falling over him". His wife mentioned bizarre, useless movements of his left hand which were present from the beginning of the disease.

On admission, he was awake, bradyphrenic, and partially collaborative. His conversation was often disrupted by hallucinations. The affect was sad and he had partial insight for his mental dysfunction. He was disoriented for time, place, and situation. He could understand speech and was able to follow oral instructions involving two consecutive components. Naming was preserved. Prominent dysgraphia and dyscalculia were noticed. Immediate recall and short term memory were severely disturbed, whereas long term memory, especially for personal life events, was relatively spared. Abstract thinking was severely affected. Bimanual movements, such as clapping, were extremely difficult.

The cranial nerves were normal as were ocular fundi. The motor examination showed normal force. Deep reflexes were symmetric and plantar responses were flexor. The right arm had a dystonic posture. His gait was ataxic on a wide base.

At times, the left arm would spontaneously rise in front of the patient during speaking or while using his right hand. He was unaware of these movements until they were brought to his attention. When questioned about their purpose, the patient denied that they were voluntary. No grasping of either hand or foot was found. The patient had no cortical sensory loss.

The laboratory data including blood chemistry, haematology, and sedimentation rate were normal, as were folic acid, vitamin $B_{12}$ concentrations, and thyroid function.Venereal disease research laboratory and HIV tests were negative. The cerebrospinal fluid had normal content. Brain CT showed mild cerebral atrophy. An EEG showed severe diffuse slowing at admission. Within a week, repeated EEGs showed triphasic waves with a periodic pattern of 1- 1.5 Hz.

During the next 2 weeks, the patient developed myoclonic jerks. Severe dysphasia and cognitive decline were accompanied by confusion and aggression. He became grossly ataxic, and unable to walk and perform any of his daily activities even with help. Transferred to a chronic care hospital, he died few weeks later. Postmortem examination was not allowed.

This short fatal neurological disease manifested by fulminant dementia, myoclonic jerks, and extrapyramidal and cerebellar dysfunction was strongly suggestive of CJD. The periodic EEG pattern reinforced this diagnosis. Our patient's alien hand was part of the otherwise characteristic clinical picture of CJD, but it occurred early in the disease course when no myoclonic jerks were present. We are aware of only one report of alien hand in CJD. MacGowan *et al*[8] described two patients with CJD with a myoclonic alien hand syndrome. In one patient the left arm "was noted to have spontaneous movements which appeared purposeful…wandered out of her view". In the second, the alien limb performed complex actions such as unbuttoning her blouse and removing a hair pin. Although our patient had no myoclonus or pyramidal signs when the alien hand appeared, in their patients it was associated with spontaneous or stimulus sensitive myoclonus, spastic hemiparesis, and cortical sensory loss.

The literature seems to describe distinct forms of alien hand. All share the occurrence of involuntary movements contrary to the patient's stated intent, but the types of movement differ. In the callosal form, there are purposeful movements of the non-dominant hand.[9] In the frontal form, there is grasping and utilisation behaviour of the dominant hand.[9] In the corticobasal degeneration, there are aimless movements of either hand.[5 7] When a consequence of tumorous or vascular pathology,[9] alien hands can perform complex acts such as trying to tear clothes or undoing buttons. The description by MacGowan *et al*[8] has characteristics of the callosal form (especially in patient 2). However, our case suggests that the alien hand sign in CJD may appear in a different type, performing less complex movements which resemble those reported by Riley *et al* in corticobasal degeneration.[7] These authors described the alien limb as " involuntarily rising and touching the mouth and eyes" (patient 1). The patient thought that she "was powerless to stop this movement" and when directed to stop responded that "she can't". Another patient's left arm was at times "elevated in front of him", while he was "unaware of this situation until his attention was called to it" (patient 10).

Another related phenomenon coined as "arm levitation" was reported in progressive supranuclear palsy. In these patients the arm involuntarily raised and performed semi-purposeful movements.[10]

One common denominator between CJD, corticobasal degeneration, and progressive multifocal leukoencephalopathy,[6] in which an alien hand sign has also been described, is multifocality. In corticobasal degeneration, it was proposed that more than one site is affected or that a "release" phenomenon occurs accounting for the aetiology of alien hand.[7] In CJD, bilateral cortical damage to motor areas might be the origin of their subsequent isolation and disconnection.

We suggest that CJD should be added to the differential diagnosis of diseases presenting with an alien hand with or without myoclonus.

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## Recurrent peripheral neuropathy in a girl with celiac disease

The involvement of the peripheral nervous system (PNS) in children with celiac disease is particularly rare. Furthermore, in both children and adults with celiac disease, neurological complications are chronic and progressive.[1]

We report on a 12 year old girl affected by celiac disease, who on two separate occasions presented with an acute peripheral neurological syndrome after accidental reintroduction of gluten in her diet.

This patient was born uneventfully to healthy non-consanguineous parents with no family history of neurological or metabolic diseases. At the age of 6 months she was diagnosed as having celiac disease according to the European Society of Paediatric Gastroenterology and Nutrition (ESPGAN) criteria. Since then she was on a strict gluten free diet and was asymptomatic until the age of 10 years when severe diarrhoea, vomiting, and abdominal pain manifested 6 days after the intake of corn flakes erroneously thought to be gluten free. No previous infections had been noticed. One week after the onset of these symptoms she experienced acute weakness and pins and needles sensation confined to her legs. At that time her parents stopped her intake of corn flakes on the suspicion that these were responsible for the symptoms. Despite this, symptoms worsened during the next 2 days, confining her to bed.

At hospital admission, she was alert and mentally stable. Results of general physical examination were unremarkable. Neurological examination disclosed symmetric, predominantly distal, weakness of the legs; the knee jerks and ankle reflexes were depressed; plantar reflexes were flexor. Distal stocking glove decreased in pin prick and temperature with sparing of propioception and light touch. Coordination tests were normal.

Laboratory investigations showed a white cell count of 9300/$mm^3$. The results of the following investigations were within the normal limits: haemogram, erythrocyte sedimentation rate, serum urea, nitrogen, electrolytes, creatinine, glucose, transaminase, bilirubin, immunoglobulins (Igs), lead, iron, copper, urinalysis, urinary porphyrin, folic acid, and vitamins A, $B_1$, $B_6$, $B_{12}$, and E. Antibodies to *Campylobacter jejuni*, neurotropic antivirus antibodies, specific and non-specific organ autoantibodies, IgA and IgG antigliadin antibodies (AGAs), IgA antiendomesium antibodies (EMAs), and IgA antireticulum antibodies (ARA), assayed by enzyme linked immunoadsorbent assay (ELISA) and immunofluorescence (IF) were also negative. Lumbar puncture was not performed. Antibodies against gangliosides GM1 and GQ1b, myelin associated glycoprotein and myelin

*Electrophysiological study suggestive in both episodes of an acute demyelinating peripheral neuropathy confined to the lower limbs. Values were within normal limits in the upper limbs*

| | *1st Episode* | | *2nd Episode* | |
|---|---|---|---|---|
| | *Peroneal* $^{L}_{R}$ | *Tibial* $^{L}_{R}$ | *Peroneal* $^{L}_{R}$ | *Tibial* $^{L}_{R}$ |
| MCV (ms) | 26 | 27 | 22 | 24 |
| | 24 | 28 | 20 | 23 |
| DL (ms) | 7.3 | 8.0 | 7.2 | 8.8 |
| | 7.5 | 8.4 | 7.0 | 9.0 |
| F wave latency (ms) | 70 | 72 | 83 | 84 |
| CMAP (μV) | 3 | | 2.7 | |
| | Sural $^{L}_{R}$ | | Sural $^{L}_{R}$ | |
| SCV (ms) | 38 | | 40 | |
| | 42 | | 41 | |
| AMP (μV) | 16.2 | | 17.4 | |
| | 16.8 | | 18 | |

MVC=motor conduction velocity; DL=distal latency; CMAP=compound motor action potential; SCV=sensory conduction velocity; AMP=amplitude; L=left; R=right.

basic protein were not tested. Nerve conduction studies were consistent with a predominately motor demyelinating peripheral neuropathy (table). Her symptoms improved spontaneously and she was discharged home after 2 weeks. For 2 years she was asymptomatic on a gluten free diet.

At the age of 12 she presented acutely with severe abdominal pain 8 days after a weekly intake of bread meant to be gluten free. Two weeks later, due to persisting gastrointestinal symptoms, her parents excluded the bread from her diet. After 2 further weeks, while the abdominal pain was gradually improving, she had a new episode of acute weakness in the lower limbs and sensory abnormalities including burning paraesthesiae. On neurological examination the legs showed marked diminution in muscle power; absent deep tendon reflexes, and a reduction in pain and temperature; light touch, perception of position, and vibration were preserved. Walking was impaired and the patient was bedridden. Otherwise the examination was normal.

A haemogram showed white cell counts of 9700/mm$^3$. Laboratory investigations were within normal values as in the past. IgA and IgG AGA, IgA EMA, and IgA ARA assayed by ELISA and IF were again negative. Nerve conduction studies confirmed the presence of a predominantly motor demyelinating neuropathy (table). The parents refused consent for a lumbar puncture or nerve biopsy.

Over the next 2 weeks her neurological disabilities spontaneously improved until full recovery was complete. After 4 weeks, AGA, EMA, and ARA were still negative.

On her most recent admission, 1 year after the onset of her first neurological symptoms, she is still on a strict gluten free diet and has no residual symptoms or signs.

The natural history of celiac disease is well known and the typical celiac enteropathy is often associated with several other disorders. However, as celiac disease is a relatively common and lifelong condition, it is likely that some of these associations may occur by chance.

This patient, who was diagnosed as having frank celiac disease at the age of 6 months, experienced two episodes of acute peripheral neuropathy, at the age of 10 and 12 years, respectively. Two major pieces of evidence strongly support the assumption of a gluten derived disease: (1) the episodes occurred on both occasions when gluten was accidentally reintroduced in the diet; and (2) the response to a gluten free diet was reasonably rapid, occurring within weeks.

The present case, however, differs clinically from those with neurological involvement previously reported. In the paediatric age group, in fact, neurological complications of celiac disease are rarely encountered and are mostly confined to the CNS[2]: to the best of our knowledge, there are only two previously reported cases of PNS involvement in children with celiac disease. In both cases, however, these were chronic axonal polyneuropathies presenting during a gluten free diet.[3 4]

In both episodes in the present case neurophysiology was strongly supportive of a demyelinating peripheral neuropathy, which is most commonly attributed to a direct immune mediated attack to the myelin. By contrast, wallerian and axonal degeneration may be caused by vasculitis, and nutritional, metabolic, and toxic factors.

An autoimmune pathogenesis in association with strong evidence of a genetic susceptibility has been proposed for celiac disease. Although it is well established that AGA, EMA, and ARA are reliable indicators of sensitisation to gluten at least at the time of diagnosis, in the clinical practice at follow up, during a gluten challenge, pathological values of these antibodies may not be detected.[5] In the present case the time course of the disease might be suggestive of an antibody mediated response. However, we could not detect pathological concentrations of AGA, EMA, or ARA antibodies either during the course of the disease or at follow up.

It is known that in celiac disease many immunological perturbations can occur outside the gastrointestinal tract. Crossing of the antigens through a damaged small intestinal mucosa, deposition of immune complexes in target organs, a reduction in immune surveillance, mechanism of molecular mimicry, and activated T cell response may contribute to the pathogenesis of the diseases associated with celiac disease. Direct toxic effects of gliadin and vitamin deficiency are other possible pathogenic mechanisms of damage to the nervous system. Although we ruled out a vitamin deficiency it is still questionable whether a toxic neuropathy can be the case.

In conclusion, this case shows two major issues: an acute polyneuropathy can be a complication of celiac disease in childhood and its benign course could help in the understanding of the underlying pathogenic mechanisms.

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## Frontal release signs in older people with peripheral vascular disease

A growing body of research examining neurological aspects of clinically "silent" cerebrovascular disease suggests that neurological signs indicative of generalised organic brain damage may occur in the absence of completed stroke.[1] These soft signs include primitive reflexes (frontal release signs), representing an anatomical and functional deafferentation of cortical from subcortical structures. Primitive reflexes are known to occur in a wide variety of dementias, including Alzheimer's disease[2] and vascular dementia.[3] It is likely that the presence of undetected cerebrovascular disease accompanying peripheral vascular disease is underestimated, as peripheral vascular disease is known to be a risk factor for transient ischaemic attacks. A study assessing 373 older patients with peripheral vascular disease found that 72 of the 144 patients who had not experienced a transient ischaemic attack or stroke were found to have a degree of carotid stenosis of between 60% and 99%.[4]

In the present study, the prevalence of primitive reflexes was examined in older people with peripheral vascular disease and a non-vascular control group. Independent predictors of these reflexes were also examined in peripheral vascular disease. Both groups were drawn from the same geographical area. All were interviewed and examined outside hospital by myself. Interviewees were community residents from the catchment area of an inner city London teaching hospital.

Twenty five consecutive non-amputees on the waiting list for femoropopliteal bypass operation were compared with 25 postoperative patients who had undergone elective hip or knee replacement and a period of inpatient rehabilitation. All participants were aged 65 and over at the time of interview. Patients with peripheral vascular disease all had clinical and Doppler proved evidence of peripheral ischaemia. Controls were interviewed between 6 months and 1 year after their operation. Both groups had no history of stroke or transient ischaemic attack.

A more detailed description of instruments is provided elsewhere.[1] All subjects were