LETTERS TO THE EDITOR

Magnetic resonance imaging in Creutzfeldt-Jakob disease: evidence of focal involvement of the cortex

Creutzfeldt-Jakob disease is a prion disease clinically characterised by rapidly progressing dementia, cerebellar and extrapyramidal signs, and myoclonus. Cerebral imaging procedures are considered to be of little value for definite premortem diagnosis, which still depends on brain biopsy. Corresponding to cognitive deficits neuropathological changes mostly affect the cerebral cortex, and less severely other grey matter areas such as the caudate, putamen, and thalamus.[1] The following case report suggests that MRI using a fluid attenuated inversion recovery (FLAIR) sequence might detect pathological changes in the cerebral cortex.

A 45 year old man presented with a three month history of progressive memory deficit, listlessness, and loss of speech. He repeatedly lost his orientation in the forest where he had worked as a wood cutter for many years. His history was remarkable for bulbectomy of the right eye at the age of 15 months, probably due to retinoblastoma. On examination he complied with simple requests, only. He spoke very little with multiple perseverations. Severe deficits of memory and orientation were obvious. Pronounced irritability with bursts of aggressiveness made neuroleptic therapy necessary. Deep tendon reflexes were brisk but plantar responses were flexor. Rigidity affecting all limbs and hypomimia indicated involvement of the extrapyramidal system. On walking the right arm did not swing. The gait was broad based and fixation did not suppress the oculocephalic reflex suggesting cerebellar involvement. Serial electric ECG recordings disclosed a progressive general slowing and a left frontotemporal, non-periodic slow wave activity. Cerebrospinal fluid cell count and protein composition were normal. Caeruloplasmin and urinary copper concentrations were within the normal range. In accordance with a negative family history for prion disease a single strand conformation polymorphism analysis did not detect any mutations in the coding sequence of the prion protein (PrP) gene. At residue 129 the patient was homozygous for valine.

Two months after onset of clinical symptoms MRI was performed. T1 weighted images before and after infusion of a contrast agent were normal, whereas on T2 and proton density weighted images the left frontal cortex appeared thicker and returned a higher signal than the other hemisphere (figure). However, when using a FLAIR sequence the patchy hyperintense signal of the cortical layer was more apparent.

An open brain biopsy of the left frontal lobe was performed. Histopathological examination disclosed spongiform changes of the cerebral cortex, loss of neurons and astrogliosis, but no inflammatory infiltrates. A diagnosis of spongiform encephalopathy (Creutzfeldt-Jakob disease) was made based on typical pathological changes. Immunhistochemistry showed no PrP deposits.

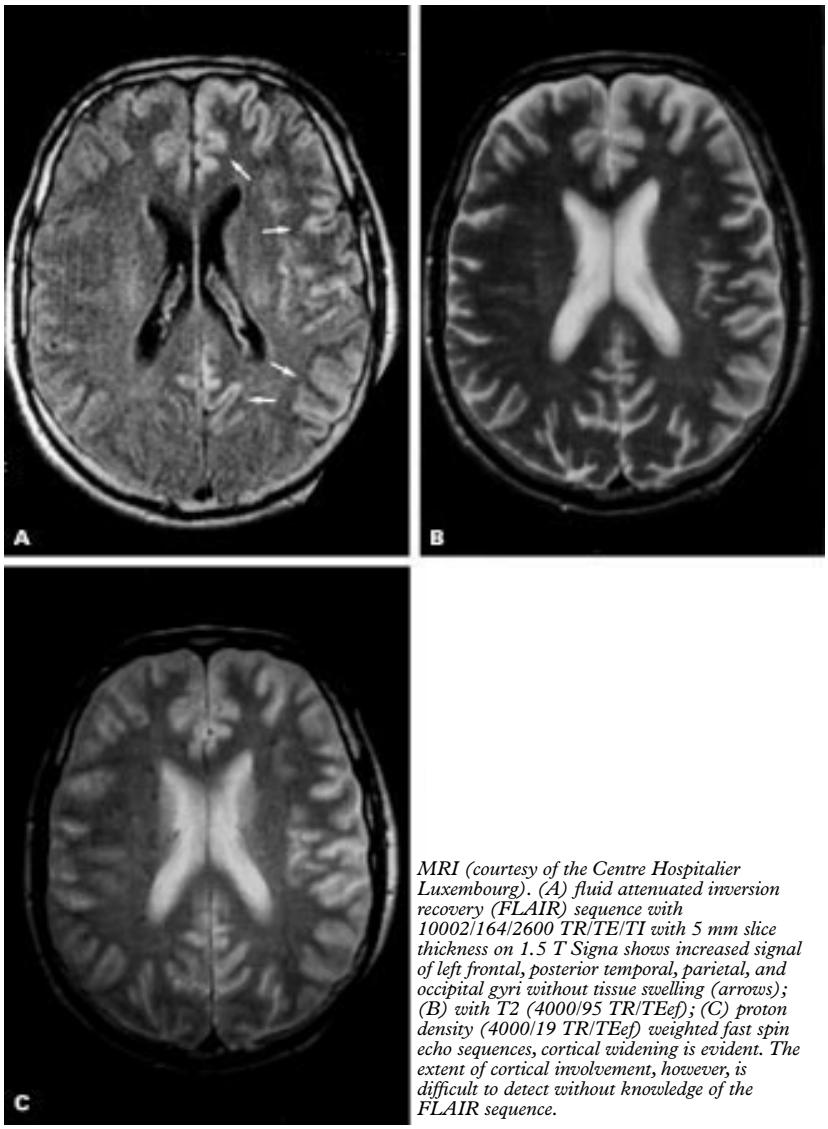
On follow up, the patient continued to deteriorate. Eight months after onset of symptoms he was reported to be completely unresponsive. At that time myocloni of the arms were seen. He died 16 months after onset of symptoms.

At necropsy the brain showed pronounced frontal cortical atrophy. The ventricular system was enlarged and atrophy of the caudate nucleus was seen. No cerebellar atrophy was detectable. Histology showed severe spongiform degeneration, severe gliosis, and nerve cell loss in the cerebral cortex. Severe changes were also found in the putamen and to a lesser extent in the thalamus. In the cerebellum only mild spongiform changes in the molecular layer were seen. The granular cell layer seemed unaffected. Immunhistochemistry was performed using the antibodies Gö138 and 3F4. As in the brain biopsy no prion protein deposits were detectable in the neocortex or cerebellum. In western blot analysis, proteinase K resistant prion protein was found.

This patient presented with the clinical features of Creutzfeldt-Jakob disease. Diagnosis of spongiform encephalopathy was confirmed by brain biopsy. Whereas T1 weighted MRI was normal, and T2 and PD weighted images showed only subtle findings, a cortical hyperintensity could be easily seen on FLAIR images. This hyperintensity predominantly affected the left frontal, insular, and parietal cortex; the right frontal cortex was also involved (figure). Findings in MRI have been reported in several cases of pathologically established Creutzfeldt-Jakob disease. Brain MRI might be normal or show either brain atrophy or symmetric, hyperintense signals of the basal ganglia in T2 weighted images.[2 3]

Occasionally, hyperintense signals of the cerebral cortex have been reported.[2] The low incidence of cortical involvement reported on MRI contradicts neuropathological data. In a series of 21 necropsied cases, the cortex was the earliest and most severely involved by spongiform changes.[1] The basis of this discrepancy may be that on conventional T2 weighted MRI the high intensity of CSF interferes with a sensitive display of cortical signal.

To our knowledge, application of the FLAIR sequence in Creutzfeldt-Jakob disease has not been reported so far. The FLAIR sequence is a heavily weighted inversion recovery sequence with an inversion time



MRI (courtesy of the Centre Hospitalier Luxembourg). (A) fluid attenuated inversion recovery (FLAIR) sequence with 10002/164/2600 TR/TE/TI with 5 mm slice thickness on 1.5 T Signa shows increased signal of left frontal, posterior temporal, parietal, and occipital gyri without tissue swelling (arrows); (B) with T2 (4000/95 TR/TEef); (C) proton density (4000/19 TR/TEef) weighted fast spin echo sequences, cortical widening is evident. The extent of cortical involvement, however, is difficult to detect without knowledge of the FLAIR sequence.

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designed to null the CSF signal but allow recovery of most of the brain magnetisation. This sequence reduces the CSF artefact and enhances contrast of pathology at the surface of the brain or adjacent to the ventricles.

There was a left frontotemporal accentuation of the hyperintense changes of the cortex in our patient. A focal involvement of the cortex has been reported as an early neuropathological finding in Creutzfeldt-Jakob disease.[4] Experimental data suggest that the infectious process begins focally and spreads via an axonal trans-synaptic pathway.[5] Spread of the infectious agent via commissural pathways to the contralateral cortex could explain the partially symmetric distribution of the hyperintense signal seen in our case.

The present case suggests that MRI using FLAIR sequences may be helpful in the diagnosis of Creutzfeldt-Jakob disease antemortem and provides a tool for characterising the pathological process in cases of Creutzfeldt-Jakob disease.

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Primary central nervous system lymphoma presenting with multiple myeloma-like clinical picture

Primary cerebral lymphoma is a unique and infrequent CNS malignancy in which the B lymphocyte subtype constitutes most cases.[1] B cell neoplasms other than multiple myeloma including non-Hodgkin's lymphomas, and acute and chronic leukaemias might also exhibit lytic bone lesions, hypercalcaemia, and monoclonal gammopathy via the particular actions of interleukin (IL-1), IL-6, or tumour necrosis factor-α secreted by the neoplastic B cell clone, but not reported previously secondary to a primary cerebral lymphoma.[2] We describe an unusual presentation of a B cell primary cerebral lymphoma mimicking a plasma cell dyscrasia.

A 64 year old woman was admitted with complaints of headache, ataxia, and urinary incontinence. Physical examination disclosed motor dysfunction in the legs, dysphasia, and impaired cerebellar function. On initial evaluation, a mass of 6×4 cm in diameter was shown in the left frontal lobe by MRI of the cranium (fig 1). Haematological and blood biochemistry values were within normal limits. Direct skull radiography disclosed multiple lytic lesions (fig 2). Serum immunoglobulin (Ig) G concentration was high (3400 mg/dl; normal<1800) and a monoclonal protein band of IgG-κ type was detected by immunoelectrophoresis. Total excision of the lesion disclosed large lymphocytes with oval and vesicular nuclei, and prominent nucleoli consistent with "intermediate grade large cell malignant lymphoma" according to the working formulation.[3] Methyl green pyronine stain was positive indicating cytoplasmic RNA accumulation and lymphoplasmocytoid differentiation. Staining with CD10 was also positive confirming the diagnosis of B cell lymphoma. The tumour margins showed infiltration into the surrounding white matter and extending to perivascular spaces with absence of involvement of subarachnoid spaces, dura, or bony structures. Pathological examination of the largest lytic skull lesion disclosed "osteolysis without a neoplastic infiltration". Immunoelectrophoresis of CSF showed a monoclonal IgG-κ band similar to the results of serum assays whereas biochemical and cytopathological CSF examinations were normal. Enzyme linked immunosorbent assay (ELISA) tests for HIV and antibody titres against Epstein-Barr virus were also negative in both serum and CSF samples. Slit lamp examination was normal, with no lymphomononuclear deposits in the uvea or vitreous fluid. Staging procedures including CT of the abdomen and pelvis, bilateral bone marrow aspiration, and biopsies were within normal limits precluding the diagnosis of primary cerebral lymphoma. She received 4920 cGy radiotherapy to the whole cranium followed by COPP (cyclophosphamide, vincristine, procarbazine and prednisone) chemotherapy, repeated every fourth week. By the third month of follow up, serum and CSF paraprotein disappeared and lytic skull lesions regressed. Concurrent cranium MRI disclosed no residual or recurrent mass and repeated investigation for systemic lymphoma was also negative. She is still being followed up and has so far survived more than a year.

Despite the differences in localisation and biology, non-Hodgkin's lymphomas arising from the CNS are not histologically different from the ones arising at extraneural sites, except that almost all have intermediate or high grade histology, predominantly of B cell subtype.[4] The monoclonality of intracellular immunoglobulins and cell lines obtained from primary cerebral lymphoma tissue cultures is well established.[5] These specific clonal products might be detected in CSF but not reflected in systemic circulation probably owing to the presence of an intact blood-brain barrier that, to the our knowledge, a B cell primary cerebral lymphoma with raised serum monoclonal paraprotein and lytic skull lesions simulating multiple myeloma has not been previously reported. The probable factors of disturbed blood-brain barrier, tumorous penetration of vascular spaces, or stimulation of angiogenetic collateral formation secondary to neoplastic outgrowth might be, alone or in combination, responsible for those remote effects of primary cerebral lymphoma. This remains to be verified. The contradictory pattern of overlapping symptomatology of B cell neoplasms makes it obligatory to achieve the definitive histopathological diagnosis particularly in the case of primary cerebral lymphoma , in which the therapeutic algorithm as well as the prognosis have diverse features.

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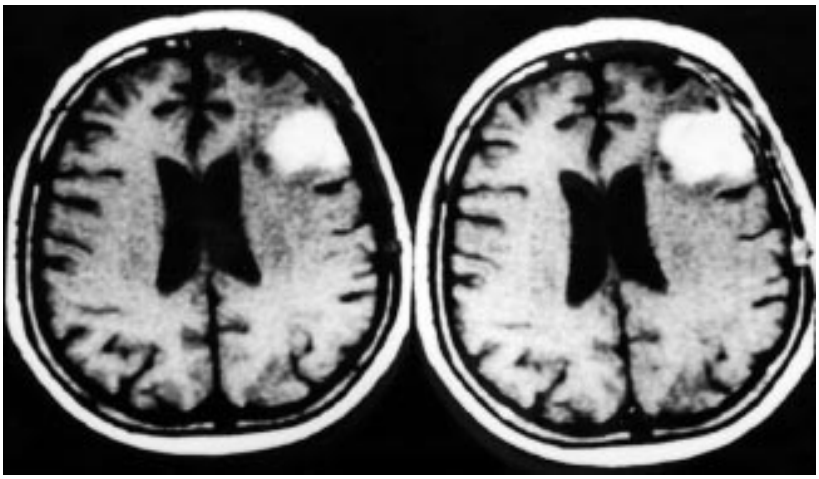

Figure 1 MRI of cranium showing a mass of 6×4 cm in diameter, located in the left frontotemporal lobe, showing moderate enhancement after intravenous contrast material injection.

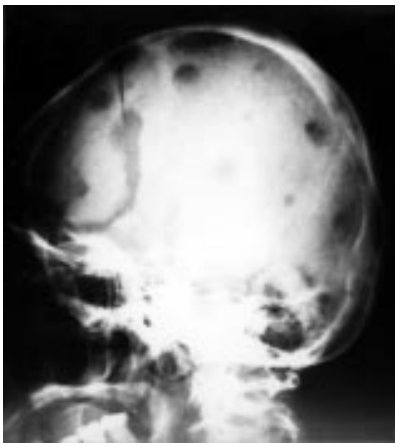

Figure 2 Direct lateral radiography of the skull of the patient, showing multiple punched out lytic lesions of the cranial vault, with no evidence of a periosteal reaction.

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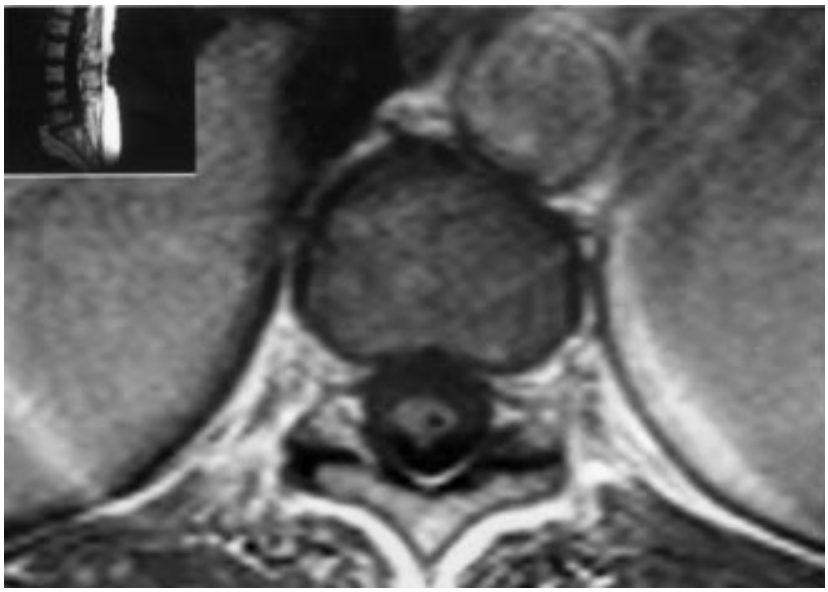
Attacks of pain in the leg from classic syringomyelia

Neurologists should not be surprised if the cause of a disorder is remote from its effect, such as a parasagittal meningioma causing foot dragging, or a sacral ependymoma leading to deafness as the first sign of siderosis of the nervous system. Yet we were for some time bewildered by the following problem.

A 67 year old woman consulted us in 1996 for attacks of pain in the left leg that had started in 1978 and had gradually increased in severity and frequency up to three to four attacks an hour, each lasting a few minutes and so severe that she had to stop anything she was doing to nurse her pain. It was sharp and stabbing in character and radiated from the gluteal region to the groin, and further down to the lateral part of the upper and lower leg. Between attacks she was completely free of pain. The stabs also woke her up at night, six or seven times. In 1988 investigations at another hospital had established the diagnosis of cervical syringomyelia, secondary to tonsillar ectopia (Chiari I malformation); a year later a syringopleural drain was inserted. Subsequently the syrinx collapsed, but the attacks of pain continued unabated. Examination (in 1996) showed normal power and sensation in the arms, a thoracic kyphosis, and on the left side of the trunk a suspended level of hypaesthesia and hypalgesia, extending from just under the nipple down to the left leg, as far as 10 cm below the knee; vibration sense was abolished below the sternum on both sides. Power in the legs was normal; the tendon jerks were very brisk on the right and sluggish on the left, both plantar responses flexor. Repeated MRI studies confirmed a collapsed syrinx in the cervical region, extending throughout the thoracic cord, and deviating to the left at the level of the lumbar cord (figure). Many analgesic, antidepressive, antiepileptic, and antiarrhythmic drugs had previously failed or failed again in our hands, as did sympathetic blockade or transcutaneous electrostimulation. Implantation of an epidural stimulator gave considerable relief, the intensity of the pain decreasing by more than half; this was sustained up to the last contact, nine months after implantation.

Leg pain with syringomyelia has so far been reported only in patients with a syrinx confined to the lumbosacral cord, secondary to trauma or tumour.[1 2] In our patient bouts of pain in the leg were associated with classic syringomyelia, which starts at the level of the cervical cord and results from obstruction of the CSF flow at the foramen magnum, most commonly by tonsillar ectopia.[3 4] We propose that the pain resulted from disturbed impulse transmission in the posterior grey matter at the left side of the lumbar cord, the pain partially matching the area of sensory loss. It is not unusual for symptoms to correspond to paracentral cavitations only, the central part of the syrinx being clinically silent.[5] Dysaesthetic pain from a paracentral syrinx is known to occur in the arm.[6] Also in those cases the response to surgical treatment is unpredictable.[6] Epidural stimulation was the only measure that made our patient's life again bearable.

We are grateful to Dr HE van der Aa (Enschede) for referring the patient and to AL Liem (St Antonius hospital, Nieuwegein) for implantation of the epidural stimulation device.



T1 weighted MRI at the level of the D10-D11 intervertebral disc. Hypointense lesion in the left dorsolateral region of the lumbar cord, corresponding to the posterior horn.

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Anti-GQ1b and anti-GT1a IgG antibodies in a patient with acute demyelinating polyradiculoneuropathy without ophthalmoplegia

Anti-GQ1b IgG antibodies have been often detected in the serum of patients with Miller Fisher syndrome or Guillain-Barré syndrome with ophthalmoplegia. These antibodies may participate in the development of ophthalmoplegia. Our patient with acute demyelinating polyradiculoneuropathy had no ophthalmoplegia despite having anti-GQ1b and anti-GT1a IgG antibodies in her serum.

An 80 year old woman was admitted because of weakness of her limbs. Ten days before admission to our hospital, after a common cold, she developed difficulty standing and paraesthesia in her lower legs. Within a few days, walking and prolonged sitting were nearly impossible and her arms became weak. On the day of admission, she developed dysphagia. There was no diplopia or ptosis at any time.

Her ocular and facial muscles were normal. She had difficulty in drinking water. Her limbs were weak (upper limbs MRC grade 3/5 and lower limbs 2 to 3/5). Deep reflexes were diminished or abolished. Pathological reflexes were not elicited. Superficial and deep sensation were abnormal below the knees. Stool culture was negative for *Campylobacter jejuni*. The CSF contained 159 mg protein/dl and no cells.

The right tibial motor nerve conduction velocity (MCV) was slow and the peroneal nerve did not respond. The median and ulnar nerves showed delayed distal latencies. Slowing of sensory nerve conduction velocity (SCV) was found only in the median nerve. F waves could not be elicited from the median and tibial nerves. A sural nerve biopsy on the 24th day showed loss of myelinated fibres without cell infiltration.

Dysphagia disappeared on the 27th day. Strength in her upper limbs recovered to MRC grade 4/5 a week later. One month after admission, she could walk with a little help. The protein concentrations in her CSF were 82 and 57 mg/dl after a month and four months respectively. Three months later, the median and tibial MCVs were still slow and could not be elicited in the peroneal nerve.

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The distal and F wave latencies in both the median and ulnar nerves were delayed. F waves could not be elicited in the peroneal or tibial nerves. Median SCV did not improve. The patient was discharged with no disability in activities of daily life four months after admission.

The patient's serum was tested at intervals for antiganglioside antibody activities by enzyme linked immunosorbent assay (ELISA).[1] GM1a, GM2, GM3, GD1a, GD1b, GT1a, GT1b, and GQ1b were prepared from bovine brain.[2] The antigenic solution contained 20 pmol/50 µl of each ganglioside. Each patient's serum was tested in triplicate at 1:100 dilution, and binding detected with horse radish peroxidase conjugated goat antihuman IgM or IgG antibody (Jackson Immunoresearch Laboratories, Inc, West Grove, PA, USA) at 1:1000 dilution. On admission, the serum reacted with both GQ1b and GT1a at a dilution of 1:3200. These two antibody activities, expressed as optical densities, fell to 1/2 in parallel with her improvement, but they could still be detected in her last blood sample (at 16 weeks). IgG antibodies against the other gangliosides were not detected at any time, nor were IgM antibodies to any ganglioside detected.

To determine whether these two antibodies react independently with each ganglioside or react with a common epitope sharing with GQ1b and GT1a, an absorption study was performed using GQ1b or GT1a coated polystyrene beads as described previously.[1] The titre of anti-GQ1b IgG antibody decreased when preincubated with GT1a coated polystyrene beads, and vice versa for the anti-GT1a IgG antibody. Based on these results, we hypothesised that these antibodies reacted with a common epitope sharing GQ1b and GT1a.

Chiba *et al*[3] found anti-GQ1b IgG antibodies in patients with Miller Fisher syndrome and also with Guillain-Barré syndrome with ophthalmoplegia. They showed immunochemically that GQ1b was rich in the paranodal regions of the human oculomotor, trochlear, and abducens nerves. These anti-GQ1b IgG antibodies also reacted with GT1a. Yuki *et al*[4] found anti-GQ1b IgG antibodies in eight patients with acute paresis of the extraocular muscles but without ataxia. These results suggested that anti-GQ1b IgG antibodies had a part in the development of ophthalmoplegia. We have also detected anti-GQ1b and anti-GT1a IgG antibodies in six patients with Miller Fisher syndome and two with Guillain-Barré syndrome accompanied by ophthalmoplegia.We also found that these antibodies reacted with a common epitope sharing GQ1b and GT1a (unpublished data). Kimura *et al*[5] have already reported a patient with acute relapsing sensory dominant polyneuropathy without ophthalmoplegia who had an anti-GQ1b IgG antibody which did not react with GT1a. Further clarification of the relation between anti-GQ1b IgG antibody and the development of ophthalmoplegia in Miller Fisher syndrome or Guillain-Barré syndrome is required.

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Can trauma alone to the trigeminal root relieve trigeminal neuralgia? The case against the microvascular compression hypothesis

Idiopathic trigeminal neuralgia (ITN) is increasingly regarded as being due to microvascular compression of the trigeminal sensory root, either by an artery or a vein close to the brainstem.[1] Yet vascular contacts are found in entirely asymptomatic cases, no vascular contacts are found in some asymptomatic patients, and, most importantly, ITN suddenly switches off, even for years, only to return later, in the face of continuing vascular compression.[2] Despite this, microvascular decompression produces immediate virtually complete (98–100%) relief in 82% of the cases and 64% after 10 years.[3] Adams has suggested that, ITN being a hyperfunctional disorder of the brainstem, microvascular decompression "produces chronic trauma to a sensitive zone of the cranial nerve... by the dissection necessary and by the manipulation required microvascular decompression produces sufficient trauma to achieve interference of normal functioning of that nerve", thus dampening the abnormal brainstem activity responsible for ITN.[2] Failure to achieve an initial result or early recurrence would imply insufficient surgical trauma.[2] We evaluated this hypothesis in our patients submitted to microvascular decompression. Forty one out of 410 patients with ITN have had keyhole microvascular decompression in the posterior fossa from December 1986 to February 1996 at the neurosurgical pain relief unit of the University of Turin. Twenty six patients showed pronounced arterial or arterovenous compression, three distally (group 1), three mild or disputable contacts (group 2), two slight and three pronounced venous compressions (group 3), five with arachnoiditis, two with a sharp root kink, four distally (group 4). In four cases (group 5), no anomaly whatsoever could be found, despite adequate magnification and careful exploration; vessels were noted close to the root, but no contact or groove could be seen. Thus the root was gently "massaged" with a microdissector; no other manoeuvre was attempted. These four patients included one woman and three men, with a mean age of 59 (range 54–66). All had typical ITN which at some point could no longer be controlled by drugs at adequate dosage. In all other cases, the vessels were separated from the root by interposing Surgicel; the arachnoiditis was dissected to free the root and, in one patient with slight venous compression partial (25%) rhizotomy was also carried out. In several patients, "massage" of the trigeminal root was performed.

All patients were relieved by surgery. Follow up disclosed the following recurrences: two in group 1 (follow up 4 months-9 years), none in group 2 (follow up 2.3–5 years), none in group 3 (follow up 1.1–5 years), two in group 4 (follow up 1–6 years), one in group 5 six years postoperatively (follow up 6 months-8 years). Importantly, one of the group 1 recurrences was operated on and no vascular contact whatsoever could be found (partial rhizotomy was elected). The only group 5 recurrence could be controlled by drugs. Whereas this was seen in other groups as well, all four group 5 patients showed transient slight to moderate hypaesthesia in two to three branches after surgery, a hallmark of trauma.

In 1961, Taarnhøj reported that simple manipulation of the trigeminal root by running a nerve hook along the root obtained 60% long term pain free results over a mean of 6.5 years (longest follow up 10 years).[4] Gardner and Miklos also obtained 67% pain free results over 4.5 years by manipulating the trigeminal sensory root at the point of crossing the apex of the petrous bone,[5] suggesting that manipulation not at the root entry zone (as suggested by Jannetta), but peripherally at the petrous apex produces as good results as microvascular decompression. As no other report considered the problem, the microvascular compression hypothesis for ITN gained favour. Our data suggest that (1) trauma alone can ensure long term relief; (2) this relief is similar between patients showing microvascular compression and those without; it should be stressed that several patients of the microvascular compression group were "massaged" to ensure a control with the group without.

The trigeminal nerve root is surrounded by many arteries. In 60% of the roots, the trigeminal vessels form arterial rings encircling at least half of the root or its entry zone in asymptomatic patients,[6] justifying the frequency of vascular contacts at large. Despite a plethora of vessels reported to compress the trigeminal nerve in a recent series,[3] initial relief could not be achieved in 18% of the patients. Recently, a group reported electrophysiological data supporting the concept of trauma during microvascular decompression, despite attempts to limit the procedure to simply moving the vessel.[7] The trauma hypothesis would explain recurrences of successful microvascular decompression in which no new compression is found (for example, our case and see Yamaki *et al*[8]) at re-exploration.

Adam's contention is being appreciated in the case of hemifacial spasm. Payner and Tew,[9] discussing their results with microvascular decompression for this disorder, stated that "...perhaps there is truth that the early success in most patients results from minor trauma... to support this theory, additional analysis is needed of the long term follow up in patients without vascular compression and...treated by "manipulation" alone". This is what has been done in this study.

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Microvascular decompression entails a risk of death (although this is small) and other serious complications requiring surgery (much more often) in the face of a painful, but benign disorder. Perhaps, "trauma surgery" would be best to ensure equal results with a much lower complication rate. A minimally invasive approach (endoscopy) could be studied in this regard.

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About the original description of cerebellar tonsil herniation by Pierre Marie

Transfalcial and transtentorial herniation and the engagement of the cerebellar tonsils into the foramen magnum are well recognised consequences of increased intracranial pressure. They were discovered through both experimental findings carried out in the 19th century,[1] and pathological and clinical experiences reported in the first decades of this century.[2] Harvey Cushing (1869–1939) is usually acknowledged as the first clinician who, in 1902, correlated the clinical picture of neurological disturbances and cardiorespiratory failure with the herniation of the cerebellar tonsils into the foramen magnum.[3] However, when in his book on pontocerebellar angle tumours Cushing made use of the notion of "cerebellar pressure cone",[4] he was employing a term first introduced into the English language by Collier,[5] as Cushing himself acknowledged in an earlier article.[6]

Here we report on the observations of Pierre Marie (1853–1940) that bear on the same issue and antedate those of both Cushing and Collier. On l July 1899, during a session of the Societé de Biologie, Pierre Marie[7] reported on two cases of cerebral haemorrhage that resulted in secondary compression of the cerebellum. In the first case, a haemorrhage of the external segment of the lenticular nucleus flattened the superior face of the left cerebellar lobe and shifted the vermis to the right. In the second case, a thalamic haemorrhage resulted in compression of the superior face of the left cerebellar hemisphere and caused a protrusion of the cerebellar tonsils that "appeared to have engaged the occipital foramen".

Pierre Marie drew attention to the pathophysiological research of Leonard Hill. "In his *Hunterian Lectures* in 1896, he showed that the brain does not transmit the pressure on one point in all directions. Indeed, a clear pressure difference is created between the main cranial cavity and the posterior fossa. According to Hill, the pressure gap is due to: (1) the viscosity of the cerebral substance; (2) the interposition of the falx cerebri and the tentorium cerebelli. This explains why a haemorrhage lesion exerts a localised compression on a particular part of the cerebrum, instead of creating a uniform pressure growth on the whole cerebral mass, as some think. In the present circumstance, the compression is exerted on a cerebellar hemisphere.

Furthermore, according to Leonard Hill

"the compression exerted by the haemorrhaged cerebral hemisphere upon the superior surface of the cerebellum can have very serious consequences. In fact, if the compression is sufficiently strong, the downward push on the cerebellum causes the engagement of its inferior surface into the foramen magnum. In this process the cerebellum takes the form of two cones constituted by the cerebellar tonsils. As a result the medulla oblongata is trapped within the foramen magnum, and if the pressure is strong enough its vessels will be compressed to the point of failing to supply the organ. Hence a severe bulbar ischemia will ensue."[7]

Pierre Marie concluded his communication by considering the possibly severe consequences of cerebellar tonsillar penetration into the occipital foramen and the resulting bulbar hypoperfusion, exactly devising the mechanism of cerebellar herniation. In the next year, Pierre Marie reported the pathological findings of another two cases of raised intracranial pressure.[8] In the first case with a thalamic haemorrhage the rise in intracranial pressure caused the caudal shift of a cerebellar tonsil, that consequently "engaged into the occipital foramen". The second case was of increased intracranial pressure of unknown origin, disclosed by pronounced hydrocephalus. "Both cerebellar tonsils had shifted into the occipital foramen such as to form a sort of cone enclosing the bulbus for more than half of its circumference." In his conclusions, Pierre Marie suggested that the compression of the medulla could have contributed to the fatal outcome.

A few years later, in 1905, Louis Pierre Marie Alquier (1872–1956) described two further cases of cerebellar tonsils herniation into the occipital foramen.[9] In Alquier's article the discussion of Jean Athanase Sicard (1872–1929) and Pierre Marie on the topic is reported. Mentioning his personal experience in similar cases, Pierre Marie also made the somewhat surprising suggestion that Alquier's pathological findings might be attributed to a postmortem process. We could find no further contribution by Pierre Marie on this topic in his subsequent scientific production.

Recently, Fisher[10] has pointed out that cerebellar herniation is not necessarily a terminal event, except, in cases in which cerebellar herniation occurs in posterior fossa infarcts, acute subdural haematomas, or during a lumbar puncture. In such cases, acute herniation is justifiably considered among the determinant factors of clinical outcome. The first clinical description of this important phenomenon was made by Pierre Marie.

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Blepharospasm induced by flunarizine

Flunarizine is a calcium channel antagonist that has been widely prescribed for vertigo, cerebral or peripheral vascular diseases, migraine, and epilepsy.[1 2] At doses of 10-40 mg/day, it can produce side effects such as parkinsonism or abnormal involuntary movements, especially in elderly people.[1 2] A case of blepharospasm in a 67 year old woman who had been taking 20 mg/day flunarizine for 18 months has been reported.[2] However, the cause of the disorder in this instance may be questionable as this patient had also been treated with cinnarizine and her dystonic movements did not disappear 13 months after the discontinuation of both drugs.[2] We have seen a 30 year old woman who was treated with 10 mg/day flunarizine for migraine prophylaxis. After two months of treatment she developed a progressive blepharospasm which eventually prevented her from reading or watching television. Three weeks after the appearance of symptoms, flunarizine was withdrawn, and the patient made a gradual and complete recovery over the next month.

Dopaminergic, cholinergic, serotoninergic, or other poorly understood mechanisms might be implicated in the pathogenesis of blepharospasm.[3] Flunarizine has been reported to have antihistaminic, antiserotoninergic, and antidopaminergic activities.[2] This interference with dopaminergic transmission seems to be both complex and particularly

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relevant. On the one hand, flunarizine blocks dopamine receptors and might have a toxic effect on dopaminergic neurons.[4] On the other hand, its calcium channel antagonism leads to inhibition of dopamine neurotransmission.[4] In addition, the antihistaminic activity of flunarizine may also have some importance. The blepharospasm that occasionally follows the use of decongestants has been explained by the antihistaminic component of these drugs.[5] Whatever the mechanisms involved, the early development of blepharospasm in a young adult on a low dose of flunarizine would suggest that individual susceptibility played a part in its emergence. The present case would favour the inclusion of flunarizine among the causes of isolated blepharospasm.

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Expression of tenascin in astrocytic tumours: too much ado about nothing?

The stroma of astrocytic tumours has been investigated in the past years by various authors. Among the proteins of the extracellular matrix tenascin is considered a very important molecule because of presumed links with the malignancy of the tumours and with the angiogenesis[1 2] and also a possible target for therapy. To verify these opinions we have performed an immunohistochemical analysis of 10 astrocytic tumours of the cerebral hemispheres. The series of patients comprised six men and four women, ranging in age from 43 to 72 years; seven underwent gross total resection and three subtotal resection. The study focused on the following molecules of the extracellular matrix: tenascin, laminin, fibronectin, and type IV collagen. The results were evaluated in relation to the following indices: grading according to the St Anne/Mayo System,[3] proliferating cell nuclear antigen labelling index,[4] dimensions of the tumour evaluated radiologically (CT and MRI) and expressed according to the criteria of the manual for staging of cancer by means of the parameter "T".[5]

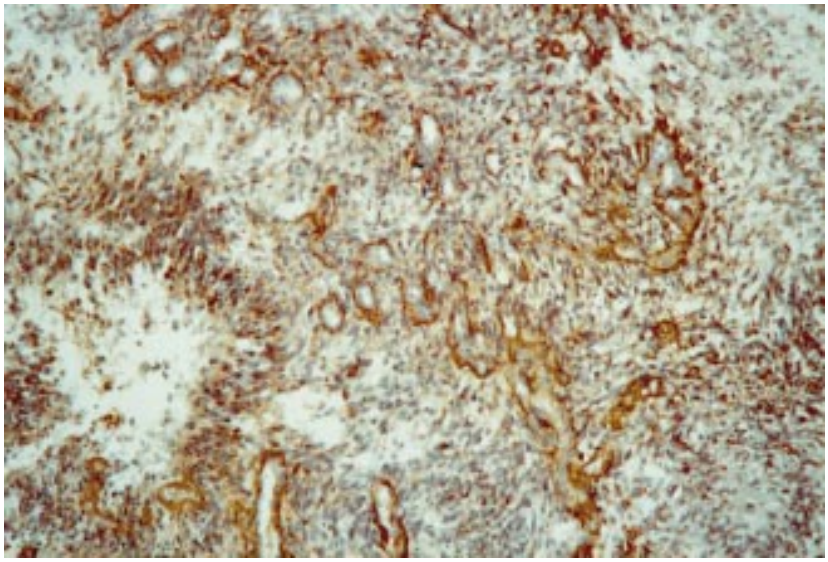
Primary monoclonal antibodies were purchased from Dako and staining was performed by the labelled streptavidin biotin staining method on 10% formalin fixed and paraffin embedded tissue.

The tumours were grade II in two cases (one gemistocytic), grade III in three cases, and grade IV in five cases. Tenascin was present in the extracellular matrix in all grade IV astrocytomas and in the gemistocytic astrocytoma. In two grade III astrocytomas and in all grade IV astrocytomas the basement membranes of the vessels with or without endothelial proliferation showed a positive immunohistochemical staining for tenascin (figure).Tenascin and fibronectin were detected in some neoplastic cells of grade IV tumours and also in the gemistocytes. Laminin, fibronectin, and collagen type IV were found around the vessels of tumours of all grades.The PCNA labelling index was <1% in tumours of grade II and grade III. In grade IV tumours the areas of highest PCNA staining did not correspond to the greater expression of tenascin on serial sections. In some areas with strong staining for tenascin the PCNA labelling index was <5%, whereas the total percentage in grade IV tumours ranged from 5% to 18%.

Evaluation of the parameter "T" failed to provide a correlation between the size of the tumour and the presence of the molecules of the extracellular matrix. For instance, a grade IV tumour evaluated as T1 expressed the tenascin as well as a grade IV tumour evaluated as T4.

In conclusion, we have shown that tenascin does not correlate with the indices of malignancy we have studied—namely, grading, PCNA labelling index, and size of the tumour. The presence of tenascin in the extracellular matrix could only be a signal of progression of astrocytic tumours. This could explain its presence in the gemistocytic astrocytoma, which is well known as a tumour with a high probability of progression.

Furthermore, it is well known in oncology that the size of the tumour must correlate with neoangiogenesis.[6] Our hypothesis is that if the expression of tenascin does not correlate with the dimension of the tumour it cannot really correlate with the angiogenesis.



Glioblastoma. Immunohistochemical staining for tenascin is in the basement membrane zone of tumour vessels and also in the extracellular matrix (originally ×125).

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Multiple sclerosis associated with duplicated CMT1A: a report of two cases

The concomitant involvement of both the peripheral and central nervous system myelin is rare and may occur in the course of inherited lysosomal storage diseases. In inflammatory autoimmune diseases of the peripheral nervous system or CNS, a mild involvement of central or peripheral myelin has sometimes been reported.[1 2] In such conditions, a single pathogenetic mechanism has been tentatively considered as responsible for the nervous tissue damage and the association of peripheral nervous system and CNS demyelinating disorders due to different pathogenetic mechanisms has never been reported.

We describe two patients with definite multiple sclerosis and hereditary peripheral neuropathy of Charcot-Marie-Tooth type 1A (CMT1A).

Patient 1, a 38 year old woman, was admitted to hospital because of episodes of gait disturbances and optic neuritis. Neurological

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examination showed ataxia, lower limb weakness, bilateral Babinski's sign, increased tendon reflexes, mild sensory loss in all four limbs, impaired bladder function, and bilateral pes cavus. Her CSF showed an IgG index of 0.89 and IgG oligoclonal bands. Electrophysiology disclosed features of CNS and peripheral nervous system demyelination (table).

Patient 2, a 30 year old woman, had had recurrent episodes of hemiparesis and paraparesis, optic neuritis, and facial palsy since the age of 22. When admitted to our department, she had spastic paraplegia, absent ankle tendon reflexes, bilateral Babinski's sign, distal loss of vibration in the legs, impaired visual acuity, internuclear opthalmoplegia, and ataxic speech. Bilateral pes cavus was found in the patient as well as in several members of her family. Her CSF showed an IgG index of 0.98 and IgG oligoclonal bands. Brain MRI showed diffuse foci of demyelination in the white matter of the cerebral hemispheres and in the spinal cord. Neurophysiological studies disclosed aspects of CNS and peripheral nervous system demyelination (table).

In both patients sural nerve biopsy showed loss of myelinated fibres and aspects of demyelination and remyelination with onion bulb formation.

Genetic molecular analysis was performed by CHEF-DRIII pulsed fields gel electrophoresis of the CMT1A Sac II junction fragment.[3] The detection of the novel junction fragment of 500 kb in both cases indicated the presence of duplication.

Both patients had clinically definite multiple sclerosis; in addition, the neurophysiological, neuropathological, and genetic analysis investigations disclosed a demyelinating and remyelinating neuropathy of CMT1A.

The involvement of the peripheral nervous system in the course of multiple sclerosis has been previously reported.[1 2] The authors suggested the diagnosis of chronic inflammatory polyradiculoneuropathy (CIDP) as the consequence of a peripheral nervous system invasion by the same pathological process affecting the CNS. Our patients did not fulfill laboratory criteria for CIDP. In addition, the anamnestic presence of foot abnormalities in family members suggested inherited neuropathy. Finally, the detection of characteristic genetic alterations in chromosome 17 confirmed the diagnosis of CMT1A.

Aspects of CNS involvement have been reported in CMT1 and also in hereditary neuropathy with liability to pressure palsy,[4] the last being caused by a reciprocal deletion of the region duplicated in CMT1A; these changes have been tentatively attributed to an increased or decreased expression of peripheral myelin protein (PMP) 22 within the CNS. However, this is the first report describing an association of multiple sclerosis and CMT1A. CMT1A encompasses most of the cases of CMT and is associated with a duplication in chromosome 17 p11.2-12 where the PMP22 gene is located. PMP22 is mainly expressed in the peripheral nervous system, but it shares similarities with other proteins of the CNS such as the proteolipid protein. In duplicated CMT1A, myelin development is normal, but an overexpression of PMP22 may affect the maintenance of the peripheral nervous system myelin, which undergoes progressive destruction.[5]

The present finding raises the question whether the concomitant presence of CMT1A and multiple sclerosis represents a chance association or whether the genetic defect responsible for the peripheral neuropathy can play a part in triggering the autoimmune disorder of CNS myelin. We speculate that the PMP22 overexpression may also involve its antigenic properties, thus inducing modifications of self tolerance. In this context, the partial homology among peripheral nervous system and CNS proteins, such as the proteolipid protein, could account for the occurrence of autoimmune disorders targeted to the CNS myelin.

We suggest that patients with multiple sclerosis must be carefully evaluated for the presence of peripheral nervous system involvement. In such circumstances, neurophysiological, neuropathological, and genetic analyses may greatly contribute towards a correct diagnosis.

Table 1 Neurophysiological studies

		Patient 1	Patient 2		Normal
MNC	Ampl(mV)	0.5	12.0		
Median	DL (ms)	10.0	13.0		
	CV (m/s)	18.6	24.7		
	Ampl(mV)	−	8.0		
Ulnar	DL (ms)	−	9.0		
	CV (m/s)	−	20.1		
	Ampl(mV)	1.0	NE		
Peroneal	DL (ms)	8.7	NE		
	CV (m/s)	18.6	NE		
SNC	Ampl (μV)	4.0	NE		
Sural	DL (ms)	5.8	NE		
	CV (m/s)	26.0	NE		
SSEPS:					
Median		NE	NE		
Tibial		NE	NE		
VEPs:					
Right	Lat (ms)	151.0	149.0	P100	<118.0
	Ampl (μV)	14.7	6.4		>7.0
Left	Lat (ms)	105.0	150.0		
	Ampl (μV)	17.9	5.4		
BAERs:					
Right	I (ms)	1.66	1.66		
	III (ms)	3.80	4.07		
	V (ms)	5.56	NE	I	<1.72
Left	I (ms)	1.54	1.59	I–III	<2.37
	III (ms)	3.68	3.64	I–V	<4.30
	V (ms)	5.48	NE		
MEPs:					
Thenar	PCT (ms)	26.0	28.9		<14.5
	CCT (ms)	15.0	32.8		<10.0
Tibial ant	PCT (ms)	28.0	NE		<15.4
	CCT (ms)	32.0	NE		<18.0

MNC=Motor nerve conduction; SNC=sensory nerve conduction; Lat=latency; Ampl=amplitude; DL=distal latency; CV=conduction velocity; BAERs=waves I-III-V; VEPs=P100; MEPs=hand and leg muscles; PCT=peripheral conduction time; CCT=central conduction time; −=not performed; NE=not evoked.

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Distal myasthenia gravis and sensory neuronopathy with anti-50 kDa antibody mimicking sensory-motor neuropathy

Bilateral foot drop, paraesthesiae, and absent tendon reflexes in the lower limbs are, for the clinical neurologist, the hallmarks of a duration dependent sensory-motor neuropathy. We report a patient in which this clinical picture was sustained by the combination of an atypical distal presentation of myasthenia gravis with a probable immunomediated sensory neuronopathy.

A 69 year old woman presented with a three month history of progressive walking difficulties and paraesthesiae in the lower limbs. Examination showed bilateral foot drop with pronounced weakness of the tibioperoneal muscles (MRC= 2) and posterior leg muscles (MRC= 3), slight weakness in arm abduction (MRC=4+), tactile and pain distal sensory loss, and absent tendon jerks in the lower limbs. There were no oculobulbar symptoms and signs nor ataxia.

Motor conduction velocities and compound muscle action potential (CMAP) amplitudes were normal (ulnar= 57 m/s, 9.7 mV; peroneal= 44 m/s, 3.9 mV). Sensory conduction velocities were slowed with reduced amplitude sensory nerve potentials (ulnar=44 m/s, 5 μV; sural= 30.6 m/s, 1.8 μV). H reflexes were absent with normal latency F responses. Tibialis anterior muscle EMG did not show spontaneous activity and

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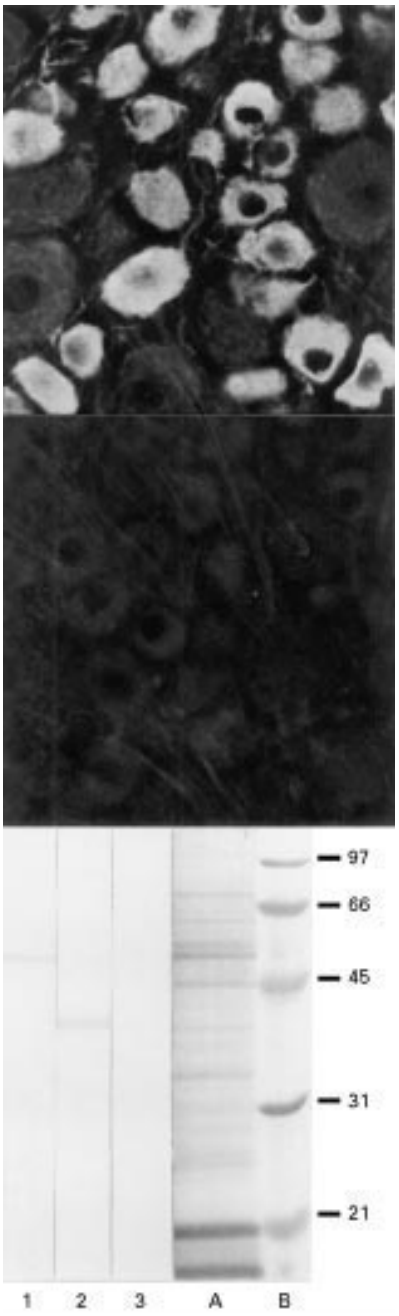
recruitment was full but during prolonged maximal voluntary activation there was a pronounced reduction of the interferential pattern amplitude. Quantitative motor unit analysis showed a 20% reduced mean duration with 4% of polyphasics. Repetitive stimulation at 3 Hz documented in the ulnar nerve-abductor digiti minimi system a 10% decrement whereas in the peroneal nerve-extensor digitorum brevis system the decrement was 33%. Amplitude CMAPs in the abductor digiti minimi after 15 seconds of maximal voluntary activation increased by 29%. A tensilon test, assessing strength in the tibioperoneal muscles, was strongly positive. Sural nerve biopsy showed a loss of myelinated fibres. Anti-AChR antibody titre was 3.3 nM (normal value<0.8). Voltage operated calcium channel antibodies were negative. Antibodies (IgG and IgM) against gangliosides (GM1, GD1a, GD1b, GM2) , SGPG, and sulphatides were negative. Chest CT excluded a thymoma or a lung cancer. A screening for breast, ovarian, and other gynaecological malignancies was negative. Tumorous markers were negative. Foot drop was greatly improved with pyridostigmine bromide and prednisone (75 and 25 mg every other day) and after three months the patient did not complain of paraesthesiae and could walk on her toes and stand on her heels.

By indirect immunofluorescence,[1] the patient's IgG strongly reacted with the cytoplasm of rat small size dorsal root ganglia neurons up to a dilution of 1:1280, whereas it did not react to large size dorsal root ganglia neurons (figure). With an indirect immunoperoxidase technique,[1] using sections of rat cerebellum, the patient's serum strongly immunostained the cytoplasm of Purkinje cells in a fine granular pattern up to a dilution of 1:2560. The patient' serum did not react with neurons of the molecular layer and Golgi neurons. To determine whether the binding to Purkinje cells and dorsal root ganglia neurons was due to the same antibody, the patient's serum was adsorbed either with whole cerebellum homogenate or with dorsal root ganglia homogenate. The pretreatment with each of the two homogenates removed the tissue binding activity, whereas liver homogenate was without effect. In the western immunoblot of whole human cerebellum homogenate, the IgG from our patient reacted with a 50 kDa protein band at dilutions up to 1:8000 (figure). Using whole dorsal root ganglia homogenate, the IgG from our patient reacted with a 50 kDa protein band at dilutions up to 1:1000. The pretreatment of serum either with whole cerebellum homogenate or with whole dorsal root ganglia homogenate removed their blot binding activity, whereas liver homogenate was without effect.

Clinical presentation in this patient pointed to a sensory-motor neuropathy. Neurophysiological studies documented an axonal sensory neuropathy but normal motor conduction. Normal CMAP amplitudes and the borderline reduced mean duration value of motor unit potentials in tibialis anterior muscle indicated that the foot drop did not have a neurogenic origin. Repetitive stimulation showed an unequivocal decremental response in the peroneal nerve (whereas the ulnar nerve was still in the normal range) indicating a defect in neuromuscular transmission, more pronounced in leg muscles. The normal CMAP amplitudes, the absence of incremental response, and the negativity of voltage operated calcium channel antibodies ruled out a Lambert-Eaton myasthenic syndrome. Myasthenia gravis was confirmed by the raised titre of serum anti-AchR antibodies and the positive tensilon test. In myasthenia gravis distal limb muscles are reported to be almost never affected in absence of oculobulbar signs.[2] Peroneal nerve repetitive stimulation, as recently described by Oh *et al*,[3] was crucial to the confirmation of myasthenia gravis in this patient.



Top: binding of patient's serum at a dilution of 1:1280 to an unfixed frozen section of rat dorsal root ganglia by immunofluorescence microscopy. The patient's IgG intensely immunostains the cytoplasm of small size dorsal root ganglia neurons (arrows) but not with large size dorsal root ganglia neurons (arrowhead) (originally×170). Middle: control serum does not bind and stain the cytoplasm of rat dorsal root ganglia(originally×170). Lower: lane 1: immunoblot of human whole cerebellum homogenate shows that at a serum dilution of 1:8000 the patient's IgG (lane 1) binds to a 50 kDa protein. Lane 2: positive control with anti-Hu antibodies binding to a 40 kDa protein. Lane 3: negative control. Lane A: whole cerebellum homogenate; lane B: molecular weight standard. Lanes 1–3, peroxidase conjugated assay. Lanes A and B, amido black staining.

Clinical, electrophysiological, and histological findings also showed an axonal sensory neuropathy. Although there are no electrophysiological or morphological ways to distinguish between an axonal sensory neuropathy and a sensory neuronopathy, the reactivity of our patient's IgG against small size dorsal root ganglia (figure) suggests a primary, probably immunomediated, involvement of sensory neurons. The patient's serum strongly immunostained, in a fine granular pattern, the cytoplasm of Purkinje cells and in western immunoblotting the IgG reacted with a 50 kDa protein band present in whole cerebellum and dorsal root ganglia homogenates (figure). These immunostaining and immunoblot findings are clearly different from the features required for the identification of anti-Yo and anti-Hu antineuronal antibodies.[4 5]

In conclusion this case is unique for several reasons:

(1) Clinical presentation pointed to a sensory-motor neuropathy but the foot drop was sustained by an atypical, distal presentation of myasthenia gravis.

(2) Peroneal nerve repetitive stimulation (not usually performed in EMG laboratories) played an important part in confirming myasthenia gravis.

(3) Myasthenia gravis has been reported to be associated with other autoimmune disorders but never to a sensory neuronopathy with antibodies reacting with dorsal root ganglia neurons and Purkinje cells.

(4) 50 kDa antineuronal antibodies reacting with small size dorsal root ganglia neurons and in a fine granular pattern with the cytoplasm of Purkinje cells have never been described previously.

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BOOK REVIEWS

Fronto-Temporal Lobar Degeneration: Fronto-Temporal Dementia, Progressive Aphasia, Semantic Dementia. Edited by: J S SNOWDEN, DAVID NEARY, AND D M MANN. (Pp 227; £55.00). Published by Churchill Livingstone, Edinburgh 1996. ISBN 0443047650.

The three editors of this book have played a central part in the renaissance of interest in the clinical, neuropsychological, and neuropathological aspects of non-Alzheimer dementias. This book is based on their truly remarkable experience of some 200 patients with lobar atrophy studied over the past decade, 40 of whom have reached postmortem. It represents, therefore, an unequalled source of information and is essential reading for all those working in the area.

After a historical introduction, the initial chapters are dedicated to the three princinpal syndromes under consideration: frontotemporal dementia, progressive aphasia, and semantic dementia. Each section integrates clinical neurology with neuropsychology, radiology, and pathology. There are also very useful chapters which deal with differential diagnosis and the relation of lobar atrophy to motor neuron disease. The final chapters are more theoretically oriented and cover the role of the frontal lobes in behaviour and aspects of semantic memory. Besides the integrated approach and the highly readable style, the other strength of the book is the liberal use of clinical vignettes and useful summaries at the end of each chapter. The quality of illustrations is very high but more MRI images would perhaps have been desirable.

Some readers naive to the field may emerge confused by the current terminologies, which cross levels of analysis: the newly adopted term, frontotemporal dementia (which has replaced dementia of frontal type), has obvious neuroanatomical connotations, whereas semantic dementia and progressive aphasia are syndrome terms which do not imply any direct anatomy or pathology. The relation between frontotemporal dementia and semantic dementia is perhaps one of the more perplexing aspects of the current classification. Personally I would prefer use of the older term for a dementia of frontal type.

The fact that neurodegenerative diseases can produce very circumscribed cognitive deficits has been one of the most surprising and fascinating discoveries in recent years. This book admirably illustrates the value of careful analysis of such cases, both for the understanding of the dementias and of normal cognitive processes. I can wholeheartedly recommend it.

JOHN HODGES

The Neurobiology of Disease. Contributions from Neuroscience to Clinical Neurology. Edited by: H BOSTOCK, P A KIRKWOOD, AND A H PULLEN. (Pp 443; £65.00). Published by Cambridge University Press, Cambridge 1996. ISBN 0 521 45132 9.

It may seem a mighty task to produce a book dealing with most of the major aspects of neurobiological research and its relevance to disease, particularly when that book weighs in at less than 21lbs. This volume, however, goes a long way in achieving these admirable goals.

The volume is dedicated to Tom Sears who has recently retired from the Chair of the Sobell Department of Neurophysiology, at the Institute of Neurology in London. The editors have gathered together an impressive list of contributors, and it is a tribute to Tom Sears that most of the authors acknowledge the influence of Professor Sears and his coworkers in their chapters. There are over 40 chapters, and most are only a few pages long. When trying to distill essential contributions made in any one field, there is inevitable variation in the extent to which this is achieved and in the readability between chapters.

The book is split into four sections: the first deals with physiology and pathophysiology of nerve fibres, the second with pain, the third with the control of nervous system output, and the fourth with development, survival, regeneration, and death. There are concise contributions from Ritchie and Waxman on ion channels and the molecular anatomy of the node of Ranvier which introduce the first section. Further chapters consider normal central and peripheral nerve conduction before dealing with disease. Throughout the book the authors attempt to direct their contributions of assessing why and how disease occurs. Newsom-Davis provides a chapter on autoimmunity at the neuromuscular junction, Feasby on the pathophysiology of human demyelinating neuropathies, and McDonald on the mechanisms of relapse and remission in multiple sclerosis. There is a well written chapter by Smith on conduction properties of central demyelinated axons and the generation of symptoms in demyelinating disease. Pain is dealt with in the second section, and this includes a readable chapter on myofacial pain syndromes by Westguard, as well as Shen's attempt to assess the neurophysiological basis of pain relief by acupuncture.

Part III deals with the control of central nervous system output, and obviously contains the widest range of topics. I would single out the chapters by Prochazka, Gorassini, and Taylor on the cerebellum and proprioceptive control of movement, together with Jefferys' chapter on cortical circuit synchronisation and seizures. There are also several contributions relating to respiration. The final section considers development, survival, regeneration, and death. This is the least inspiring part of the book, which is disappointing as this is currently the most exciting area of neuroscience.

Overall the editors have succeeded in condensing a huge amount of information in a readable and educative fashion. This book will appeal to all those interested in clinical neurology, both in training and practice, as well as those neuroscientists who seek to broaden their own field of research.

JOHN ZAJICEK

Clinical Disorders of Balance, Posture and Gait. Edited by: A M BRONSTEIN, T BRANDT, AND M WOOLLACOTT. (Pp 350; £85.00b). Published by Arnold, London 1996. ISBN 0340601450.

This multiauthored book sets out to explore the neuroscientific basis, clinical examination, and evaluation of disorders of balance and locomotion. The book has an opening section on the organisation of the sensorimotor systems involved in balance, posture, and walking with particular reference to the vestibular system. This forms an essential basis for the rest of the book but is somewhat intimidating to the naive reader who may fail to get beyond discussions—for example, on the role of strategies or synergies in the control of posture in response to balance disturbances. This would, therefore, prevent the reader from entering the excellent section on clinical disorders of balance and gait, and the assessment of such patients, a section that will appeal to most general neurologists. In this section of the book we are entertained by some excellent chapters especially with respect to the diverse and sometimes devastating symptoms and signs of vestibular disorders and the range of different gait disorders that can now be distinguished. Such disorders include the well recognised isolated gait ignition failure as well as less widely known states such as those gathered under the rubric of subcortical disequilibrium states (including thalamic astasia). In addition, there are detailed discussions on the cautious gait and psychogenic disorders of gait and balance—cases of which abound in every neurological clinic. The classification and clinical features of different disorders of gait and balance are complemented by chapters on the analysis and investigation of such patients from an orthopaedic, neurological, and neuro-otological point of view. This serves not only to highlight a strength of this book—namely, the multidisciplinary approach, but also highlights the shortcomings of most neurological practices, which have limited access to specialist neuro-otological units. In most centres the patients are reviewed by non-specialist neurologists and ear, nose, and throat surgeons and then referred on to physiotherapists for treatment, as pharmacological treatments are generally not helpful. This aspect of the management of patients with gait or balance disorders is discussed in the three chapters forming section four of this book, in which the discussion concentrates on the psychological and physical approach to treatment.

The book closes with a rather repetitive section on the specific problems of gait disorders and falls in elderly people—an important and often neglected area of medicine which will no doubt become more of an issue as the elderly population continues to grow. These chapters I found the most disappointing as they tended to be too wordy with little detail given to summary points—for example, in chapter 20 there is an eight page table on all the studies that have analysed the effects of medications on the risk of falls!

Overall this book sets out to define and explore a much neglected area of neuroscience and clinical neurology and goes a long way to achieving this aim. The problem with a book such as this, however, is in trying to combine detailed technical accounts and models for the specialist while holding the interest of the neurologist. Ultimately the book has chapters of great value to the non-specialist neurologist, but these have to be looked for and the opening and closing sections of the book will scare off many possible readers. However, for those who are prepared to do battle with these chapters the rewards are worth seeking, because the book does give one of the best overviews on the control of posture, balance, and locomotion and with this comes an understanding of such disorders as camptocormia, otolith Tullio phenomenon, and Tumarrkin's otolithic crisis.

ROGER BARKER

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