature of epilepsy.

There is somewhat less controversy about the anatomical substrate of memory. It is well known that damage to the medial temporal regions of the human brain will cause a profound disturbance of memory. More specifically, the amygdalahippocampal complex appears to play a central role (9, 10) although the thalamus is also important (11, 12).

The early authors presented TGA as an essentially benign condition with excellent prognosis. Subsequent papers, however, described cases of TGA with more sinister lesions in the medial temporal region. The first report of a mass lesion in association with TGA was that of Hartley et al (13) who described a chromophobe adenoma of the pituitary gland extending laterally into the medial 2 cm of the left temporal fossa. This was discovered in a 62 yr old man. Then followed reports of a glioblastoma multiforme of the left hippocampus (14), a small left temporal haemorrhage (15), and a single metastasis (of a transition-cell carcinoma of the bladder) to the non-dominant temporal region (16) all causing cases of TGA. Drugs like clioquinol (17) and diazepam (18) have also been associated with TGA. Caplan (7), however, has pointed out that these cases often have other accompanying neurological signs atypical of TGA. For example, the patient with the chromophobe adenoma had persistent memory deficits and superior defects in the visual fields while the patient with the metastatic tumour had weakness of the left hand. The patients who took clioquinol had a toxic encephalopathy.

The relationship of TGA to classical atherosclerotic cerebrovascular disease has again been discussed recently. Kushner and Hauser (19) compared 18 patients and found that a prior episode of cerebral ischaemia was the most significant risk factor for TGA. They concluded that there was a close link between cerebrovascular disease and TGA and postulated that prior damage to anatomical structures may be necessary for the expression of TGA. Nevertheless the experience of most centres that see a large number of such cases confirm that this is an essentially benign disorder. Naturally any history of prior ischaemic cerebrovascular events should be treated on its own merits but an episode of TGA by itself would not justify extensive and invasive investigations like angiography.

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