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References

1 **Mori M**, Kuwabara S, Fukutake T, *et al*. Clinical features and prognosis of Miller Fisher syndrome. *Neurology* 2001;**56**:1104–6.
2 **Willison HJ**, Veitch J, Paterson G, *et al*. Miller Fisher syndrome is associated with serum antibodies to GQ1b ganglioside. *J Neurol Neurosurg Psychiatry* 1993;**56**:204–6.
3 **Byrd RP Jr**, Roy TM. Pasteurella multocida respiratory infection: an important cat-associated zoonosis. *Arch Intern Med* 2003;**163**:1239.
4 **Proulx NL**, Freedman MS, Chan JW, *et al*. Acute disseminated encephalomyelitis associated with Pasteurella multocida meningitis. *Can J Neurol Sci* 2003;**30**:155–8.
5 **Yuki N**. Infectious origins of, and molecular mimicry in, Guillain-Barre and Fisher syndromes. *Lancet Infect Dis* 2001;**1**:29–37.

Coagulopathy and NICE recommendations for patients with mild head injury

Management of patients with mild head injury (MHI) is open to debate.[1] In the last few years, there has been a trend towards earlier diagnosis, implying an extensive use of computed tomography (CT), rather than admission and observation. The National Institute for Clinical Excellence (NICE) has recently proposed new evidence based recommendations on all steps of the management of patients with MHI.[2] In the diagnostic algorithm, coagulopathy (history of bleeding, clotting disorder, or current treatment with warfarin) is not considered a predictor variable necessitating early CT in subjects without loss of consciousness (LOC) or amnesia since injury. This statement conflicts with previous guidelines, where history of coagulopathy, independently of symptoms, indicated CT.[3]

Since 1999, all cases with MHI attending the Emergency Department of our district hospital have been treated and registered in a comprehensive database according to predefined procedures.[3] Our criteria for CT and/or hospital admission are wider than the NICE criteria; in particular, there is routine detailing of NICE variables, but in addition, all subjects with coagulopathy have an early CT, independently of symptoms and signs after injury. This provides the opportunity to determine the risk related to coagulopathy and the accuracy of the NICE recommendations.

We analysed the data of 7955 consecutive patients within 24 hours from trauma, who had been triaged for an acute MHI. MHI was defined as an injury of the head, other than any superficial injury to the face, Glasgow Coma Score (GCS) definitely 14 or 15, in subjects aged ⩾10 years. We excluded 1258 more patients because of unclear history of the trauma as primary event, major trauma with unstable vital signs, GCS <14, penetrating injuries, pregnancy, or voluntary discharge. All patients re-attending for complaints after discharge (282 cases) underwent a CT scan and in this study were considered only once. All patients received written recommendations at discharge for home observation and complaints that would require referral back to hospital for further evaluation. Observers were instructed to check for symptoms and signs, and for any change in patients' clinical status for 7 days.

According to NICE, CT scan is recommended in the presence of: (*a*) GCS <13 at any point and/or equal to 13 or 14 at 2 hours after injury, (*b*) any sign of basal skull fracture, (*c*) any focal neurological deficit, (*d*) post-traumatic seizure, (*e*) vomiting (>one episode), and (*f*) amnesia of events before impact >30 minutes, (*g*) risk factors (coagulopathy, age ⩾65 years, dangerous mechanism of injury), provided that patients have experienced some LOC or amnesia since injury. In our protocol,[4] CT is mandatory for subjects with risk factors, in particular amnesia and/or LOC (but excluding old age), independently of signs and symptoms.

Following our protocol, 4081 out of 4547 (89.8%) eligible patients had an early CT scan. In 3580 early CT was also indicated according to the NICE protocol; in 501, CT scans were performed in subjects outside the NICE protocol. These patients had CT because of coagulopathy (warfarin therapy) in 66 cases (13.2%), diffuse headache in 178 cases (35.5%), previous neurosurgical intervention in 26 cases (5.2%), history of seizures in 22 cases (4.4%), dangerous mechanism of injury in 172 cases (34.3%), and recent alcohol and/or drug misuse in 58 cases (11.6%).

Clinically important intracranial lesions were demonstrated in 477/3580 (13.3%) patients of the NICE group. Neurosurgical intervention was required within 7 days in 97 patients (2.7%) for haematoma evacuation or for elevation of depressed skull fracture. At follow up (6 months), 36 patients (0.1%) had an unfavourable outcome (death, persisting vegetative state, or severe disability by the Glasgow Outcome Scale), rated by an expert physician on the basis of a structured telephone call.

In the 501 NICE negative cases, 40 patients (8.0%) had an intracranial haemorrhagic lesion: intracerebral haematoma (20 cases); intracerebral haematoma plus subarachnoid haemorrhage (2); intracerebral haematoma plus subdural haematoma (3); subarachnoid haemorrhage (2); subarachnoid haemorrhage plus subdural haematoma (1), subdural haematoma (11); and epidural haematoma (1). This prevalence is lower compared with NICE positive cases (Fisher's exact test, p = 0.0006), but nevertheless NICE recommendations would not have led to early detection of these 40 lesions, for which neurosurgical intervention was required in five (12.5%): intracerebral haematoma evacuation (1 case), subdural haematoma (3), subarachnoid haemorrhage plus subdural haematoma (1). At follow up, only one patient died after 9 days for causes related to intracerebral haematoma, the remaining having a favourable outcome. In these 40 NICE negative cases with haemorrhagic lesions, coagulopathy was the main factor leading to CT scan in 16 cases (40%), and was associated with a fivefold increase in the risk of intracranial lesions (table 1). With logistic analysis, coagulopathy was the only predictor variable associated with CT lesions in asymptomatic patients not fulfilling NICE criteria for early CT. Six patients, re-evaluated for complaints after a median (interquartile range) time of 144 hours (66 to 168), had an intracranial lesion detected by a second CT; four belonged to the NICE positive group, two were in the NICE negative. None had coagulopathy.

The post hoc analysis of our prospective database demonstrates that NICE recommendations for CT scanning identify the majority of patients with intracranial lesions in subjects attending the ED for MHI. However, the exclusion of coagulopathy as a factor always indicating CT impairs the diagnostic accuracy of NICE guidance. Routine use of CT scanning is not cost effective; more than 90% of CT scanning are negative in subjects with MHI, and at least 98% are negative for epidural haematoma, the event requiring immediate intervention. A more liberal policy for CT use, making CT mandatory in patients with coagulopathy, independently of head trauma severity, would indicate only 66 additional CT in our total cohort of 3581 (less than 2.0%), with a 1:4 probability of identifying an intracranial lesion.

The indications for CT use in MHI are subject to a continuous debate.[5] Our data strongly suggest that the restrictive use of CT proposed by NICE in the presence of risk

Table 1 Characteristics of the 501 patients, submitted to early CT scan according to protocol, and not considered by NICE recommendations

	CT negative (n = 461)	CT positive (n = 40)	Odds ratio (95% CI)	p value*
Median (IQR) age, years	53 (29 to 77)	68 (46 to 78)	–	0.054
Median (IQR) INR†	2.3 (2.0 to 2.8)	2.2 (2.2 to 2.6)	–	0.464
Cause of injury				
Fall	204 (44.3%)	19 (47.5%)	1.14 (0.59 to 2.18)	0.741
Crash	179 (38.8%)	15 (37.5%)	0.94 (0.48 to 1.84)	1.000
Assault	15 (3.3%)	2 (5.0%)	1.56 (0.34 to 7.10)	0.637
Occupational	32 (6.9%)	2 (5.0%)	0.71 (0.16 to 3.06)	1.000
Risk factors				
Coagulopathy	50 (10.8%)	16 (40.0%)	5.48 (2.73 to 11.00)	<0.001
Dangerous mechanism	156 (33.8%)	16 (40.0%)	1.30 (0.67 to 2.53)	0.488
Age ⩾65 years	191 (41.4%)	22 (55.0%)	1.73 (0.90 to 3.31)	0.133
History of epilepsy	20 (4.3%)	2 (5.0%)	1.16 (0.26 to 5.15)	0.692
Previous neurosurgery	26 (5.6%)	1 (2.5%)	0.43 (0.06 to 3.25)	0.713
Alcohol and/or drugs	51 (11.1%)	7 (17.5%)	1.71 (0.72 to 4.05)	0.205

CI, confidence interval; *Mann-Whitney *U* test or Fisher's exact test: p<0.05; †international normalised ratio in patients with coagulopathy.

factors may be generally accepted. However, in the light of our data we suggest that CT should also be considered for all subjects with coagulopathy.

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REFERENCES

1 **Jagoda AS**, Kantrill SV, Wears RL, *et al*. Clinical policy: neuroimaging and decision making in adult mild traumatic brain injury in the acute setting. *Ann Emerg Med* 2002;**40**:231–49.
2 **National Institute for Clinical Excellence**. *Head Injury in Infants, Children and Adults: Triage, Assessment, Investigation and Early Management*. National Collaborative Centre for Acute Care. Available at: http://www.nice.org.uk/pdf/headinjury_full_version_completed.pdf. Accessed November 2003.
3 **Servadei F**, Teasdale G, Merry G, on behalf of the Neurotraumatology Committee of the World Federation of Neurosurgical Societies. Defining acute mild head injury in adults: a proposal based on prognostic factors, diagnosis and management. *J Neurotrauma* 2001;**18**:657–4.
4 **Fabbri A**, Servadei F, Marchesini G, *et al*. Prospective validation of a proposal for diagnosis and management of patients attending the emergency department for mild head injury. *J Neurol Neurosurg Psychiatry* 2004;**75**:410–16.
5 **Li J**, Brown J, Levine M. Mild head injury, anticoagulants, and risk of intracranial injury. *Lancet* 2001;**357**:771–2.

Neurogenic T wave inversion in pure left insular stroke associated with hyperhomocysteinaemia

Alterations in cardiac depolarisation and repolarisation are reported in 74% of patients with cerebrovascular events.[1] They are more frequent after subarachnoid and intracerebral haemorrhage, but may also occur in acute ischaemic stroke (15–30%) and are related to an increased incidence of malignant arrhythmia and sudden death (6%).[2]

The most common ECG alterations are QT prolongation, ST segment alterations, T wave flattening or inversion, and abnormal U waves.[1] ECG changes may be similar to those commonly observed in patients with coronary artery disease,[2] but they have also been demonstrated in the absence of autopsy proven heart disease.[1] This suggests a neurogenic rather than a primary cardiac cause, mediated by unbalanced autonomic control.

Experimental evidence implicates the insular cortex in cardiovascular control and heart chronotropic organisation,[2] and suggests its involvement in the genesis of adverse neurogenic ECG alterations.

Case report

A 68 year old right handed female was admitted after the acute onset of mild right ataxic hemiparesis, right facial and hypoglossal nerve palsy, and dysarthria. The patient was vegetarian, had no history of diabetes or cardiac disease, and was a non-smoker without relevant family history. Blood pressure was 150/100 mm Hg and heart rate (HR) was 94 beats per minute (bpm). The admission brain CT and Doppler ultrasounds were normal. A left anterior hemiblock was detected at ECG (fig 1C).

Standard blood chemistry showed macrocytic anaemia, with other parameters within normal range, including serum lipids (lipoprotein a, total, HDL, and LDL cholesterol, and triglycerides). Antithrombin III, PT, PTT, fibrinogen, protein C and S activity, and activated protein C resistance were normal. Searches for lupus anticoagulant, antinuclear antibodies, antibodies to extractable nuclear antigens, anti-neutrophil cytoplasm autoantibodies, anticardiolipin antibodies, and cryoglobulins were negative.

A homocysteine serum level of 35.7 µmol/l (normal values: <20 µmol/l), vitamin B12 deficiency (90 pg/ml; normal values: 200–1000 pg/ml), and normal folic acid were detected. Vitamin B12 and antiplatelet therapy were started. The patient's clinical condition improved and 5 days later she was discharged.

The day after discharge she was readmitted because of the recurrence of moderate right ataxic hemiparesis, dysarthria, and non-fluent aphasia with phonemic paraphasia, anomia, and with essentially preserved comprehension and repetition. Blood pressure was 130/90 mm Hg and HR was 92 bpm. Blood examination showed the previously detected macrocytic anaemia, and a C reactive protein (CRP) value of 2.14 mg/dl (normal value: <0.8 mg/dl). Brain CT and MRI (fig 1A and B) showed an infarct limited to the left insular cortex with no other lesions on the diffusion weighted images.

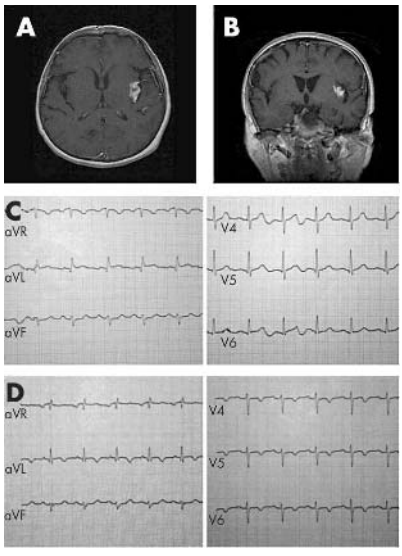

Figure 1 (A, B) T1 weighted spin echo axial and coronal scan (repetition time, TR = 500 ms; echo time, TE = 10 ms), showing the pure left insular stroke; (C) admission ECG showing only a left anterior hemiblock; (D) ECG performed 7 days after the second stroke showing the presence of neurogenic T wave inversion.

The admission ECG showed a global T wave inversion (fig 1D), which persisted on subsequent monitoring, and disappeared only after 2 months. No other ECG alterations were detected, including QT prolongation (QT = 0.34; QTc = 0.42 s). The patient had no cardiac symptoms and transthoracic echocardiography was normal as was serum potassium, calcium, and cardiac enzyme (creatine kinase-MB, troponine I, and myoglobin) investigation repeated over 5 days.

Following 3 weeks of therapy, vitamin B12 and homocysteine levels were normal, CRP value was 1.87 mg/dl, and the macrocytic anaemia had improved.

By 2 months after the cerebrovascular events, macrocytic anaemia was absent, homocysteine, vitamin B12, and CRP were normal, and the ECG had nearly normalised. An adenosine-thallium scan performed 6 months after stroke onset showed no evidence of coronary artery disease. To date there have been no cardiac events.

Comment

Acute insular stroke may present with various clinical presentations, due to the anatomic and functional complexity of the insular lobe and its wide connections with the frontal, temporal, parietal, and olfactory cortex, and with the basal ganglia, thalamus, and limbic structures.[3 4] It is an important gustatory, somatosensory, and visceral motor sensory processing area, a component of the vestibular and limbic cortex, and is implicated in pain processing, volitional swallowing, cardiovascular control, and cerebrogenic sudden death.[2–4]

Pure insular strokes, rare entities in clinical practice, are defined as infarcts restricted to the insula in which coexisting brain lesions are exclusion criteria, with the exception of some involvement of the claustrum and capsula extrema.[4] This definition is justified by the complex insular arterial supply which principally supplies the insular cortex, the capsula extrema, and the claustrum, and, sporadically, the capsula externa.[4]

The prominent clinical features of our case were neuropsychological disorders (expressive aphasia, dysarthria, verbal memory impairment), and electrocardiographic alterations, represented by persistent T wave inversion.

Neurogenic ECG alterations are often transient, but cause diagnostic problems, mimicking acute myocardial infarction. Some features of T waves may be suggestive of heart pathology, but they are non-specific, making it important to consider a neurogenic genesis to avoid unsuitable therapies.

The neurogenic nature of T wave inversion in our case was demonstrated by the lack of evidence of coronary artery disease or cardiac pathology, both of which were ruled out by echocardiography and adenosine-thallium scan. Myocardial enzymes, which have also been reported to be elevated mainly in large size stroke, were normal probably because of the limited extent of cerebral infarction.

In insular stroke the pathophysiology of abnormalities of rate, rhythm, and conduction is related to an imbalance of autonomic cardiovascular control and to increased circulating and local myocardial tissue catecholamines, suggesting an underlying sympathetically mediated mechanism. The insular cortex has been shown experimentally