and serological features of a demyelinating polyradiculoneuropathy.

Documented overlap of acquired acute central and peripheral system demyelination is very rare. Gamstrop and Blennow used the discriptive diagnosis of encephalomyeloradiculoneuropathy to designate paediatric cases of Guillain-Barré syndrome with presumed CNS involvement.[1] Again in children, Amit *et al.* coined the entity of acute severe combined demyelination for cases in which central and peripheral nervous system pathology equally contributed to the overall clinical picture.[2] An acute or subacute combined central and peripheral myelinopathy has been very rarely reported in adults,[3 4] with no successful treatment regimens being documented.

In our patient, no improvement was seen after high dose intravenous prednisone therapy (5 g), but she dramatically improved on intravenous immunoglobulin and plasma exchange therapy. This finding extends the previous reports of the effectiveness of this therapeutic strategy in the patients with central or peripheral inflammatory demyelination who failed to respond to high dose steroid therapy. Even a delayed treatment (7 weeks after onset of the symptoms) with immunoglobulin induced a significant remission. Further clinical improvement was achieved with subsequent plasma exchange. Our finding supports the concept of immunomodulation using immunoglobulin and plasma exchange in steroid resistant combined central and peripheral inflammatory myelinopathy.

Acute demyelinating diseases are often preceded by an infection or vaccination and considered to be immune mediated. This case of a severe unrestricted demyelinating syndrome encourages the concept that an immunological attack can be directed against central and peripheral myelin in susceptible individuals.

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Miller Fisher syndrome associated with *Pasteurella multocida* infection

Miller Fisher syndrome is characterised by ataxia, areflexia, and ophthalmoplegia and was first described by Charles Miller Fisher in 1956 as an unusual variant of acute idiopathic polyneuritis. There is frequently an antecedent illness[1] and the syndrome is associated with a high titre of anti-GQ1b antibodies in approximately 90% of cases.[1 2] *Pasteurella multocida* is a Gram negative bacteria, commonly found in the saliva of animals, particularly cats.[3]

We present the case of a 70 year old lady who developed Miller Fisher syndrome with positive anti-GQ1b antibodies 11 days after *P. multocida* was cultured from a blood sample. Miller Fisher syndrome associated with *P. multocida* infection has not, to our knowledge, been described previously.

Case report

A 70 year old lady presented with a one day history of a painful left hip, fever, sweats, and lethargy following a bite from her pet cat on her left leg on the preceding day. She reported no other recent illnesses. She had had a total left hip replacement four years previously. On examination she was hypotensive and pyrexial with local tenderness of her left hip and decreased range of movement. She had puncture marks on her left shin from the cat bite with surrounding erythema tracking proximally to the groin. Initial blood cultures revealed heavy growth of *P. multocida* sensitive to penicillin. Intravenous benzylpenicillin (1.2 g four times daily) was administered.

The patient's pyrexial illness improved over the next 11 days but then she developed diplopia. The attending orthopaedic surgeon recorded that the cranial nerve examination was normal. By the following day the patient had also become ataxic, and she was referred for a neurological opinion. Examination at this stage revealed marked truncal ataxia and complete internal and external ophthalmoplegia with bilateral ptosis. Limb examination revealed areflexia and ataxia although limb power and sensation were normal. The patient was unable to stand.

A computed tomography brain scan was normal. Magnetic resonance imaging was precluded by claustrophobia. The cerebrospinal fluid was clear, containing 0.5 g/l protein, 3.3 mmol/l glucose, no white cells/mm^3, and 255 red cells/mm^3. No organisms were seen or cultured. There was no clinical response to pyridostigmine and acetylcholine receptor antibodies were negative. A sample of blood taken seven days after the onset of neurological symptoms was positive for anti-GQ1b antibodies at a titre of 1:1600 using enzyme-linked immunosorbent assay (ELISA). The testing laboratory considered a titre above 1:100 to be positive for anti-GQ1b antibodies. Other antiganglioside antibodies and follow up anti-GQ1b antibodies were not tested.

A diagnosis of Miller Fisher syndrome was made and intravenous immunoglobulin (0.4 g/kg daily for five days) was administered with gradual improvement in symptoms and signs over the next six weeks leading to the patient's discharge. At follow up five months later she had fully recovered.

Discussion

This patient developed the typical neurological symptoms of Miller Fisher syndrome with positive anti-GQ1b antibodies 11 days after *P. multocida* was cultured from a blood sample. To our knowledge this is the first reported case of any form of Guillain–Barré syndrome associated with *P. multocida* infection.

P. multocida is a small Gram negative coccobacillus[4] and is an important animal and human opportunistic pathogen. In humans it can cause soft tissue, respiratory, urinary tract, and meningeal infections. The mechanisms by which *P. multocida* might cause Miller Fisher syndrome (we are assuming causation and accept we have only demonstrated temporal association) are unknown but molecular mimicry is a possibility. There is considerable evidence supporting the theory of molecular mimicry between lipopolysaccharide (LPS) from *Campylobacter jejuni* and the GQ1b ganglioside.[5] As *P. multocida* is Gram negative, its capsule similarly has LPS. However, we were unable to find any research specifically suggesting a similarity between the *P. multocida* LPS and the GQ1b ganglioside. *P. multocida* has previously been reported in association with acute disseminated encephalomyelitis[4] but not, to our knowledge, with any other diseases with a presumed autoimmune basis.

Although an antecedent illness has frequently been noted before the onset of Miller Fisher syndrome the causative agents are not as well described as in Guillain–Barré syndrome.[5] While *C. jejuni* has been implicated in the pathogenesis of Miller Fisher syndrome following enteritis, a recent study[1] of 50 patients with the syndrome found that 76% had respiratory symptoms in the month preceding onset of the syndrome compared with only 4% with gastrointestinal symptoms. *Haemophilus influenza, Staphylococcus aureus, Mycoplasma pneumoniae, Coxiella burnetii*, cytomegalovirus, Epstein–Barr virus, varicella zoster, and mumps virus have also been reported as antecedent agents in Miller Fisher syndrome. However, a statistical correlation with Miller Fisher syndrome has only been shown for *M. pneumoniae*[5]—serological evidence of recent infection was found in 7% of Miller Fisher patients compared with 2% of patients with Guillain–Barré syndrome.

From the above discussion it is clear that the antecedent illness in Miller Fisher syndrome commonly takes the form of a respiratory infection of unknown aetiology. *P. multocida* can cause respiratory infection. It is often difficult to isolate this organism from sputum samples[3] and it has been reported as causing indolent and asymptomatic pulmonary infection,[3] including asymptomatic lung abscess. For these reasons *P. multocida* infection is possibly underdiagnosed. Therefore, while we believe this is the first *reported* case of an association between Miller Fisher syndrome and *P. multocida* we believe it highly unlikely to be unique.

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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.