

Unexpected outcome (positive or negative) including adverse drug reactions

Neuropsychiatric manifestation after a stroke: newly developed symptoms or side-effect of drug?

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Summary

A 55-year-old woman presented with sudden onset of left-sided body weakness and numbness, which was diagnosed as multifocal cerebral infarct with right thalamic bleed. She had concurrent hypertension, diabetes mellitus and chronic kidney disease. She suffered from central poststroke pain and reactive depression as poststroke complications, for which amitriptyline was prescribed. Unfortunately, she developed symptoms suggestive of mania and psychosis upon initiation of medications, which resolved upon withdrawal of amitriptyline. Amitriptyline is effective for treatment of poststroke pain and particularly useful in concomitant depression. Unexpectedly, this patient developed new psychopathologies after initiation of this medication. This case highlights the development of new psychopathologies that could be due to the antidepressant, underlying bipolar disorder or a complication of the stroke itself. Primary care providers need to actively enquire regarding neuropsychiatric symptoms because they can adversely affect the patient's quality of life as well as impede rehabilitation efforts.

BACKGROUND

Stroke is a condition that affects a person in many aspects; from early mortality to various physical disabilities. However, not many are aware that neuropsychiatric problems are one of the major complications of stroke, which remains undiagnosed in many stroke patients.¹ The following case illustrates how treatment for common stroke complications was complicated by the presence of new neuropsychiatric symptoms as well as renal insufficiency. It is important for primary care providers to identify psychiatric symptoms in stroke patients because they will adversely affect the quality of life as well as rehabilitation efforts.^{2,3}

CASE PRESENTATION

A 55-year-old woman with no known chronic medical or psychiatric illnesses developed sudden onset of left-sided body weakness and numbness upon waking up from sleep. She did not have any amaurosis, palpitations, headache, slurred speech or seizures. She was brought to an urban teaching hospital in Kuala Lumpur for medical treatment.

An urgent CT scan of the brain taken at the emergency department showed the presence of a hyperdense lesion measuring 1.6×1.3 cm, which was consistent with intraparenchymal bleed at the right thalamus. Perilesional oedema was also present. There were also multiple hypodense areas at both right and left external capsule, corona radiata and frontal regions. Periventricular lucencies were present, indicating small vessel ischaemia. There was no midline shift. The CT scan findings were consistent with a multifocal infarct with thalamic bleed.

She was also found to have hypertension, diabetes mellitus and renal impairment, which was previously undiagnosed. In her 5 days of admission, she was started on oral captopril 25 mg three times a day, felodipine 10 mg once

daily, atenolol 50 mg once daily, metformin 1 g twice daily, gliclazide 80 mg twice daily and lovastatin 40 mg once daily. Neuropsychiatric assessment was not done as the primary team found no overt abnormalities of her cognitive function. Due to limited resources, neuropsychiatric assessment was only performed for specific cases where the patient's cognitive function was in doubt.⁴ Physiotherapy intervention was also initiated in the ward. She was discharged with residual left-sided hemiparesis, paraesthesia and instability on walking, with outpatient physiotherapy intervention and oral medications.

She was later followed up at the primary care clinic 2 weeks following discharge. She revealed that the weakness and numbness still troubled her. As a result, she could not perform certain housework such as sweeping or cooking, although she was still able to perform her basic activities of daily living. She also admitted to feeling sad most of the day for 2 weeks prior to the first visit at the primary care clinic. She had difficulty falling asleep and her appetite was poor. She claimed that her neighbours had been gossiping about her, saying that she would not get well. Therefore, she refused to venture out of her own home. She denied any loss of concentration, guilt or suicidal ideation. There were no obvious manic or psychotic symptoms.

Her instability also made it inconvenient for her to go out. She was afraid she would fall and no one would be there to help her. Instead, she spent her days watching television alone in her home while her son worked. She also defaulted her rehabilitation sessions because there was no one to take her.

She was a divorcee, who stayed with her bachelor son. Prior to the stroke, she supported her family by selling pastries, which contributed significantly to her household income, after her divorce. Her instability and mood lability made it difficult for her to prepare pastries and this affected the family's quality of life.

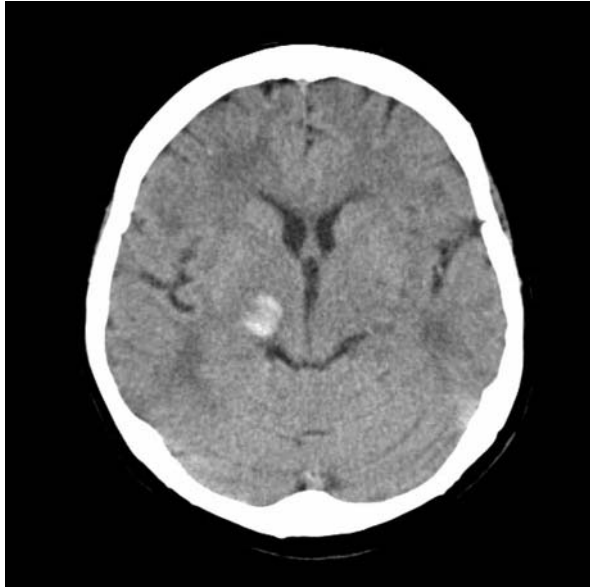


Figure 1 Right thalamic bleed with multifocal infarcts at right frontal region.

On examination, her gait was unstable and she required the aid of a walking stick. There was no abnormal movement noted. Her blood pressure was high, measuring 170/100 mm Hg, whereas her pulse rate was 92 beats per minute. Her body mass index was 20.3 kg/m². There were no obvious neurological deficits, except for slight reduction of power (4/5) for left elbow flexion and hyperreflexia over the left upper and lower limbs. Tone and power for both lower limbs were normal. There were no objective sensory deficits to fine touch or pin prick over her limbs. Cardiorespiratory examination and funduscopy were unremarkable. There was no pedal oedema. Apart from low mood, mental state examination was normal.



Figure 2 Right thalamic bleed with multifocal infarcts at the right frontal region and both external capsules.

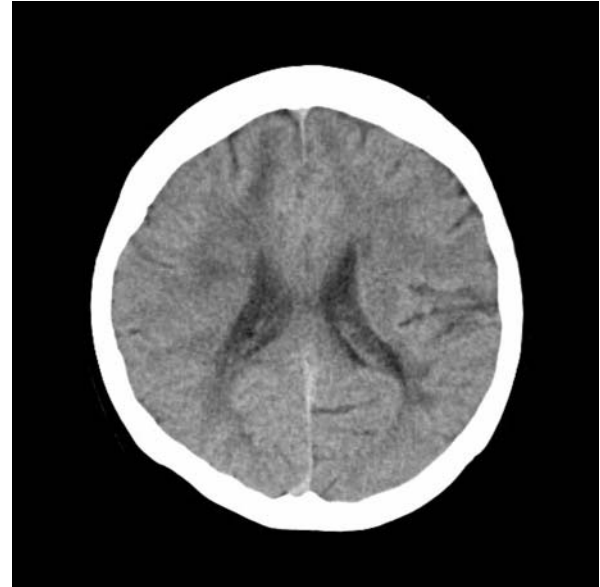


Figure 3 Infarcts of both corona radiata.

Blood investigations done at the clinic showed impaired renal function; her estimated glomerular filtration rate (eGFR) was 45 ml/min/1.73m². She had poor glycaemic control with an HbA1c of 11.6%.

In view of the new depressive symptoms and concurrent paraesthesia, she was started on oral amitriptyline 25 mg once daily. She was given an appointment within the same week to review her blood pressure after titration of her antihypertensives.

During the subsequent visit, she reported that her paraesthesia and sleep had improved. Her low mood persisted because she held to the thought that her neighbours had said that she would not recover. Her random capillary glucose was within the target range. However, blood investigations revealed that renal function had deteriorated to an eGFR of 25 ml/min. Doppler ultrasound of the renal arteries ruled out renal artery stenosis. However, she was found to have bilateral renal parenchymal disease. At that point, amitriptyline was retained at the current dose.

During the fourth visit, she appeared happy and attributed it to feeling good after a visit by her relatives. She was able to sleep well on amitriptyline.

However, by the next visit, she was apparently elated. She was dressed in bright red attire. At times, she smiled for no particular reason. There were no other symptoms of mania such as pressure of speech, grandiosity or pleasure-seeking behaviour. The paraesthesia of her lower limb had improved. She claimed that she had a better relationship with her neighbours. As a result, she had been overindulging in sweet and fatty food. However, she also complained of drowsiness and still chose to isolate herself at home. Amitriptyline was discontinued due to her hypomanic symptoms, excessive drowsiness, as well as resolved paraesthesia.

Two weeks later, the drowsiness and hypomanic symptoms persisted. She revealed her plans to restart her business and subletting her home for extra income. She giggled for no apparent reasons. Upon further probing, she claimed that other people could read her mind and

also believed that something had entered her body, causing her paraesthesia. There were no overt auditory or visual hallucinations or bizarre delusions.

She was referred for psychiatric assessment. She was diagnosed with adjustment disorder and subsequently defaulted follow-up at the psychiatry clinic after the second visit.

DISCUSSION

This patient had symptoms of central poststroke pain, commonly found in strokes involving the thalamic region.⁵ Central poststroke pain is a condition where persisting neuropathic pain develops due to a lesion in the central nervous system after a stroke.⁶ This patient had persisting paraesthesia over the left side of her body, which began within 6 months of stroke in the contralateral side of the body, corresponding to the lesion in the right thalamus, which were features of central poststroke pain.⁶ This condition can be very distressing for stroke patients and affects their quality of life.

Low-dose amitriptyline, a tri-cyclic antidepressant, is the standard first-line therapy for central poststroke pain, which has been found to be safe and effective.^{5,6} Onset of relief can be as early as 2 weeks from initiation of therapy,⁶ and could also benefit her depressive symptoms. Amitriptyline worked well for this patient, and she did not complain of the anticholinergic side-effects commonly caused by tri-cyclic antidepressants. However, over time, she developed excessive drowsiness and mood changes.

The mood changes were not the result of altered drug metabolism or excretion due to her renal insufficiency. It has been shown that plasma levels of amitriptyline are reduced in patients with renal insufficiency.⁷ In fact, patients with renal insufficiency would require higher doses of amitriptyline to achieve the desired effect for either neuropathic pain or depression.

Stroke itself is often associated with neuropsychiatric symptoms. The commonest neuropsychiatric complications are poststroke depression (35% prevalence), anxiety (25%), apathy (20%) and catastrophic reactions (20%).^{1,8} Mania and psychosis have also been reported to occur poststroke; however, they are very rare.⁸ An early neuropsychological assessment while she was still warded may have been beneficial by detecting any cognitive or psychological complications which were not readily apparent.⁴ This will facilitate rehabilitation efforts to include management of any psychological complications of stroke.⁹

This patient initially had depressive symptoms. However, after 4 months from the initiation of low-dose amitriptyline, she started demonstrating hypomanic symptoms, such as elated mood and increased appetite. Nevertheless, her hypomanic symptoms did not fulfil the Diagnostic and Statistical Manual-IV criteria for hypomania.

Her hypomanic symptoms could be attributed to several causes. Antidepressants, such as amitriptyline, have been shown to induce mania and hypomania in patients with underlying bipolar disorder.⁸ It could be possible that she had soft hypomania,¹⁰ which became apparent after the initiation of amitriptyline.

Her symptoms could also be at the milder end of the spectrum of poststroke mania.¹¹ This rare condition has a prevalence of 1% among acute stroke patients and is usually associated with strokes involving the right

hemisphere of the brain.¹¹ Despite preliminary evidence that right hemisphere strokes may be associated with poststroke mania,^{12,13} the link between stroke location and mood disorders are still unclear.¹⁴

With the discontinuation of amitriptyline, her mood gradually returned to normal. The presence of psychotic symptoms, such as somatic passivity and thought broadcasting, prompted the need for in-depth psychiatric evaluation.

After psychiatric evaluation, her symptoms were diagnosed to be due to adjustment disorder. However, adjustment disorders tend to present with symptoms of depression and anxiety or conduct disorder rather than manic or psychotic symptoms.¹⁵ Unfortunately, discontinuation of follow-up hindered the confirmation of diagnosis because the full evolution of psychopathology could not be assessed. The possibility of an underlying bipolar disorder could not be excluded in this case.

Learning points

- ▶ Neuropsychiatric complications of stroke are common, but are often not screened or detected by primary care doctors.
- ▶ We need to inquire regarding symptoms suggestive of neuropsychiatric disorders in all stroke patients.
- ▶ Central poststroke pain can be treated with antidepressants, which will also help to improve symptoms of depression. Despite the small risk of inducing hypomania, treating central poststroke pain with antidepressants will improve patients' quality of life and facilitate rehabilitation efforts.

Competing interests None.

Patient consent Obtained.

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