Unusual association of diseases/symptoms

Viral encephalitis and atherothrombotic stroke

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Summary

The clinical hallmark of viral encephalitis is an acute febrile illness, but stroke-like presentations have been rarely described. We report a patient who arrived at A&E with an acute right middle cerebral artery syndrome, without fever. Following thrombolytic treatment, clinical deficit almost disappeared and a critical ipsilateral carotid stenosis was identified. Stenting was implemented and 7 days later the patient started with high fever and reappearance of the initial deficit. Hyperperfusion syndrome and pneumonia were initially considered as the diagnosis but herpetic encephalitis (HE) was the final diagnosis. A very good response to antiviral treatment was achieved. We discuss whether the patient suffered from an unusual sudden stroke-like onset HE without encephalitic features or whether a stroke led to delayed HE.

BACKGROUND

Herpetic encephalitis (HE) is the most common sporadic necrotising encephalitis in the Western world.¹ The main modifiable predictor of outcome is the delay between admission and initiation of acyclovir treatment. In a small retrospective study,² there appeared to be a tendency towards a poorer outcome associated with a longer delay between symptom onset and treatment initiation. A further, larger, study³ showed that a delay of >2 days between hospital admission and initiation of therapy was associated with poor outcome at 6 months of follow-up. We present, here, a complex clinical case to highlight the importance of avoiding treatment delays while awaiting definitive HE diagnosis, especially when a high level of clinical suspicion exists.

CASE PRESENTATION

At 21:50 on 12 March 2008 a 71-year-old man telephoned the emergency ambulance service because he suddenly noticed weakness in the left arm and leg and left side of the face, and slurred speech. The patient and his family confirmed that it was the first time these symptoms had occurred and there were no accompanying abnormal movements or loss of consciousness.

His medical history was that of dyslipidaemia and hypertension since 2002; the latter controlled with β -blockers and diuretics. No statin had been prescribed. Tobacco consumption had been 20 cigarettes/day for 12 years but he had quit smoking from past 4 years.

On examination in A&E, his temperature was 36.4°C, blood pressure was 157/58 mm Hg and heart rate regular at 76 beats/min. Neurological evaluation revealed eye deviation to the right side, left complete hemianopia, anosognosia, left visual hemineglect, mild dysarthria and left hemiplegia. His score on the National Institutes of Health Stroke Scale (NIHSS) was 15, with a normal level of consciousness. No additional pathological findings were found on systemic exploration.

A complete blood test (cell count, biochemistry and coagulation) and cranial CT were performed immediately (figure 1A,B). A 12-lead ECG showed sinus rhythm.

Since the patient was considered to have had a stroke and the platelet count was normal, intravenous thrombolysis with alteplase was started at 23:08. The procedure was completed without any complication. The patient improved, with a NIHSS score of 9 within 2 h of the bolus drug administration. Cranial CT was performed (figure 1C,D) 24 h later, at which time the NIHSS score was 1. Brain imaging showed an inferior division of the right middle cerebral artery stroke with H1 bleeding. Antiplatelet treatment was prescribed.

To assess stroke aetiology, we performed a carotid artery duplex scan which showed a critical stenosis of the right internal carotid (figure 1E): internal carotid peak systolic and diastolic velocities were significantly increased, with clear asymmetry between middle cerebral arteries; and right middle cerebral artery damping (table 1, 24 h after transcranial Doppler (TCD)). Echocardiography and Holter-ECG were normal.

Early carotid stenting was planned for 18 March. Twelve hours before the procedure, the patient developed slight fever (37.5°C) with no additional clinical abnormalities. There were no neurological symptoms and the revascularisation technique proceeded uneventfully.

Nevertheless, the patient had a high fever the day after the procedure. A repeat complete evaluation was performed which identified hyponatraemia (129 mEq/l) and leucocytosis with 89.8% neutrophils. Intravenous levofloxacin was empirically administered as pneumonia was suspected despite a normal chest x-ray.

On 22 March, the clinical situation worsened and the fever did not respond to treatment. Sustained lymphocytopenia (800/ μ l) was found (lymphocyte count on admission was 1600/ μ l). Level of consciousness dropped and left hemianopia and visual hemineglect appeared, without changes in a non-contrast control cranial tomography. MRI was not available during that weekend. We opted to reassess carotid and cerebral basal arteries using ultrasound. Stent stenoses or occlusions were not observed, but the right middle cerebral artery velocities were significantly increased (table 1; 10th day TCD).

Figure 1 (A and B) Basal non-contrast cranial tomography. (C and D) A 24 h follow-up non-contrast cranial tomography. (E) Right internal carotid triplex echography. (Notes: V_{max} = systolic peak velocity; V_{min}=final diastolic velocity; PI=pulsatility index; angle measure=56°.) (F) Axial fluid attenuated inversion recovery-weighted MRI. (G) Coronal T2-weighted MRI.

Table 1 Patient's clinical evolution following admission

	Base line	24 h later	7th Day	10th Day	11th Day
NIHSS scores	15	1	1	5	5
Temp (°C)	36.4	37.0	38.5	38.5	38.0
Na (mEq/l)	137	N/A	129	129	128
TCD	N/A		N/A
Suspected diagnosis	Stroke	Stroke	Stroke and pneumonia	Hyperperfusion syndrome	?? MRI requested

Carotid stenting

N/A, not available; NIHSS, National Institutes of Health Stroke Scale; TCD, transcranial Doppler; Temp, temperature.

A diagnosis of hyperperfusion syndrome was considered at this point. However, as seen in table 1 (11th day TCD), Doppler spectra of the right middle cerebral artery normalised 24 h later, but the patient's condition worsened. Could fever and hyponatraemia explain this clinical evolution? What had we missed? Status was very atypical. Were we lacking some important data? The patient was stuporous, and we had no insight as to why. Hence, we decided to begin again with diagnosis options. There were two possibilities: something new and untoward was happening to our patient, or our initial diagnosis was wrong. Hence, we solicited an urgent MRI (figure 1EG).

Herpetic encephalitis was diagnosed after MRI. Lumbar puncture was not performed because of the right temporal lobe swelling. Intravenous acyclovir (10 mg/kg) every 8 h was administered for 21 days with good outcome.

INVESTIGATIONS

- ▶ Basal non-contrast cranial CT
- ▶ 24 h control non-contrast cranial CT
- ▶ Carotid artery duplex scan
- ▶ TCD
- ▶ MRI

DIFFERENTIAL DIAGNOSIS

- ▶ Stroke
- ▶ Hyperperfusion syndrome
- ▶ Herpetic encephalitis

TREATMENT

- ▶ Intravenous thrombolysis
- ▶ Antiplatelet treatment
- ▶ Carotid stenting
- ▶ Levofloxacin
- ▶ Acyclovir

OUTCOME AND FOLLOW-UP

The patient was asymptomatic at discharge from hospital (NIHSS 0).

DISCUSSION

This clinical case posed a considerable challenge to our Stroke Unit, where the procedures we decided upon are still debated.

HE was clearly responsible for clinical deterioration and fever, but the question is whether the initial syndrome was related to this herpes process, or whether two different pathologies were concurrent in the patient.

HE without fever, headache, altered level of consciousness and neurological signs is rare; the hallmark symptom of viral encephalitis is the acute onset of fever.^{1 4} Although unusual, a sudden stroke-like onset without encephalitic features has been previously reported by Abdul-Jabbar *et al*⁵ in an immuno-competent patient. There had been no fever on admission and serum sodium concentration was normal. However, the patient was younger than ours, without known risks factors.

Lumbar puncture and cerebrospinal fluid analysis, although considered the gold standard at the moment for HE diagnosis, is not compulsory for diagnosis; there are cases with negative PCR and a clear diagnosis of herpetic encephalitis.⁶ When the risk of cerebral herniation is high (in a patient with low level of consciousness and cerebral swelling), MRI can be diagnostic.⁷

Basal cranial tomography findings at initial HE stages can be similar to those found in stroke patients, so a clinical diagnosis must be reached at symptom onset. There are diagnostic pit-falls even when MRI is performed in the A&E; cytotoxic oedema may be observed at initial stages⁸ and patients with HE may even present with cerebral intravascular enhancement.⁹ Besides that, at early stages of encephalitis MRI can be normal.⁴

Hence, thrombolytic treatment administered under conditions mimicking a stroke, although uncommon, is possible even in the best clinical settings.

However, our patient's hemiplegia completely recovered after thrombolysis, and an ipsilateral carotid stenosis to the affected hemisphere had been observed. The most plausible explanation is, usually, 'one disease for every case' although sometimes patients present with several disorders simultaneously. We were unable to find descriptions in the literature of encephalitis after an ischaemic stroke, but stroke and reperfusion can damage the blood-brain barrier and lead to immunosuppression.¹⁰ Infarct

volume is the main predictor associated with lymphocytopenia.¹¹ Furthermore, HE following central nervous system surgical damage occurs with an average delay of 6 days,^{12 13} a period that is similar in our case.

A 1.5-fold increase in the middle cerebral artery mean flow velocity following carotid revascularisation indicates a high risk of hyperperfusion syndrome.¹⁴ Unfortunately, transcranial Doppler is not of much help at acute stages since hyperperfusion can occur in HE.¹⁵ Nevertheless, as previously reported by van Mook *et al*¹⁶ MRI is recommended if transcranial Doppler velocities normalise without patient improvement.

After careful reading of the literature, we conclude that there are grounds for both diagnostic possibilities. Confusing? Perhaps, but certainly difficult!

Learning points

- ▶ Although unusual, a sudden stroke-like onset without encephalitic features viral encephalitis has been previously described.
- ▶ Clinicians should have a high level of H&E suspicion when facing patients with stroke and fever and level of consciousness impairment, if other more frequent complications have not been confirmed.
- ▶ Herpetic encephalitis (HE) may produce haemodynamic changes in cerebral circulation that can be misleading. This fact should be taken into account in the interpretation of diagnostic tests.
- ▶ Thrombolysis administration under conditions mimicking a stroke is possible even in the best clinical settings.
- ▶ Stroke and reperfusion can damage the blood–brain barrier and lead to immunosuppression. It is well known that central nervous system lesions can be followed by HE.

Competing interests None.

Patient consent Obtained.

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