CASE REPORT

Hyponatraemic encephalopathy:
an unusual stroke mimic

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SUMMARY

We present a case of a 74-year-old man who was admitted to our stroke unit with symptoms and signs suggestive of a left total anterior circulation stroke. Subsequent MRI failed to support this diagnosis and, furthermore, correction of an incidental finding of hyponatraemia due to syndrome of inappropriate antidiuretic hormone secretion led to a complete recovery of symptoms. Investigation and subsequent exclusion of other potential differential diagnoses confirmed the diagnosis of hyponatraemia mimicking acute stroke.

BACKGROUND

Consideration of stroke mimics in the differential diagnosis of patients admitted with symptoms and signs of stroke is essential to avoid the risks of associated treatment including thrombolysis and antithrombotic agents. Further, the psychological impact of mislabelling patients with cerebrovascular disease can be devastating.

Common stroke mimics including space occupying lesions, sepsis, hypoglycaemia and seizures are well documented in the literature. Although rare, electrolyte disturbances are an important differential and if not considered and investigated, significant pathology may go undetected. We present a rare case of hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH) mimicking acute stroke.

CASE PRESENTATION

A 74-year-old man with a medical history of cervical myelopathy, type 2 diabetes mellitus complicated by sensory neuropathy and retinopathy, and pernicious anaemia, presented with confusion, vomiting, headaches and reduced mobility. He was afebrile and agitated on admission, with normal cardiorespiratory and gastrointestinal examination findings. Neurological examination identified a receptive and expressive dysphasia, however, no focal limb weakness was found. Serum sodium on admission was 120 mmol/L. On day 2 of admission, the patient had developed a right homonymous hemianopia and pronator drift of the right arm with pyramidal distribution weakness. He had a positive Babinski on the right and plantar response was equivocal on the left. The National Institute of Health Stroke Score (NIHSS), a score used routinely in the assessment of physical impairment in patients with stroke, with greater scores indicative of greater disability was 10, constituting a moderately severe stroke. It is noteworthy that serum sodium had dropped to 118 mmol/L on this day.

On review of symptoms, there was no history of weight loss, change in bowel habits or rectal bleeding. The patient's regular medication included omeprazole 20 mg once daily, metformin 850 mg thrice daily, pregabalin 150 mg twice daily and loratadine 10 mg once daily. He lived with his wife and was independently mobile with a crutch. He was an ex-smoker and drank alcohol occasionally.

An assessment by the speech and language therapist confirmed global aphasia and dysphagia, and the patient was placed nil by mouth with a view to nasogastric feeding.

INVESTIGATIONS

Admission blood tests demonstrated hyponatraemia, with serum sodium of 120 mmol/L, and microcytic anaemia (haemoglobin 120 g/L, mean corpuscular volume 77 fL). White cell count and C reactive protein (CRP) were within normal limits. Iron profile results were in keeping with anaemia of acute/chronic disease.

Further investigations into the hyponatraemia demonstrated low serum osmolality (265 mmol/L (normal range 285–295), normal 9:00 cortisol, and elevated urine osmolality and urine sodium values (679 mOsm/kg/L and 49 mmol/L, respectively). The results were in keeping with the SIADH.

CT of the brain at the time of admission demonstrated minimal cerebral atrophy with no acute changes. Chest X-ray demonstrated clear lung fields with no evidence of malignancy.

MRI with routine sequences including diffusion-weighted imaging (DWI) was performed following the deterioration noted on day 2. This demonstrated mild periventricular ischaemic changes on fluid-attenuation inversion recovery sequences (FLAIR), but no changes on DWI (figure 1), excluding acute infarction. Further, there was no abnormality of the temporal or frontal lobes or deep grey nuclei on T2 sequences (figure 2).

An EEG demonstrated normal findings, with no evidence of an encephalopathy.

A lumbar puncture was considered to investigate the possibility of a viral encephalitis, however, several attempts were unsuccessful.

DIFFERENTIAL DIAGNOSIS

A number of differential diagnoses were considered on admission. The working diagnosis was stroke due to the identification of a global aphasia and vascular risk factors, namely diabetes and being an ex-smoker. The normal CT of the brain on admission did not exclude this diagnosis as this can be normal in early ischaemia. The focal neurological

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Figure 1 Normal axial MRI diffusion-weighted imaging.

deterioration noted on day 2 led to the suspicion of stroke progression and an urgent brain MR was performed. Appearances of the brain were within normal limits and, significantly, with no changes on DWI, excluding ischaemia as the cause of symptoms.

Encephalitis was considered as a differential diagnosis given the subacute onset of symptoms over 48 h and the presentation with an acute confusional state. Unfortunately, despite several attempts, cerebrospinal fluid sampling was unsuccessful. This diagnosis was discounted clinically on the basis of the lack of fever and the absence of any raise in inflammatory markers (white cell count 6.7 and CRP 11). EEG, a sensitive indicator of cerebral dysfunction including in early encephalitis, was normal.¹ Finally, MRI of the brain is highly sensitive and specific for encephalitis, particularly when performed with diffusion-weighted sequences,¹ and this was normal. There was

Figure 2 Axial MRI T2 sequence demonstrating mild periventricular ischaemic changes.

no recent history of vaccinations or infectious processes and so acute disseminated encephalomyelitis was considered unlikely.

Cerebral vasculitis is a complex disease that poses considerable diagnostic and therapeutic challenges. This was considered a possibility due to the subacute encephalopathy, headache and stroke-like symptoms. Although there were no inflammatory signs or symptoms, and normal serum inflammatory markers and a normal autoantibody screen, these can be observed in isolated angiitis of the central nervous system. Unfortunately, we were unable to obtain a cerebrospinal fluid sample; however, cerebral vasculitis is associated with a mild pleocytosis or elevated protein. Although imaging findings are not diagnostic of cerebral vasculitis, MR FLAIR and DWI changes can be observed, though these were not present in our patient.² Although cerebral vasculitis was considered unlikely, it could not initially be excluded.

Focal neurological deficits have been described in patients with hypoglycaemia from any cause and was considered in our patient. Though rare, metformin may cause hypoglycaemia. This differential was discounted due to persistent neurological deficits in the absence of hypoglycaemia.

Sepsis may mimic stroke, however, this is usually in the context of the debilitated state exaggerating features of a previous stroke. Further, there was no history of stroke, the patient was afebrile and investigation findings did not identify any systemic source of sepsis.

TREATMENT

Following the exclusion of haemorrhage on admission CT of the brain, the patient was started on aspirin as treatment of presumed acute ischaemic stroke and placed on fluid restriction 1/L per day. The patient presented outside the time window for intravenous thrombolysis (as confirmed with his wife) and so this treatment was discounted.

Empirical aciclovir was started following the neurological deterioration noted on day 2, pending the lumbar puncture and MR of the brain for possible encephalitis. Further, the serum sodium had fallen to 118 mmol/L and omeprazole (known to cause hyponatraemia) was discontinued and fluid restriction continued.

OUTCOME AND FOLLOW-UP

On day 7 of admission, the patient was found to be communicative, alert and orientated to time, place and person. He was unable to recall his journey into hospital, however, he did recall that he was not able to understand speech nor express himself. Serum sodium at this point had improved to 134 mmol/L. The following day, the hemianopia fully resolved. A reassessment by the speech and language therapist confirmed normal speech, comprehension and a coordinated swallow. The patient was discharged from hospital on day 10 with complete neurological recovery and an NIHSS of 0. Aciclovir was discontinued on day 4 due to lack of supporting evidence for encephalitis. [Figure 3](#) illustrates serial serum sodium values during the admission.

Since discharge, the patient's haemoglobin and serum sodium levels have remained within normal range and he has had no further neurological events.

DISCUSSION

Up to 30% of patients presenting to emergency departments with suspected stroke at initial assessment are discharged with a diagnosis of stroke mimic.³ Common mimics include psychogenic disorders, migraine, seizures, toxic/metabolic disorders

Figure 3 Serial serum sodium values during the admission.

and mass lesions.^{3 4} In one prospective stroke study, metabolic disorders accounted for 30% of stroke mimics and severe hyponatraemia accounted for one-third of these.³ Interestingly, aphasia was the most frequent presentation of stroke mimics accounting for up to 42.9% of stroke mimics.³⁻⁵

Hyponatraemia is the most common electrolyte disorder encountered in clinical practice and is associated with increased morbidity and mortality. Despite this, hyponatraemia is frequently underdiagnosed and undertreated.⁶ Hyponatraemic encephalopathy is defined as central nervous system dysfunction secondary to hyponatraemia. Severe hyponatraemia generally refers to serum levels below 120 mmol/L, however, factors such as the rate of decline in serum sodium, age and gender will influence observed features. Symptoms include lethargy and confusion at mild levels of hyponatraemia to seizures, coma and respiratory arrest at significantly lower levels. Symptoms of hyponatraemic encephalopathy can be reversible if treated promptly, however, one must be cautious due to the risk of osmotic demyelination syndrome with aggressive correction. A sodium increase of no more than 12 mmol/L in the first 24 h is recommended.

Neurological features manifest in 21% of patients with severe hyponatraemia.⁷ Further, in one case series of patients with hyponatraemic encephalopathy, focal neurological symptoms were present in 18%.⁸ In another case series of 184 patients with severe hyponatraemia, neurological features included seizures (3.3%), hemiplegia (2.7%), psychosis (0.5%) and quadraparesis (0.5%).⁹

The SIADH is defined by hyponatraemia and hypo-osmolality resulting from continued secretion or action of the hormone despite normal or increased plasma volume, and resulting in impaired water excretion. Causes of SIADH include disorders of the nervous system (eg, abscess, encephalitis, meningitis); neoplastic disorders including those involving the pulmonary, gastrointestinal and genitourinary systems; pulmonary disorders (eg, pneumonia, fibrosis, emphysema); and drugs (eg, opiates, haloperidol, barbiturates, etc).¹⁰ In view of the anaemia, our patient underwent gastrointestinal investigations, which were normal.

Hyponatraemia is a recognised complication of treatment with omeprazole and has been documented in several case reports.¹¹ In these cases, hyponatraemia was refractory to conventional corrective treatments, however, it did resolve on discontinuation of such treatment. Hyponatraemia is thought to

arise as a consequence of increased renal sodium excretion and SIADH.¹¹ Metformin itself has been implicated as a possible cause of hyponatraemia in one case report.¹²

Homeostasis within the brain and cerebral cortex is maintained largely by astrocytes and their foot processes, which form the major part of the blood-brain-barrier. Astrocytes respond to neurons by calcium dependent release of various gliotransmitters (ie, transmitters of glial origin), including the principle excitatory transmitter glutamate, which can influence neuronal and synaptic functions as well as the overall performance of the central nervous system.¹³

Aquaporin 4 (AQP4) is a predominant water channel protein, present in highest density in astrocyte membranes surrounding the blood-brain-barrier. They act as water-conducting pores and are upregulated in hypo-osmolar conditions (including hyponatraemia),¹⁴ thereby raising membrane permeability 5–20 fold. Thus water is shunted into astrocytes, preserving neuronal cell volume, to the detriment of their own neuromodulatory role.¹⁵ The variation in clinical features observed in severe hyponatraemia include factors such as the chronicity of the electrolyte disturbance; however, AQP4 polymorphisms have been detected in humans and are associated with differing osmotic permeabilities, and may also be a contributing factor.¹⁶

No further imaging was considered necessary to exclude stroke. First, symptoms were present for over 48 h and second these symptoms were suggestive of significant involvement of the left middle cerebral artery territory, factors that would make MRI with DWI highly sensitive and specific for stroke. Finally, one would not expect a full neurological recovery in a patient with stroke with an NIHSS of 10 within 10 days. The IScore (Ischemic Stroke Predictive Risk Score) is a validated tool that is useful in estimating the risk of death, disability and institutionalisation in the initial assessment of patients with acute ischaemic stroke using clinical parameters and chronic comorbid conditions. Using this tool, our patient's risk of death or disability at 30 days was 76.8%.¹⁷

A rapid assessment of the patient presenting with suspected stroke is essential to help guide treatment, particularly with thrombolytic agents. The earlier such treatment is given, the greater the benefit in functional performance. Stroke mimics present a diagnostic challenge in these pressured situations. In one case series, factors favouring a stroke mimic included a history of cognitive impairment, loss of consciousness or seizure activity at onset, and examination findings demonstrating a lack of lateralising symptoms, signs in non-vascular territories (eg, chest crackles) and symptoms that could not be attributed to one vascular territory.¹⁸ Reassuringly, studies have shown that the risk of thrombolysis associated complications in stroke mimics is exceedingly small and so unless the physician is convinced to the contrary, administering treatment promptly in suspected acute ischaemic stroke is preferable to delaying treatment in the search for mimics.

In summary, this case illustrates hyponatraemic encephalopathy masquerading as a stroke mimic, and has been described previously in the literature. The pathophysiological basis centres on functional as opposed to structural dysfunction and thus focal and generalised neurological symptoms of hyponatraemia can be reversible if treated promptly. In the case presented, the clear correlation between correction of serum sodium and improvement in function, in the absence of an alternative diagnosis, strongly suggests a causal relationship.

Learning points

- ▶ In patients with suspected acute ischaemic stroke, thrombolytic therapy should be considered and, if appropriate, administered quickly due to benefits of early therapy and low risk of complications in stroke mimics.
- ▶ Multiple conditions may mimic acute stroke and should be actively considered and investigated from the time of presentation.
- ▶ Electrolyte disturbance can mimic acute stroke and is a potentially reversible pathology.
- ▶ Correction of sodium should be cautious, with a target increase of no greater than 12 mmol/L over a 24 h period.

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